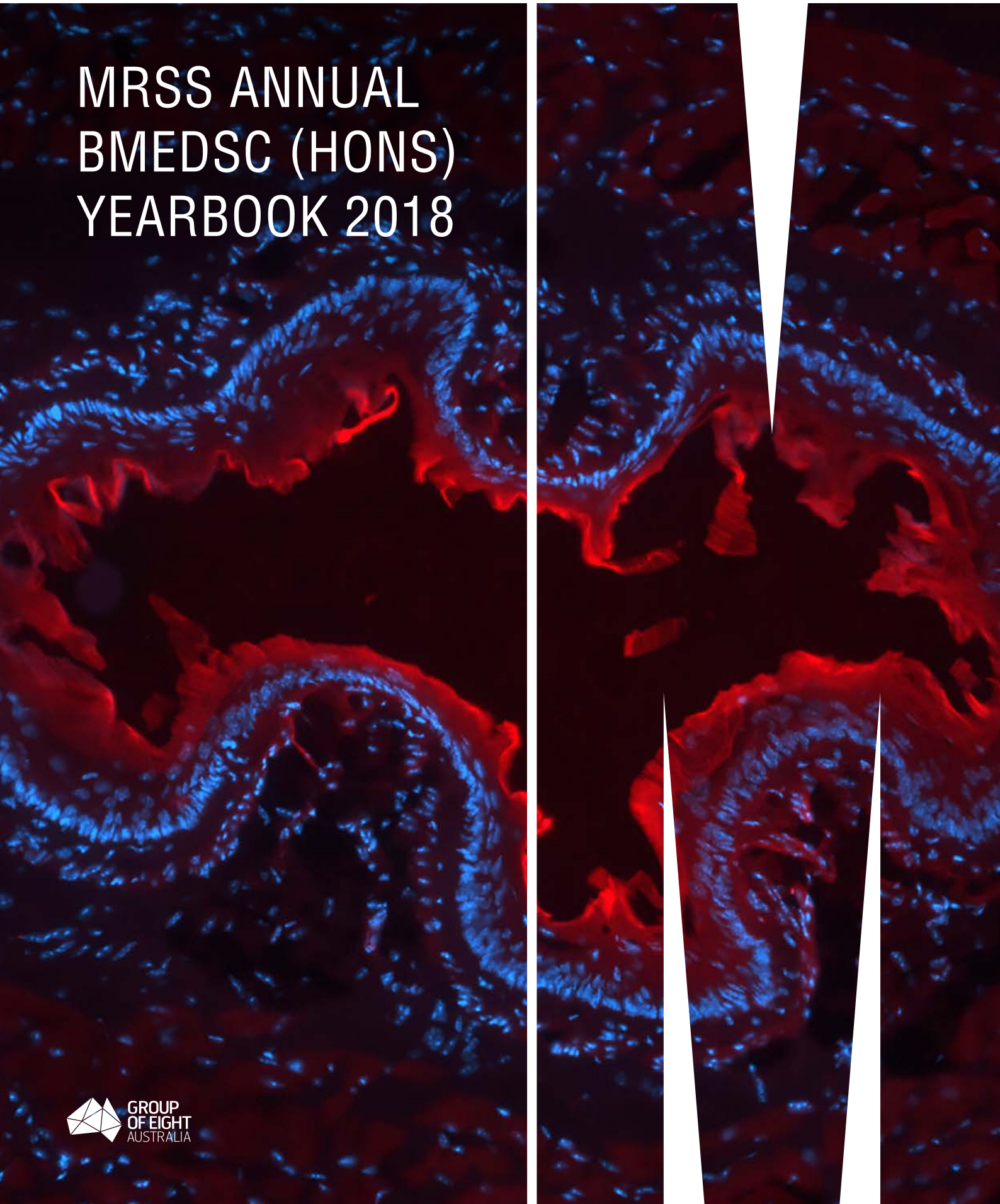
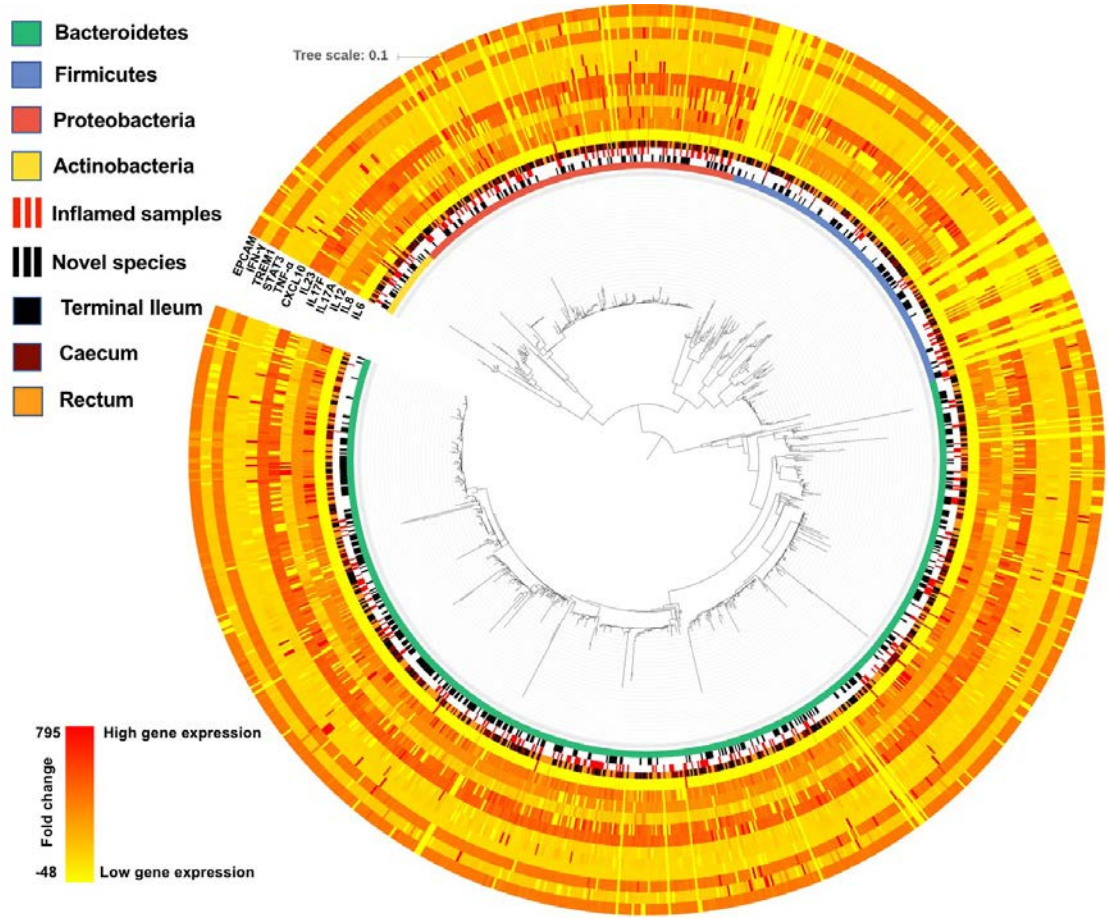
MONASH University

MONASH
MEDICINE
NURSING AND
HEALTH SCIENCES

MRSS ANNUAL BMEDSC (HONS) YEARBOOK 2018



GROUP OF EIGHT AUSTRALIA



FRONT COVER

Nishat Siddique “Luminal rhodamine”

This is the result of fluorescent rhodamine dye injected into the lumen of a mouse’s oesophagus. The dye is caught in and partially penetrates the stratum corneum in this mouse which has decreased expression of the epithelial transcription factor Grainyhead-like 3.

INSIDE FRONT COVER

Gemma D’Adamo “Phylogenetic tree of cultured isolates and the strength of inflammatory responses initiated”

Phylogenetic tree of cultured isolates displaying the distribution of isolates among the four main phyla – *Bacteroidetes* (green ring), *Firmicutes* (blue ring), *Proteobacteria* (red ring) and *Actinobacteria* (yellow ring). The overlay shows isolates cultured from inflamed mucosal samples (red bars), isolates classified as a putative novel species (black bars), the site of biopsy in the colon (shades of brown), and the intensity of inflammatory gene activation, in relation to the 12 genes investigated (shades of yellow and red), being IL6, IL8, IL12, IL17A, IL17F, IL23, CXCL10, TNF-a, STAT3, EPCAM, TREM1, IFN-y. Each ring around the phylogenetic tree represents one of the genes investigated.

Message from the BMedSc(Hons) Course Management Committee

Dear BMedSc(Hons) Students,

Congratulations on completing your BMedSc(Hons) degree! Well done, it is a very significant achievement.

The Course Management Committee would like to thank you for choosing to embark upon a formal year of research in BMedSc(Hons). We hope that the BMedSc(Hons) year has challenged you both personally and academically. The Honours year is meant to give you a new appreciation of how much more there still is to learn about medicine, about how new knowledge is created, how medical research is translated into changes in clinical practice and how important evidence-based medicine is for ensuring that changes to practice are justified. By the end of the year most students will feel like they have undergone an exponential learning curve, not just in their research area, but also in their confidence to critically evaluate new research findings, to communicate in written and oral formats and in their ability to work independently, as well as a member of a team. We hope that your Honours year has equipped you with all of these skills and many more.

We would also like to express our thanks to your supervisors and to the large number of unsung heroes who have devoted their time this year to help you learn. The Course would not be possible without them. We are also very grateful to the large number of examiners who willingly volunteer their time every year to assess the oral and poster presentations, literature reviews and theses. Thank you also to the MRSS committee, particularly your BMedSc(Hons) Chairperson Stephanie Davies. Stephanie has worked hard to organize information nights and to feed back your questions and comments, helping to improve your own experience as well as that of future cohorts.

On behalf of the BMedSc(Hons) Course Management Committee, we wish you all the very best for a bright future.

Dr Megan Wallace, Director of Medical Student Research

Message from MRSS

Congratulations to the BMedSc(Hons) Class of 2018 on completing the year!

As I am sure you are all aware this is no mean feat. There have certainly been some highs and lows for all of us. You should all be proud of what you have achieved during this year, whether it was trying something new, writing a paper or just getting through that never ending workload.

The advantage of the BMedSc is that everyone's experience is different. No two projects are the same and the outcomes even more so. The diversity of the projects in this yearbook is a testament to this.

I hope that you have all gained something unique and valuable from this year as well as a passion to answer the big questions of medicine. I am sure you will go on to do great things in the future and I wish you all the best of luck!

Stephanie Davies, BMedSc(Hons) Representative

Jawad Abidi

Uncovering the Macrophage Migration Inhibitory Factor (MIF) Interactome

Doctor James Harris, Doctor Nadia Deen, Professor Eric Morand

Institute Affiliations:

Rheumatology Group, Centre for Inflammatory Diseases, School of Clinical Sciences,
Monash University Faculty of Medicine, Nursing and Health Sciences, Monash Biomedical Proteomics Facility

I decided to commence a BMedSc (Hons) year after completing Yr 4 since I thought it would be best to pursue research after completing my major exams. I chose my project since I have been interested in Rheumatology for a few years now and decided that it would be good to get a taste of what it is like to be in the specialty before committing who knows how many years of my life to it down the line! In retrospect now that the year is complete, I can firmly say that I have a greater understanding of what the specialty stands for, what the average day as a Rheumatology fellow is and what lab-based Rheumatology research is like.

In addition, I learnt several life skills, ranging from dealing with adversity and maintaining focus and determination in the face of repeated failures and challenges. It was a very transformative year and I sincerely hope that you consider taking on the challenge for yourselves!

ABSTRACT

Background

Macrophage Migration Inhibitory factor (MIF) was one of the first immune active molecules discovered in the 1960s, and while it has been shown to be associated with multiple inflammatory pathologies, the exact role of MIF in such diseases remains unclear. Despite this, MIF is known to influence several biological processes, including (but not limited to) apoptosis, inflammasome activation, autophagy/ mitophagy, pattern recognition receptor signalling, cytokine activity and immune cell proliferation and migration. However, some contention regarding the role of MIF as a cytokine exists, with numerous studies pointing to CD74, CD44, chemokine receptors CXCR2 and CXCR4 being the protein's physiological receptors. However, there are multiple aspects of MIF biology pointed toward it being an intracellularly acting protein as opposed to a traditional cytokine. The goal of this project was to determine whether MIF has a wide range of intracellular interacting partners - the MIF interactome.

Method

WT (wildtype)/Mif-/- /GFP-LC3 (cells stably expressing GFP-LC3) iBMM (immortalised bone marrow mouse macrophages) and THP-1 cells (human monocytic cells from a patient with acute monocytic leukaemia) were cultured. These cultured cells were stimulated in several conditions: inflammatory (lipopolysaccharide and/or nigericin), autophagy inducing (starvation, Bafilomycin A1, Torin1) and MIF-inhibiting (using a small molecular inhibitor – 4-IPP). The cells were then lysed and MIF was then immunoprecipitated out of the lysates, and the samples were either run on sodium dodecyl sulphate polyacrylamide gel electrophesis (SDS-PAGE) gels (for Coomassie stain/Western blot) or sent for liquid chromatography mass spectrometry analysis.

Results

Co-immunoprecipitation (Co-IP) was successful in iBMM using RIPA buffer and abcam175189 -MIF antibody and in THP-1 cells using the Biolegend -MIF antibody/ Abcam175189 -MIF antibody. Co-IP coupled Coomassie stain/Western blot analysis demonstrated NLRP3, vimentin (inconsistently) and LC3 (inconsistently) as binding partners of MIF in WT iBMM, whilst CD74 was not present. Co-IP coupled mass spectrometry analysis demonstrated 299 binding partners for MIF, with a broad array of functions. LPS was found to have an effect on the binding partners of MIF in the Co-IP coupled mass spectrometry analysis. Variation was also observed between the Co-IP coupled mass spectrometry results and the Co-IP coupled Western blots.

Conclusions

MIF is likely not a traditional cytokine, since many of the proteins with which it interacts are involved in the maintaining basic cellular functions. The binding partners of MIF may be affected by the treatments used during culturing and the MINOR THESIS BMedSc (Hons) 10 | P a g e elution protocol during the immunoprecipitation process. Further experimentation is required to determine the definitive biological role of MIF.

Nadya Anindita

Resolution of Hypertension with Weight Loss

Professor Wendy Brown, Centre for Obesity Research and Education, Department of Surgery, Central Clinical School, Monash University
Professor Michael Cowley, Monash Obesity and Diabetes Institute, Department of Physiology, Monash University
Dr Stephanie Simonds, Monash Obesity and Diabetes Institute, Department of Physiology, Monash University

Hi, I'm Nadya, a fourth-year medical student from Universitas Indonesia. This Honours year at Monash University is one of the best years of my life. First, I was so lucky to have the chance to work with amazing and really great (or the best) people in their fields who also happened to be really supportive and helpful during the program. These people were my supervisors and my colleagues who really inspired me a lot to do and give my best in my career in the future. Second, I got to experience both lab work (radioimmunoassay) and clinical observations (bariatric surgeries) during the program. Both were new for me and were really cool! Third, this Honours program helped me to improve not only my writing but also my presentation skill. Last, living abroad and meeting new people were really priceless experiences for me. By the end of the course, I was really amazed at what I have achieved so far. For future students, I really hope you enjoy your Honours year as much as I do. I never regret any second I spent during this Honours year because surely it was one of the best times of my life!

ABSTRACT

Background

Cardiovascular disease is the leading cause of death in the world and hypertension is one of the major risk factors. Obesity, in turn, is an important risk factor for hypertension. Leptin is a hormone produced by adipocytes and is secreted in proportion to the adipose tissue mass. It is postulated that leptin contributes to the development of hypertension in people with obesity. Substantial weight loss improves obesity-related diseases and its components, including hypertension and leptin concentration. Laparoscopic adjustable gastric banding (LAGB) is a bariatric surgical procedure which may allow patients to achieve substantial weight loss. This study aims to understand the relationship between the resolution of hypertension and changes in leptin level by studying changes in a cohort who underwent LAGB surgery. The study also aims to determine the percentage of total body weight loss (%TBWL) needed for the resolution of hypertension.

Method

This was an observational study using prospectively collected data of obese patients who underwent an LAGB procedure between April 2009 and March 2010. Demographics, comorbidities, and anthropometrics, along with blood tests measuring the causes and complications of obesity as well as for gut hormone assessment were performed before surgery. Patients were reassessed, including repeating blood tests, monthly for the first 9 months, then 3-monthly until 24 months after the surgery. Radioimmunoassay was performed to determine the leptin concentration.

Results

89 patients were eligible to participate in the study, 83 of which had hypertension at baseline. There were 56 (62.92%) women and 33 (37.08%) men in this study. The mean age of all participants was 48.23±10.75 years. The mean weight loss 24 months after LAGB was 18.37±7.6% TBWL (48.73±23.51% EWL). Leptin level was reduced to 69%, from 46.19 (26.34–71.74) ng/mL to 14.31 (4.22–33.53) ng/mL, 12 months after surgery ($p<0.0001$). A correlation between leptin and systolic blood pressure (SBP) was seen in males without antihypertensive medications ($p=0.0265$). This correlation was shifted when analysing leptin and SBP in males with antihypertensive medications ($p=0.0541$). The median time for the resolution of hypertension was 5 months. The odds ratio for the resolution of hypertension with 22.5–25% TBWL was 2.99 ($p=0.021$). A higher weight loss showed an increased probability for the resolution of hypertension to occur.

Conclusions

Leptin showed no correlation with the resolution of hypertension after LAGB in all patients, but had a correlation with SBP in males without antihypertensive medications. Meanwhile, weight loss about 22.5% TBWL (60% EWL) should be considered as a target with significant blood pressure improvement.

Eishi Bandara

How can we transform primary care? Areas of improvement in trans and gender diverse primary care: Client and GP perspectives

Dr Riki Lane, Dr Chris Barton

Department of General Practice, School of Primary Health Care, Monash University

After finishing 4th year last year, I decided I needed a break from clinical medicine and wanted to try something different. I have an interest in queer health, and trans health is something we don't learn much about in our medical course. When I found this project on the project database, I thought it would be perfect for a BMedSc year, from a personal and academic perspective. It was also very interesting to delve into the world of qualitative research, which we also get very little teaching on. It's a lot more than just chatting to people! Qualitative research makes you think deeply about your participants, their experiences and their worldviews, as well as your own lens and perspectives that might influence your research. It was a lot more work than I initially thought it would be, but well worth it – I really loved being involved in this project. If I had any advice for future students, it would be to pick a project that you are interested and passionate about. All the hard work is much more enjoyable that way!

If you have any questions, I am happy to be contacted (esban1@student.monash.edu).

ABSTRACT

Trans, gender diverse and non-binary (TGDNB) people identify as a gender differing from what is expected of their sex assigned at birth, with various gender expressions that may not fit into the traditional gender binary. The health disparities experienced by the TGDNB community suggests this is one of the most vulnerable and marginalised groups in Australia and internationally. Primary care plays an important role in reducing these health disparities. GPs can provide specific healthcare for TGDNB clients, and also holistic care as for any other client. However, primary care for TGDNB people is not optimal, and there is a lack of in-depth research focused on primary care provision for this group in an Australian context. Evaluation of client experiences is necessary to identify possible barriers to providing high quality healthcare. GP perspectives can further facilitate identifying these barriers. A combination of perspectives can enable identifying appropriate and practical solutions, increasing positive engagement with primary healthcare for this community.

Aims

This study aimed to explore the perceived barriers to providing high quality primary care to TGDNB people, from a GP and a client perspective. The secondary aim of this study was to use these perspectives and understanding to build recommendations for overcoming these barriers.

Methods

This study consisted of semi-structured qualitative interviews with GPs and TGDNB clients, using a phenomenological approach and drawing on feminist research principles. The research plan and question schedule were developed with a TGDNB Community Advisory Group. Interviews were transcribed, and the data analysed using Braun and Clarke's Approach to Thematic Analysis. NVivo 12 was used for data management. The resultant codes were then organised using the socio-ecological model of health provision, into three major themes: socio-structural influences, interpersonal influences and intrapersonal influences.

Results

This research found perceived barriers to providing high quality primary care on a socio-structural, interpersonal and individual level. Socio-structural influences included societal and political influences on healthcare provision, the healthcare system and related structural barriers. Interpersonal influences centred on the client-clinician relationship, and effects of a GP's knowledge, and perceived role in providing safe primary care. Intrapersonal influences included individual characteristics of the TGDNB clients, including their diverse intersections of identities, and perceptions, knowledge, and expectations of primary care.

Conclusions

TGDNB clients had variable experiences with GPs, with many clients finding inadequate GP knowledge to be a barrier in providing comprehensive care. However, TGDNB clients stressed the importance of practicing patient-centred care, identifying that GPs could be considered safe if they were empathetic and willing to learn. GPs highlighted the importance of protecting their clients from harm, which was complicated by different perspectives of what constitutes harm. Open and honest communication is important to mediate these tensions. Other recommendations for improving care provision included increasing education for GPs, increasing funding to medical and community services for this population, and updating medical software to more accurately identify TGDNB clients. Overall, this study suggests that with structural support and education, any GP has the capacity to provide high quality care to TGDNB clients.

Elodie Bernard

Interconception care in general practice: a qualitative study

Professor Danielle Mazza[1], Dr Cathy Watson[1]

[1] Department of General Practice, School of Primary and Allied Health Care, Faculty of Medicine, Nursing and Health Sciences, Monash University

With an interest in women's health and primary care, I decided to do a BMedSc at the Department of General Practice after completing my fourth year. I wanted to gain insight into the world of research and experience the other side of medicine after having done two years of clinical placements. From interviewing participants to using NVivo software and analysing data, I have gained valuable experience in performing qualitative research which I'd not previously encountered in medical school. I would definitely recommend the Department of General Practice to anyone considering an honours year – it is a friendly, supportive environment where everyone is willing to help you, even if they are not directly involved in your research! If anyone has any further questions, feel free to send me an email at ember2@student.monash.edu.

ABSTRACT

Background

Interconception care (ICC) aims to reduce the effect of maternal risk factors on subsequent pregnancies, particularly if a poor outcome has occurred in a first pregnancy. General practitioners (GPs) are leading providers of care for women between pregnancies yet there is a knowledge gap regarding GP understanding and experiences of ICC in the literature. To address this gap, we aimed to explore GPs' knowledge, perspectives and experiences of ICC using qualitative interviewing.

Method

18 GPs from metropolitan Melbourne were recruited using purposeful sampling from the Monash Practice-Based Research Network (MonRen). Semi-structured telephone interviews (30 to 60 minutes) were conducted. Interviews were audio-recorded and transcribed verbatim. The software NVivo 11 was used for data management and generation of codes. Data were analysed using thematic analysis guided by the Framework Method.

Results

Participants were unfamiliar with the term 'interconception'. Most GPs conceptualised ICC as routine care of childbearing age women as opposed to interventions aimed at improving health for a subsequent pregnancy. GPs reported some key ICC activities reflected in existing literature but described providing this care opportunistically after the scheduled postpartum visit. GPs perceived a lack of engagement in ICC from mothers with high competing demands. Participants questioned whether women prioritise health optimisation for a subsequent pregnancy whilst raising a young child. Participants attributed this absence of prioritisation on ICC by women as a result of general lack of awareness on the importance of pre-pregnancy health optimisation. GPs also reported time constraints in general practice and a lack of clarity on the content and timing of ICC as provider barriers. Continuity of care and education materials for women and GPs were viewed as facilitators to ICC by participants.

Conclusions

Our findings indicate that GPs do not conceptualise ICC as a particular subset of their practice but rather routine opportunistic care for women. GPs also perceived many patient barriers to the delivery of ICC, including a lack of awareness on the value of pre-pregnancy care. Further research to evaluate patient perspectives on ICC may be necessary before a complex intervention to improve ICC in general practice can be developed, trialled and evaluated.

Nadia Bogatzke

Comparison of a one and two-tiered trauma activation protocol at a Metropolitan Trauma Service

Associate Professor Robert Meek (Monash Health, ACEM)
Department of Emergency Medicine, Monash Health, Melbourne.
School of Clinical Sciences, Department of Medicine, Monash University, Melbourne.
Monash Emergency Research Collaborative, Dept. of Medicine, Clinical Sciences at Monash Health, Monash University, Melbourne.

Professor Andis Graudins
Clinical Toxicology Unit and Emergency Medicine Service, Monash Health, Dandenong Hospital, Melbourne.
Monash Emergency Research Collaborative, Dept. of Medicine, Clinical Sciences at Monash Health, Monash University, Melbourne.

I chose to undertake a BMedSc (Hons) year after completing MED IV. Throughout my early medical years, I developed an interest in the management of emergency situations, surgical interventions and the world that is acute care. As I was undecided between several specialties, I thought an understanding of emergency medicine, and acute trauma, would be useful knowledge for my future career, regardless of where I end up. I decided to undertake a BMedSc (Hons) to gain skills in clinical research, as I hope to continue contributing to medical research throughout the course of my career as a doctor.

The best part of the year has definitely been the connections I have made within the field of emergency medicine, as well as with other research students. We were a small cohort, but the support from my fellow BMedSc (Hons) students made completing the thesis much more manageable.

For those looking to undertake a BMedSc (Hons), I would suggest picking the supervisor, rather than the project, and ensuring you have the same expectations at the beginning. If you're planning on a relaxed year, let your supervisors know from the outset. If you want to be published, or present at conferences, be up front.

ABSTRACT

Background

Early assessment of trauma patients in the emergency department (ED) by multi-disciplinary teams has improved patient outcomes. Trauma teams are triggered when patients meet defined physiological, injury pattern or mechanism of injury (MOI) criteria. However, trauma team activations are resource intensive. Research at major trauma services report that two-tiered trauma responses reduce resource consumption without adversely affecting patient outcomes. Smaller ED-based teams manage physiologically stable patients with MOI criteria, as this subgroup is low risk for major trauma. The safety of a two-tiered trauma response at a level two, Metropolitan Trauma Service (MeTS) is unproven.

Study Aim

To determine if the safety of a two-tiered trauma response at a Melbourne MeTS is non-inferior to a one-tiered system.

Methodology

An observational, non-inferiority study was conducted at Dandenong Hospital, a MeTS within the Victorian State Trauma System. Outcomes during a retrospective one-tier period (1 June to 12 August 2017) were compared with a prospective two-tier period (1 June to 12 August 2018). Patients triggering a Trauma Call in the one-tier period, and a Trauma Call (first-tier) or Trauma Alert (second-tier) during the two-tier period were included; performance and timing of a CT scan was noted. The primary outcome measure was time to CT scan (TtCT). This was chosen as safety relies on timely diagnosis, and diagnosis is confirmed on CT. Non-inferiority required the upper 95% confidence limit of the mean TtCT in the two-tier period to be <30 minutes longer than the mean TtCT in the one-tier period. Secondary outcomes including length of stay (LOS) and disposition from ED were compared between periods, and between the Trauma Call and Trauma Alert subgroups of the two-tier period. The primary comparison of mean TtCT included only patients who had a CT scan; baseline data and most secondary outcomes compared all Trauma Response patients from both periods.

Results

Of the 140 and 172 eligible patients from 2017 and 2018, 61% [95%CI: 53-70] and 55% [95%CI: 48-63] were male; mean ages were 37 (95%CI: 34-40) and 41 (95%CI: 38-44) years. The mean TtCT for the 100 patients who had a CT scan in each period were 146 (95%CI: 135-157) and 154 (95%CI: 140-168) minutes respectively. The upper 95% confidence limit in 2018 was <30 minutes longer than the mean TtCT in 2017, meeting the a priori definition for non-inferiority. From 2017 to 2018, ED LOS was non-significantly reduced (6.6 [95%CI: 5.9-7.4] to 5.8 [95%CI: 5.1-6.6] hours), as was that for admitted patients (15.7 [IQR 5.4 – 36.8] to 6.5 [IQR 2.9 – 31.0] hours). The discharge rate was similar between periods (30% [95%CI: 23-38] vs 38% [95%CI: 30-45] respectively), but from 2017 to 2018 the Short Stay Unit (SSU) admission rate increased significantly (28% [95%CI: 19-39] vs 53% [95%CI: 43-63], p<0.01) while the inpatient ward admission rate decreased significantly (68% [95%CI: 58-78] vs 45% [95%CI: 35-55]).

Conclusions

At a Melbourne MeTS, the safety of a new two-tiered trauma response system was non-inferior to the previous one-tiered system. Apparent LOS benefits warrant further investigation.

Claudia Brick

Defining the concept of a life not worth living in paediatric treatment limitation

Dr Guy Kahane (University of Oxford)
Prof. Roger Crisp (university of Oxford)
Prof. Michael Selgelid (Monash University)

I decided to undertake my BMedSci in bioethics after hearing about the program Monash runs with the Uehiro Centre for Practical Ethics at Oxford University. It seemed like a perfect opportunity to explore my interest in ethics and the global challenges facing medicine, as well as a chance to study overseas. My project was on treatment limitation issues in paediatrics, particularly in light of the recent controversial case of Charlie Gard, so it was very topical. Studying at Oxford was an incredible experience not only in the project and research itself, but also in what I learnt about philosophy, other issues in practical ethics, and how argumentation works in these fields! It was made even more special by the other Monash students and Oxford students we met. I am happy to contacted by any future students about the program.

ABSTRACT

Background

Decisions about withdrawal of life support for infants are predominantly made through consensus between physicians and parents. Occasionally, disagreement results in controversial legal battles. Medico-legal precedent is for withdrawal of treatment only if it is in the best interests of the child, and the burdens of life outweigh the benefits. However, it is unclear how we evaluate when life is no longer worth living for an infant, and public attitudes towards treatment withdrawal and the role of parents in decision-making have not previously been assessed.

Aims

The empirical component of this study aims to assess public attitudes towards when life is no longer worth living for an infant, and whether this justifies treatment withdrawal. The ethical analysis aims to evaluate these public views in comparison to key principles within the bioethical discourse.

Methods

An online survey was conducted with a sample of the UK public (n=130). Participants were asked to judge the benefit of life for seriously ill infants in a series of case scenarios, as well as their views on treatment withdrawal and parental autonomy. Statistical analysis was conducted on IBM SPSS Statistics version 25 for Mac. The null hypothesis was rejected at $p<0.05$. The data gathered was compared against ethical principles identified in the literature review.

Results

The majority of participants agreed that at a certain level of wellbeing, an infant's life may have no benefit (93.8%) or be worse than death for the infant (87.7%). This belief varied significantly between cases: for the most severe case, 89.2% of participants did not believe life was of benefit, while for the least severe case, 13.9% of participants did not believe life was of benefit. Participants seemed to place most value on the objective goods of awareness and capacity for basic relationships when making this judgement. A significant proportion of participants in each case (up to 50%) believed it was permissible to continue or withdraw treatment for each case. Participants were reluctant to disagree with parents being allowed to continue treatment indefinitely for their child: in 5 of 6 cases, a majority of participants believed parental autonomy should be allowed.

Conclusion

Despite the controversy generated by similar legal cases and quality of life judgements, our findings indicate that there is a level at which most people reach consensus that life is not worth living: one where cognition is so limited that the infant has no awareness of themselves or their surroundings, even if suffering is minimal. The defining feature of a life that the majority believed to be worth living was a level of cognition that allows for basic relationships and a small chance of future communication. Significant support for permissible withdrawal of treatment (where it is not morally obligatory to either withdraw or continue) in the most divisive cases as well as prioritisation of parental autonomy may be useful when constructing robust guidelines for clinical practice. Further research is needed to ensure reproducibility and to investigate more specifically the factors behind these beliefs.

Quillan Chan

Evaluating the impact of pneumococcal conjugate vaccine against paediatric pneumonia and empyema in children

Main supervisor: Angela M McCullagh[1]
Co-supervisor: Rosemary SC Horne[2]

[1]Monash Children's Hospital, Melbourne, Australia
[2]The Ritchie Centre, Department of Paediatrics, Monash University and Hudson Institute of Medical Research, Melbourne, Australia

I completed my project at the Department of Paediatrics at Monash Children's Hospital because of my interest in paediatrics, especially infectious diseases and respiratory medicine.

I chose to undertake the BMedSc(Hons) year to gain a better understanding of the process of medical research. I found it especially helpful to have both a clinician and a scientist supervise me this year. With a scientist as a supervisor it allowed me to better understand scientific writing and the process. This also helped with presenting in general, as they provided me with a different perspective to my study. Furthermore, having a clinician as a supervisor helped me to integrate my findings with clinical practice.

I also gained some important research skills this year, most importantly being able to efficiently search the literature and synthesise these into succinct writing. I also learnt basic research skills, such as data collection and statistical analyses and interpretation.

ABSTRACT

Introduction

Pneumonia is a lung infection that can be complicated by empyema, defined grossly as pus in the pleural space. Pneumonia is most commonly caused by Streptococcus pneumoniae.

Pneumococcal conjugate vaccines (PCV) have been used to decrease the burden of these diseases. After the introduction of PCV7 in 2001, paediatric pneumonia rates decreased, however empyema rates paradoxically increased. This was due to "serotype replacement", where non-vaccine serotypes became more prevalent and were more likely to progress to empyema. To address this, PCV13 was released in 2011.

The aim of this study was firstly, to identify the bacterial aetiologies and S. pneumoniae serotype prevalence in pneumonia and empyema patients after the introduction of PCV13. Secondly, we aimed to identify patient factors which could predict the development of empyema in children.

Methods

63 pneumonia and 44 empyema patients were prospectively recruited from Monash Children's Hospital between November 2015 – July 2018. These groups were compared with respect to demographic and clinical features and underlying bacterial aetiologies.

Nasopharyngeal swabs, blood and pleural fluid were tested for underlying bacterial aetiologies using PCR and cultures. Pneumococcus positive samples were then serotyped. Demographic and clinical factors were compared between the groups.

Serotype prevalence was compared with the serotype prevalence prior to PCV13 introduction (Strachan, 2011).

Results

S. pneumoanie was the most commonly identified pathogen in the entire population (41.1%). Furthermore, infections more associated with empyema included S. pneumoniae (68.2% vs. 22.2%; $p<0.05$), S. pyogenes (22.7% vs. 0.0%; $p<0.05$) and a viral co-infection (17.5% vs 36.4%; $p=0.047$).

PCV13 serotypes 19A (2.3%) and 3 (41.9%) were still identified. The proportion of serotypes 1 and 19A have fallen significantly since PCV13 introduction, however the prevalence of serotype 3 has not changed.

In a multivariate analysis, S. pneumoniae (OR 19.5; 95% CI 4.3-88.9), CRP on admission over 120mg/L (OR 8.45; 95% CI 2.1- 33.4) and use of ibuprofen during hospital admission (OR 9.81; 95% CI 1.2-76.7) were predictors for empyema.

Conclusions

PCV13 appears to be effective at against caused by serotype 1 and 19A, however is ineffective against serotype 3.

Clinical predictors for the development of empyema from pneumonia include S. pneumoniae, CRP >120mg/L on admission, and use of ibuprofen during hospital stay.

Daniel Chepurin

Bony Stress in the Lumbar Spine

Dr Ashish Diwan: St George & Sutherland Hospital Clinical School
Dr Uphar Chamoli: St George & Sutherland Hospital Clinical School
Dr David Scott: School of Clinical Sciences Monash University

I started the BMedSc year after completing year 4C of the MBBS for a number of reasons. I was incredibly lucky to have been given the opportunity to conduct the year back home, in Sydney, with some of the most supportive and helpful supervisors. Of course, the chance to spend a whole year doing work in the field that I wanted, being able to control which path my work went down and seeing results from the whole journey was amazing for me to experience. Overcoming constant challenges, like teaching myself statistics from scratch in a very small time-frame, and balancing self-motivation throughout the year can only be described as fun.

Throughout a lot of school and university, you come across many topics that make you question whether you will ever actually need or use this. After finishing this year I can confidently say that I will use the skills I've learnt this year for the rest of my career. This year transformed my mindset from being a university student to being part of a medical team, and I believe it's set me up to launch into a medical career very well.

ABSTRACT

Background

The lumbar spine motion segment has multiple components that interact during normal and pathological function. Bony stress in the lumbar spine is recognised as a factor in the process of pars defects and stress fractures in the lumbar spine, but its prevalence and relationship with intervertebral disc degeneration and other pathology is not well understood.

The primary aim of this project was to explore the relationship between bony stress in the lumbar spine and disc degeneration. Secondary outcomes include prevalence of bony stress, facet osteoarthritis, lower back pain and anatomical parameters.

Method

Data were collected from a sample of patients under the age of 25 who had a lumbar MRI conducted at three radiology centres between March 2015 and March 2018. All patients (n=493) had their images screened for bony stress. Association between outcomes of interest were assessed using two case-control studies;the first study had one control group of patients without bony stress (n=75), and the second study had two age and sex-matched control groups; one with disc degeneration (n=51) and the other without disc degeneration (n=51). Images for all cases were retrospectively examined for disc degeneration, lumbar anatomical parameters and other pathology. Radiology reports were also read for the indication for MRI. The groups were analysed using Pearson's Chi Square and logistic regression, and risks were estimated as odds ratios.

Results

Bony stress was visible on MRI in 11% (55/493) (95% CI [8.4% - 14.5%]) patients. Bony stress was missed on routine assessment by radiologists in 36% (20/55) (95%CI [22.2% - 54.7%]) of cases.

The odds of disc degeneration being present among patients with bony stress was 2.3 times higher than in patients without bony stress (OR 2.3 (95% CI [1.1 - 4.8]). The odds of pain being an indication for MRI among patients with bony stress was 5.3 times higher than in patients without bony stress (OR 5.3 95% CI [2.11 – 13.3]). Facet osteoarthritis was not significantly associated with bony stress (p=.07). There were no clinically substantial differences in anatomical parameters between bony stress patients and control patients.

Conclusions

These findings suggest there is an associative relationship between bony stress in the lumbar spine and intervertebral disc degeneration and pain as an indication for MRI. Bony stress is likely to be undiagnosed in many cases which may have clinical consequences given it may be a cause of cryptogenic lower back pain. Further temporal studies need to be conducted to clarify the cause and effect of bony stress on lumbar pathology.

Roberto Bagaskara I Christanto

Determining the Surface Levels of the Thrombin Receptor, PAR4, on Human Platelets

A/P Justin Hamilton, Australian Centre for Blood Disease (ACBD), Monash University
Dr Shauna French, Australian Centre for Blood Disease (ACBD), Monash University

Hi! I am Roberto Christanto. I am currently on fourth year of medicine in Universitas Indonesia. I have taken interest in blood disease in general. Stroke and ischaemic heart disease is the most common cause of death. Finding appropriate treatment for these conditions had become my main interest for the past research. I was very grateful to both of my supervisors for giving me the chance to work in their lab and introducing me to research. My heartiest appreciation to friends in ACBD for their support and thoughtful comments in completing my research project. Throughout the year, I have gained valuable insight on how to conduct a quality research project.

My advice to future students is to enjoy your project cause you will be amazed and proud at the end of your thesis. I would highly recommend the BMedSc(Hons) year and encourage future students to consider doing project at ACBD. If you are interested in doing BMedSc(Hons), I would love to answer your question - robertobagaskara@gmail.com

ABSTRACT

Background & Aim

Cardiovascular disease (CVD) is the major cause of death in the world. The most common manifestations of CVD are myocardial infarction and stroke, both of which are caused by formation of platelet-rich thrombi in major arteries. Due to the poor efficacy of current treatment options, potential new therapeutic targets are being examined. The examples of these targets are the protease activated receptors (PARs), PAR1 and PAR4. Vorapaxar is the only clinically approved drug that targeting PAR1. However, Vorapaxar has limited clinical utility due to a high risk of bleeding. Therefore, PAR4 has recently become a prime target for the development of novel anti-thrombotic therapies. One potential limitation in developing robust PAR4 antagonists is the existence of a single nucleotide polymorphism (SNP) in PAR4 (rs773902) that impairs the efficacy of existing antagonists. PAR4 can either have an alanine or threonine at amino acid position 120 (Ala120 or Thr120) and the Thr120 sequence variant has increased sensitivity to agonists and decreased sensitivity to antagonists. The mechanism underlying this altered PAR4 function is unknown. In order to address this, this study investigated whether there is a correlation between rs773902 genotype and the absolute number of PAR4 on the platelet surface.

Method

PAR4 surface level expression was measured by quantitative flow cytometry on the platelets of 49 individuals, which were subsequently genotyped rs773902 using a Taqman SNP genotyping assay.

Results

The average number of PAR4 on the human platelet surface was 1093 ± 63 receptors/platelet. Importantly, individuals expressing the Thr120 PAR4 sequence variant had significantly more PAR4 on their platelets (1799 ± 378) than either of those expressing the Ala120 PAR4 sequence variant (1010 ± 64) or heterozygous individuals (1065 ± 89)

Conclusions

This study is the first to quantify platelet PAR4 expression level. These findings may explain the altered receptor sensitivity to agonists and antagonists of the Thr120 PAR4 variant and may therefore be an important consideration for any future efforts to target PAR4 for anti-platelet drug therapy.

Isabelle Claxton

Pre- and Post-Migration Factors Associated with Resilience Among Refugees in Australia

Prof Grant Russell, Department of General Practice, School of Primary Healthcare, Monash University
Dr Joanne Enticott, Department of General Practice, School of Primary Healthcare, Monash University

I finished fourth year last year and decided to do a BMedSc (Hons) project as a chance to not only learn some research skills, but also to explore an area that's been an interest of mine for a while: refugee health. It's not too often you get the chance to focus solely on one topic and learn about it in great detail, and this year has provided the opportunity to do so. Not only have I learned how to conduct literature searches, use data analysis software and write a scientific thesis and paper, but I have also learned more about refugees and refugee health than I ever expected I would.

Doing my project at the Department of General Practice has been great, as I had access to many researchers, not just my two supervisors, for advice. Working with such a supportive team, I have discovered my interest in research and in the future, I hope to do further research as part of a Master of Public Health.

ABSTRACT

Background

Australia's refugee and asylum seeker population is a vulnerable population at risk of both physical and mental health issues. Current refugee mental health research has focussed on risk factors for mental illness, and mental health assessment and intervention methods. Despite over 90% of refugees reporting exposure to trauma, about 50% of refugees develop mental illness. This means that 50% remain mentally healthy, exhibiting resilience in the face of potentially traumatic events. We examined the pre- and post-migration factors that are associated with resilience among refugees.

Method

We used the first three waves of data from the Building a New Life in Australia (BNLA) study, an ongoing, nationwide, longitudinal study conducted by the Australian Institute of Family Studies. The first wave of data collection included 2399 refugees aged 15 and over, who were granted permanent humanitarian visas between May and December 2013. The three data waves used in this study were collected between October and March of 2013-14, 2014-15 and 2015-16. Resilience in this study was defined as Kessler-6 and Post- traumatic Stress Disorder 8 items within normal limits in all three waves of data.

Results

30.0% of refugee participants demonstrated resilience and 37.1% of refugee families contained members who all demonstrated resilience. Financial hardship has the greatest influence on odds of resilience in individuals and families, with an OR of 0.333 (95% CI 0.267-0.415) among individuals and 0.396 (95% CI 0.329-0.478) among families for 3-6 financial hardships per day compared to no financial hardships per day. Long-term disability or illness (OR 0.408 for individuals and 0.493 for families) and exposure to trauma pre-migration (OR 0.476 for individuals and 0.497 for families) also had significant influence on the odds of resilience.

Discussion

This study is the first to examine resilience among refugees, determined by those refugees with K6 and PTSD-8 results below the clinical threshold in each wave of the BNLA data. Our study differs from previous studies in refugee mental health as we have used a longitudinal dataset of a large, nationally-representative sample of refugees. We found several factors that significantly influence refugees' odds of demonstrating resilience. While some factors are fixed and cannot be altered to increase resilience, we have identified other factors that can be modified to promote resilience. We are also able to compare the relative effect that each factor has on resilience, so can determine which factors have the greatest influence on refugees' mental health outcomes.

In the future, these predictors of resilience represent targets for intervention that can be used to assist refugees to maintain good mental health.

Assia Comella

High Resolution Oesophageal Manometry In Children With Previous Repair of Type C Oesophageal Atresia

A/Prof. Sebastian K. King – Department of Paediatric Surgery, The Royal Children's Hospital, Melbourne

Mr Ramesh M. Nataraja – Department of Paediatric Surgery, Monash Children's Hospital, Melbourne

Department of Paediatric Surgery; Institutes: The Royal Children's Hospital, Murdoch Children's Research Institute, Monash Children's Hospital, Monash University

I am an Italian International student, who graduated from high-school in Canada and then moved to Australia. I completed my 4th year of Medicine in 2017 and underwent a BMedSc(Hons) year in 2018. I decided to undertake a year of research in the light of my past research experience along Med School and to learn more about this aspect of Medicine, which has provided me with a valuable learning experience. I decided to focus on paediatric surgery, area that most interests me and that I hope to purse as future career, paired up with research and potentially public advocacy and academic work as well.

During the year I have grown immensely from an academic and personal point of view, developing long-lasting bonds with peers, friends and supervisors. This year has provided me with endless research, clinical, networking, surgical and professional opportunities. I have had the privilege to work with two amazing supervisors and paediatric surgeons, who have greatly inspired me to focus on my work, but also on myself and my personal life. I strive to be like them and become an enthusiastic and present supervisor and paediatric surgeon.

Feel free to contact me, should you have any questions.

ABSTRACT

Background

Oesophageal atresia (OA) is a life-threatening congenital disease which affects 1 in 3500 children. There are five main sub-types (Gross classification: Type A – Type E). Oesophageal atresia is diagnosed on the first days of life with surgical repair occurring on an emergency basis. Improvements in treatment have increased survival, which has changed the focus to morbidity management. Dysphagia, gastro-oesophageal reflux disease (GORD), oesophageal dysmotility, as well as, quality of life (QoL), are the main areas of interest in current OA research.

Method

Patients with repaired OA were identified from The Royal Children's Hospital OA database. Eligibility criteria included type C OA children who had undergone surgical repair and whose parents consented to the study.

Data on their demographics, previous admissions and interventions were organised in a Microsoft Excel 2016 (Washington State, USA) spreadsheet.

High resolution impedance manometry (HRIM) was performed with an 8-French solid-state catheter with 32 pressure sensors, inserted from a nostril, through the oesophagus into the stomach. Children swallowed a minimum of five 5mL sips of Standardised Bolus Media (SBM) solution IDDIS0 (thin solution) and five 5mL sips of SBM IDDIS4 solution (extremely thick solution). The catheter registered pressures in the oesophagus and plotted them in topography-pressure plots. Images were then stored for further analysis and the catheters were sterilised. The child's dysphagia symptomatology questionnaire (Dakkak) was completed by the parents.

Oesophageal manometry analysis was performed using AIMplot software (Flinders University, Adelaide). Dakkak symptomatology analysis was performed with Microsoft Excel 2016 (Washington State, USA) and GraphPad Prisma 7 (California, USA). Studies were compared with 17 retrospective HRIM studies of children investigated for suspected GORD without a history of OA repair.

A review of the literature was performed to evaluate the effects of radiation in children with OA, as well as the standardised imaging regimens currently being utilised.

Results

Forty-one children with type C OA were contacted; 17 patients underwent oesophageal manometry. Ten patients were male and 7 were female (age: 3 months to 3.5 years old).

Manometric assessments demonstrated three motility patterns: distal contraction pattern, aperistalsis, and pressurisation. No statistically significant correlation was found between oesophageal motility type and Dakkak questionnaire score ($p = 0.44$).

Children with OA had less effective oesophageal body peristalsis and bolus clearance than controls. No statistically significant difference in lower oesophageal sphincter relaxation was found.

Radiological imaging currently performed exposes children with OA to higher amount of radiation dose than the general population, putting them at an estimated 130-fold increased cancer risk.

Conclusions

Children born with OA demonstrated objective oesophageal dysmotility, with less effective oesophageal contraction and bolus transport than patients with GORD. Information about oesophageal motility, reflux and appropriate diet was gained with HRIM. No guidelines regarding standardised follow-up regime for children born with OA and recommended maximum radiation exposure exist.

Gemma D'Adamo

Identification of novel bacterial species in paediatric inflammatory bowel disease through direct mucosal sampling.

Dr Sam Forster – CiiiD, Hudson Institute of Medical Research, Wellcome Trust Sanger Institute, Cambridge, UK
Dr Edward Giles – Department of Paediatrics, Monash University, CiiiD, Hudson Institute of Medical Research

I decided to undertake a BMedSc after my 4th year of medicine. Initially, I wanted to take part in a research year in order to have a break from medicine, experience a different working environment and learn some exciting new skills. However, I found that I gained so much more. I never imagined the incredible experiences I would have or the amazing people I would meet. My BMedSci was focused on paediatric IBD and the involvement of the microbiota in disease pathogenesis. I really loved the way my project allowed me to stay connected to clinical medicine, while also experiencing the lab environment. I was lucky enough to be surrounded by an incredibly supportive group of people. I cannot thank my supervisors and fellow lab members enough for the incredible year that I have had. I think that deciding to do a BMedSc year was one of the best decisions I have made, and I would strongly encourage anyone considering it to pick a project that they are interested in and have a great year!

ABSTRACT

Background

Inflammatory bowel disease (IBD) is a chronic, incurable inflammatory condition, comprised of Crohn's Disease (CD) and Ulcerative Colitis (UC). The manifestation of IBD during childhood (paediatric IBD; PIBD) ensures that the cumulative incidence of complications is significant for these patients. Currently, there are no universally effective treatments and clinical management is complicated by a plethora of side-effects. Investigation into the genetic basis of IBD has suggested that genetic variants predispose to immune dysregulation, in response to environmental triggers and microbial factors.

Until recently, investigation of the microbiota has been limited by an inability to culture the majority of intestinal microbes. This led to reliance on microbial sequencing to gain greater taxonomic understanding of microbial communities, however, sequencing is limited by an inability to define causation. The development of novel yeast-casitone fatty acid (YCFA) culturing techniques1 means that much of the previously 'unculturable' gastrointestinal microbiota is now cultivatable. To advance from correlative studies to defining causation, a combination of functional characterisation and experimental validation is required.

Objectives

Using novel YCFA culturing techniques, we aimed to culture the microbiota populating mucosal samples, in order to characterise microbial signatures among a PIBD cohort. We further aimed to complement this mucosal-associated microbial analysis with investigation of inflammatory responses at the sampled sites, to investigate associations between the microbiota and inflammatory cascades initiated. We hypothesised that this would allow identification of novel therapeutic candidates for future experimental validation.

Methods

Mucosal samples were collected from 38 PIBD patients during endoscopy at Monash Children's Hospital. Biopsies were taken from three colonic regions (Terminal Ileum, Caecum and Rectum) and cultured using YCFA culturing techniques. Taxonomic classification of isolates was based off partial-length 16S rRNA sequences. Additionally, mucosal-associated inflammatory responses were investigated, through assessment of 12 genes (IL6, IL8, IL12, IL17A, IL17F, IL23, CXCL10, TNF- , STAT3, TREM1, EPCAM, IFN-). Correlations between the inflammatory cascades initiated and microbiota present were identified to detect novel therapeutic candidates.

Results

Mucosal samples were collected from 38 patients, across three colonic regions (RNA analysis: 95 samples, microbial analysis: 107 samples). The cohort comprised a roughly equal distribution of males (52.6%) and females (47.4%); however, most patients were 11-18 years of age (65.8%), and Caucasian (57.9%). Additionally, most samples were histologically non-inflamed (69.5%). Culturing allowed 1748 bacterial isolates to be picked, which generated 1209 high-quality sequences. We identified 415 known and 325 putative novel species. Enrichment and depletion analyses were performed and correlated with the strength of inflammatory responses initiated, which identified four therapeutic candidates. Future functional characterisation and experimental validation of these candidates will be required to assess their potential roles in disease exacerbation and control.

Conclusions

We applied novel YCFA1 culturing techniques to culture the mucosal-associated microbiota from PIBD patients for the first time. A significant number of known and novel species were cultured, and several therapeutic candidates for future functional characterisation were identified. This workflow should enable characterisation of microbial signatures implicated in the pathogenesis of PIBD, and various intestinal and extra-intestinal diseases, thereby permitting translation to other conditions.

Stephanie Davies

Cellular Investigation of Antiepileptic Dr g-Induced Cutaneous Reactions

Professor Anthony Purcell, Dr Nicole Mifsud, Dr Patricia Illing
Department of Biochemistry and Molecular Biology, Monash University

Last year I completed fourth year and decided to do a BMedSc to give research a try. I picked this project in particular as it encompassed a number of different medical fields; immunology, neurology and dermatology. I am very glad that I did and have learnt immensely from this experience. It was certainly a challenging year filled with mistakes and set backs but I could not be prouder of the results. I commenced this project with no previous experience in lab work and minimal immunology knowledge. Now that I am at the end of this year I can say that I am significantly more experienced in both areas. I was lucky enough to have incredible support and guidance from my supervisors as well as other members of my lab group. I would highly recommend undertaking a BMedSc to any students curious about research. Feel free to contact me for more information – sjdav15@student.monash.edu.

ABSTRACT

Antiepileptic drugs (AEDs) are key causes of cutaneous adverse drug reactions (ADRs), which are categorised as type IV hypersensitivity reactions and mediated by T cells. Cutaneous ADRs range from mild, maculopapular exanthema (MPE), to severe, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The mild reactions are characterised by a rash, which may extend to organ involvement in drug reaction with eosinophilia and systemic symptoms (DRESS). The severe reactions (SJS/TEN) are characterised by epidermal detachment and significant morbidity and mortality.

Carbamazepine is the AED most strongly associated with cutaneous ADRs. The mechanism proposed for the presentation of carbamazepine to T cells is via pharmacological interaction of the drug with the immune receptors, known as the p-i concept. This interaction is non-covalent and labile. Associations have been made between cutaneous ADRs and human leukocyte antigen (HLA) molecules, which are responsible for presenting peptides to T cell receptors (TCRs) for T cell activation. The most established correlations are HLA-B*15:02 with carbamazepine-induced SJS/TEN and HLA-A*31:01 with carbamazepine-induced MPE.

MPE is not as well characterised as the severe reactions and the association with HLA-A*31:01 is not as strong as HLA-B*15:02 with SJS/TEN. This project hypothesised that specific AED-responsive TCRs may also be associated with MPE. The aims were to i) characterise drug-specific T cell responses in MPE patients, ii) investigate cross-reactivity between structurally similar AEDs and iii) identify the associated TCR signatures.

In this study I was able recapitulate carbamazepine-induced immune reactions T cell responses in HLA-A*31:01+ drug hypersensitive patients who had exhibited MPE as well as drug-naïve HLA-A*31:01+ individuals. Additionally, carbamazepine-induced T cell responses were also observed in individuals with HLA alleles from the wider HLA-A19 subgroup. This novel observation suggests that drug hypersensitivity may also extend beyond HLA-A*31:01 to other members of the HLA-A19 supertype.

T cell cross-reactivity between carbamazepine and other structurally related molecules (ECBZ and oxcarbazepine) was observed, supporting current findings in the literature. Additionally an incidence of cross-reactivity between carbamazepine and lamotrigine was also observed.

Lastly variable polyclonal T cell responses were observed in most MPE patients. A clonal T cell response from carbamazepine-specific TCR clonotypes was observed in one MPE patient. The clonotypes identified were patient-specific but appeared to be cross-reactive between HLA-molecules. This suggests a private TCR response occurs in individuals with MPE.

The findings of this study corroborate previous reports of HLA association and cross-reactivity. It also provides areas for further exploration of the mechanisms underlying carbamazepine-induced MPE, namely the possibility of an association with the HLA-A19 subgroup and alternative mechanisms for activation of T cell responses namely direct interaction of the drug-TCR interaction.

Lydia Di Stefano

Viability, abortion and ectogestation

Primary Supervisor: Prof Dominic Wilkinson
Secondary Supervisor: A/Prof Catherine Mills

I completed year 4 in 2017 and decided to undertake a BMedSc(Hons) at the Oxford Uehiro Centre for Practical Ethics in 2018. Doing research in bioethics at Oxford had been a dream for a while, so I was absolutely stoked when I found out I had a place. I have always been interested in women's and children's health, and hope to one day work in this field, so it made sense to try to find a bioethics project that related to this interest. I was very lucky that the perfect project was on offer, which would focus on the ethics of 'ectogestation', a new way of extending gestation using an artificial womb. I loved my time in Oxford. In particular, I enjoyed the contrast to the MBBS: I was able to live in a small university city and spend six months focusing on one ethical dilemma which was a huge change of pace when compared to five days a week of placement and moving hospitals every 6 weeks. I had to learn to be independent and self-motivated, and to assertively express my own views. This was challenging, but I think I have gained some very valuable skills from the experience. I've also been lucky enough to sneak in a lot of European travel too. Ultimately, I decided to defer finishing my MBBS for another year and have just started a Masters of Reproductive and Sexual Health Research at London School of Hygiene and Tropical Medicine. I'm happy to be contacted if anyone considering a BMedSc(Hons) (or overseas Masters) wants to get in touch. My email is lmdi6@student.monash.edu.

ABSTRACT

Background

Abortion is sometimes restricted by law beyond the point when fetuses are 'viable'. However, viability is poorly defined and relies on access to technologies which vary temporally and geographically. Moreover, new technologies such as ectogestation – a way of extending gestation using an artificial womb – may improve outcomes for extremely premature infants who would be non-viable without this technology. Ectogestation thus appears to shift the borderline of viability. This raises questions as to whether ectogestation should impact on access to abortion.

Aims

The aim of this study was to combine empirical results with ethical analysis to investigate whether by shifting the gestational age of viability, ectogestation should result in changes in access to abortion.

Methods

Two principle methods have been adopted: theoretical analysis of ethical issues and a survey of doctors on their views and practices with regards to management at the borderline of viability.

The ethical analysis sought to explore the key arguments linking ectogestation, viability and abortion, to determine whether ectogestation should lead to changes in access to abortion.

The online survey involved consultants and fellows in obstetrics or neonatology working in Victorian tertiary hospitals who were recruited via a 'snowballing' technique. They were presented hypothetical scenarios relating to extremely premature labour in the light of current technology and ectogestation, before being asked about the appropriateness of abortion, Caesarean section, resuscitation and non-resuscitation, and to respond to general questions about abortion, ectogestation and the nature of viability. Results were presented descriptively and statistical analysis (using Chi-square and t tests) was adopted to compare the views of doctors who work in obstetrics and neonatology.

Results

The ethical analysis found consistency (treating 'like' cases like) to be the best argument in support of restricting abortion post-viability. However, a woman's autonomy represents a morally significant difference between a fetus and infant that justifies different treatment.

Ninety-one doctors completed the survey (response rate 64%). When asked directly, 69% of doctors said that viability related to the possibility of survival at a particular gestation, however they did not apply this definition: 69% of neonatologists and 89% of obstetricians did not believe that a 22+3-week infant was viable, even though survival is possible at this gestation. Surveyed doctors believed that ectogestation would shift the gestational age of viability (88% agreeing that an infant is viable with ectogestation at 22+3 weeks). Over half (55%) of respondents neither agreed nor disagreed that ectogestation should become common practice. Forty-one percent of respondents agreed that this technology would influence their views on termination of pregnancy, while 48% disagreed.

Conclusion

I conclude that ectogestation does not warrant changes in access to abortion. However, this does not exclude other reasons for limiting abortion after a certain gestation as a compromise. Surveyed doctors agreed that ectogestation will alter the point of fetal viability (a conclusion that I independently reached) however, there was contention as to whether access to abortion should be limited beyond viability. Qualitative studies are needed to determine the reasons behind such contrasting views.

Zlatikha Djuliannisaa

Mesenchymal Stem Cell Therapy for Hypoxic Ischemic Encephalopathy

Dr Courtney McDonald
The Ritchie Centre, Hudson Institute of Medical Research

Hi I am Azla! I am a medical student from Universitas Indonesia who are very lucky to have this opportunity to work on honours project in Monash University. I chose a project that involves stem cells because I believe this field is always developing and can be a key point of treatment for many incurable diseases. It has always been my dream to find a cure for diseases, especially since I am pursuing my medical year as a physician. At first, I think it would not be really relevant working on my research and my study to be a doctor but I was completely wrong. There is this captivating connection between those two which assure me that my goal to really cure people is not longer a dream. Additionally, I really enjoyed working with the project and all the people who assisted me in the processes. I recommend all my fellows to try this life-changing and mesmerizing experience on Monash University. Feel free to contact me if you have further questions or if you are curious about my full story regarding my honours year.

ABSTRACT

Background

Cerebral palsy (CP) is a permanent, non progressive motor disorder that can result from brain injury during the perinatal period. It is a complex disorder that often causes low quality of life in the patients. One of the most easily identifiable causes of CP is hypoxic ischemic encephalopathy (HIE). HIE is a brain injury due to severe acute deprivation of oxygen in infants around the time of birth. It affects 2 to 3 out of 1000 live births in the developed countries. HIE can lead to either postnatal death or in surviving patients, permanent neurophysiological disabilities. The key point of HIE treatment is to reduce inevitable brain inflammation and restore functional brain structures. The only treatment available for HIE is therapeutic hypothermia which principally reduces body temperature of infants to delay the disease progression. However, it is found to be ineffective in the majority of patients.

Recently, the use of mesenchymal stem cells (MSCs) has been proposed as a new treatment for HIE and CP. MSCs treatment has already been shown to be beneficial to treat adult brain injury, MSCs can be collected from many sources, and MSCs have been found to be safe in both preterm and term animal models. However, the way to maximize the potency of MSCs and their mechanism of actions in HIE, remain unclear. Our study aimed to reveal the therapeutic benefits of MSCs therapy in treating HIE. Moreover, our project explored the potential of human umbilical cord tissue derived MSCs (UC-MSCs) and intranasal administration route, both of which have not been tested yet.

Method

In this project, we isolated MSCs from human umbilical cord tissue collected from consented term cesarean section deliveries. Hypoxic-ischemic (HI) injury was performed using postnatal day 10 rat pups through permanent ligation of their left carotid artery, followed by a hypoxic challenge at 8% oxygen for 90 minutes. Seven days later, negative geotaxis test to analyse their behaviour was performed, followed by post mortems to collect brains for histological analysis and immunochemistry for detection of neurons, microglia, and astrocytes, cell tracking.

Results

We found the brains were smaller and had less number of neurons in the hippocampus after HI injury. Administration of UC-MSCs significantly increased the brain mass and neuronal cells in the hippocampus. Furthermore, we found that HI exaggerated brain inflammation. The improvement of brain inflammation was detected through significant reduction of astrocytes and microglial counts in the hippocampus after UC-MSCs treatment.

Conclusions

In conclusion, this study demonstrated that UC-MSCs treatment improved brain injury following HI by restoring neuronal cell numbers and reducing brain inflammation in the hippocampal area. Further improvements are needed to advance the limitations in this study including the small sample number, the histological cutting method, and the use of an unstable cell tracking marker. Future studies also need to include more complex behavioural studies, other brain areas for histological analysis, cytokine analysis, and test different UC-MSCs administration dosages, times, and routes. Finally, we have shown that UC-MSCs have potential as a therapy for HIE during neonatal period.

Zakary Doherty

Short- and Long-term Outcomes Following an In-hospital Cardiac Arrest

Associate Professor Rebecca Kippen – Associate Professor of Demography, Monash Rural Health, Bendigo VIC
Dr Belinda O'Sullivan – Research Fellow, Monash Rural Health, Bendigo VIC
Dr Jason Fletcher – Director of Intensive Care, Bendigo Health, Bendigo VIC
Ms. Kim Fuzzard – Clinical Educator / Critical Care Registered Nurse, Bendigo Health, Bendigo VIC
Dr Cameron Knott – Intensive Care Specialist, Bendigo Health, Bendigo VIC

This year has been the best part of my medical degree so far. I have had such a variation in what I do each day, and I have gotten more out of the past 10 months than I could have ever hoped. I've gone from being a student obsessed with graduating and getting on a training program to one that wants to spend each year in the way that makes me the happiest. My supervisors have taught me a lot about research, but they have taught me more about what my future career can be like.

Whilst I did spend way too much time in ICU I now feel completely at home there (I probably did spend more time then than at home!). I hope I'm back very soon to continue the great work our whole team has started.

ABSTRACT

Background

The rate of event survival and survival to hospital discharge following an in-hospital cardiac arrest (IHCA) is poor, worldwide and in Australia. Worldwide there is little data about survival outcomes beyond hospital discharge and even less in the Australian context. Many factors relating to the patient and the arrest have been previously shown to positively or negatively influence survival at different points, unfortunately little investigation has been done into how these factors influence survival beyond hospital discharge. This study aimed to measure survival outcomes following IHCA in the short (event survival and survival to hospital discharge) and long-term (survival beyond hospital discharge) and investigate how patient and arrest factors may influence outcomes.

Method

single-centre retrospective longitudinal study was done of all adult patients (aged 20 years and over) who had a cardiac arrest inside the Bendigo Hospital between the 1 February 2000 and 31 December 2017. Patient and arrest data were sourced from the existing hospital's Code Blue Database. Long-term survival outcomes were ascertained by linking the hospital data to the death data in the Victorian Death Registry on the 31 January 2018. All patient and arrest variables were included in multivariate logistic regression to determine adjusted association with survival of the event and survival to hospital discharge. A Cox regression including all variables then determined associations with long-term survival. Finally, the long-term survival of all patients that survived to hospital discharge was compared to that of a standard Australian population matched on age and sex.

Results

A total of 682 patients were included in the analysis, the median age was 73.01 years and 59% were males. Twenty six per cent of arrests were of a shockable type (Ventricular Fibrillation or Ventricular Tachycardia) and the median duration of resuscitation was 10 minutes. Fifty four per cent of patients survived the cardiac arrest and 32% survived to hospital discharge.

Shockable rhythms and arrests that occurred in recent years were independently associated with an increased rate of survival to hospital discharge as were arrests occurring in the Emergency Department. An increasing resuscitation duration and the patient having a not for resuscitation order were associated with a decreased rate of survival to discharge. When compared to the standard Australian population cohort, the annual risk of death was significantly higher for the first three years-post arrest for the IHCA group. Beyond this time there was no significant difference in mortality. Younger age was independently associated with a decreased hazard of death whereas cardiac rhythm, being Ventricular Tachycardia or Pulseless Electrical Activity, and increasing resuscitation duration were associated with an increased hazard of death in the Cox regression analysis.

Conclusions

Around half of patients who suffer an IHCA survive the event and around a third survive to hospital discharge. Over time the impact of the arrest on survival decreases. This is the first ever Australian study to investigate IHCA survival beyond 1-year post arrest and has the longest patient follow-up period following the arrest in the literature worldwide.

Shourye Dwivedi

Developing Vaccines for the Treatment of Glioblastoma

Professor Magdalena Plebanski – Department of Immunology and Pathology, Monash University
Adjunct Clinical Associate Professor Martin Hunn – Depeartment of Neurosurgery, Alfred Hospital
Dr Jennifer Boer – Postdoctoral Researcher, Department of Immunology and Pathology, Monash University
Dr Kirsty Wilson – Postdoctoral Researcher, Department of Immunology and Pathology, Monash University

After completing four years of clinical medicine, I pursued a BMedSc(Hons) year to broaden my research skillset, as well as to push myself outside of my comfort zone. With a prior interest in neurosurgery, I was fortunate enough to get a laboratory-based translational research project under the supervision of Prof. Magdalena Plebanski and Prof. Martin Hunn at the Department of Immunology and Pathology, and in conjunction with the Department of Neurosurgery at The Alfred Hospital. With the expert guidance of my postdoctoral researchers (Dr Jennifer Boer and Dr Kirsty Wilson), we pursued vaccine design for a mouse model of glioblastoma, using novel nanoparticle-based formulations, as well as whole tumour cell based vaccines.

My BMedSc(Hons) year has truly fostered an interest in science, translational medicine, and research in general. I have garnered a wide berth of skills, from culturing cells and handling mice, to optimising research methodology and planning experiments. I hope to pursue these interests in my future career, hoping to continue as a clinician-researcher. I would strongly recommend BMedSc(Hons) to anyone interested in broadening their research capability. Please feel free to conact me if you have any questions about BMedSc(Hons) in general, or specifically about laboratory based projects.

ABSTRACT

Background

Generating an artificial immune response by against glioblastoma by administering vaccines stimulating CD8+ T-cells to generate tumoricidal cytotoxic T-lymphocytes (CTLs) could improve tumour clearance. Vaccines have been trialled in the GL261 model of glioblastoma, syngeneic to C57BL/6 strain of mice. Whole GL261 vaccine with alpha-galactosylceramide (aGC) produced protective effect, yet this intravenous formulation produced some toxicity requiring reformulation. Alternatively, bioinformatics pipeline approaches have identified targeted GL261 neoantigens which could be used alongside nanoparticle-based adjuvant (nanovax) capable of producing peptide-specific CD8+ T-cell responses. Our group has also derived CD4+ T-cell epitopes (long peptides) which could also be used. Ultimately, the immunogenicity of these neoantigens is unknown and requires evaluation. To evaluate the potential efficacy of these vaccines, we had three aims:

1. To develop an immunogenic vaccine against GL261.
2. To evaluate subcutaneous and intracranial GL261 tumour growth kinetics, calibrating GL261 growth in C57BL/6 mice.
3. To investigate protective effects of these vaccines in GL261 model.

Method

We performed IFN- enzyme linked immunosorbent spot (ELISpot) to determine systemic immunogenicity of neoantigen based vaccine formulations. To confirm irradiation inactivated GL261s, we irradiated GL261 samples to 150Gy, and evaluated growth in vitro, ensuring that 150Gy irradiated cells could be used in vaccine formulations. Following these experiments, immunogenic and theoretically functional vaccines were formulated. To test the protective effects of these vaccines, we optimised a subcutaneous model of GL261 to test vaccine formulations. Finally, we performed prophylactic vaccination experiment, vaccinating mice 7 day prior to implanting subcutaneous GL261 per optimised model, to evaluate the protective effect of vaccine.

Results

To formulate vaccines, we first confirmed immunogenic neoantigens of greatest immunogenicity. Greatest immunogenicity was observed when pool of longer CD4+ T-cell epitopes (long peptides) were administered with nanovax. In particular, greatest CD8+ T-cell response was observed upon administration of CD4+ T-cell epitope peptide 4, which showed largest response upon re-stimulation with CD8+ T-cell recall antigen peptide 10-4L (the short CD8+ T-cell restricted epitope of peptide 10). Therefore, long peptide pool and peptide 4 would be useful vaccines to trial. 150Gy irradiated GL261s were definitively inactivated in vitro and could therefore also be formulated into vaccines for use.

Having identified useful formulations (long peptides, peptide 4, and 150Gy irradiated GL261s), we optimised a subcutaneous (SC) model of GL261. We found that 1×106 live GL261 administered subcutaneously generated tumours reliably and in a workable 20-day time frame, in C57BL/6 mice.

We then evaluated the prophylactic protective effect of these vaccines, observing prophylactic vaccination with irradiated GL261s (with or without aGC) produced statistically smaller tumours ($p<0.0001$) as compared to vaccine naïve mice. Long peptides pool produced no significant effect, but single peptide 4 did show statistically smaller tumours ($p=0.0001$). Nonetheless, survival was only observed to be superior in mice prophylactically vaccinated with irradiated GL261s (with or without aGC).

Conclusions

Our study demonstrated the systemic immunogenicity of neoantigen peptides in combination with nanovax adjuvant. Furthermore, we observed intradermal irradiated GL261 (with or without aGC) produced protection against growing SC GL261, but protection not clearly conferred by single peptide vaccine. This gives insight into the formulation of vaccines against glioblastoma.

Nic Ensor

Negative Pressure Dr ssing in Pilonidal Surgery (N-PIPS): A Multicentre Randomised Controlled Trial

Mr Ram Nataraja – Monash Children's Hospital, Monash University
Mr Maurizio Pacilli – Monash Children's Hospital, Monash University

I chose to do my BMedSc(Hons) after fourth year. I had always been interested in pursuing research and I thought that doing a BMedSc(Hons) would allow me to develop the skills necessary to do so. I was fortunate to meet my supervisors, Mr Ram Nataraja and Mr Maurizio Pacilli, when they ran a paediatric surgery workshop in Bairnsdale during fourth year. I am very happy that I chose to do a BMedSc(Hons) with them. I have learnt a great deal about surgical research and have developed a foundational skillset that I can build upon for further research. There were many (somewhat frustrating) times throughout the year when it felt like I was constantly 'putting out spotfires.' However, I believe that these were the most valuable aspects of the year because they allowed me to learn from my mistakes and prevent them from happening in the future. I am very grateful to my supervisors and the entire paediatric surgical team for making the year so much fun. I would highly recommend a clinical BMedSc(Hons) to anyone considering it. It is not an easy year, but it is definitely worth the effort! Please don't hesitate to contact me – ndens1@student.monash.edu.

ABSTRACT

Background

Pilonidal sinus disease (PSD) is a localised inflammatory reaction secondary to the implantation of loose hair within the intergluteal (natal) cleft. Surgical excision with off-midline primary closure is the most accepted definitive treatment method. However, it is limited by high rates of postoperative wound complications, namely surgical wound dehiscence (SWD). Negative pressure wound therapy (NPWT) reduces rates of SWD in other high-risk wounds, though it has not previously been investigated for closed PSD excisions.

Aim

Our primary aim was to investigate whether the use of a NPWT dressing (versus a conventional passive (CP) dressing) reduces the rate of SWD for primarily closed PSD excisions. Our secondary aims were to establish whether NPWT improves wound healing, short-term recurrence rates, patient quality of life (QoL) and the time taken return to normal activities.

Method

A prospective, multicentre randomised controlled trial (RCT) was conducted at 3 Australian hospitals. Patients, aged 12-40 years, with primary PSD requiring excision with primary off-midline closure were eligible for this study. The sample size of 100 patients was powered to detect a 35% reduction in SWD (power=0.9, significance=0.05). Patients were randomised by computer minimisation to receive a CP (PrimaporeTM or OpsiteTM) or NPWT (SNAPTM) dressing. Patients were followed-up on postoperative days 3, 7, 10, 14, and then weekly until wound healing. Data was collected on: the time to wound healing, analgesia utilisation, SWD, surgical site infection (SSI), and return to normal activity. De-identified photographs were taken of the dehisced wounds and classified as superficial (depth<5mm) or deep (depth≥5mm). Patients were followed-up at 2-months postoperatively with an online survey to assess: time taken to wound healing, time taken to return to normal activity, postoperative pain, patient satisfaction, and overall health. Patients will be followed up at 6-months to screen for short-term PSD recurrence.

Results

At this interim analysis, 13 patients were recruited into the study. 10 patients received surgical treatment and were randomised; there were 5 patients in each group. Six patients completed the 2-month follow-up. There were no significant differences in patient demographics or surgical variables. One SWD occurred in each group. The dehiscence rate in both groups was 20% (p>0.9). The SWD in the CP group (superficial) occurred on postoperative day 14 and the SWD in the NPWT group (deep) occurred on day 21. Both cases of SWD were associated with SSI, despite intraoperative antibiotic prophylaxis. There were no differences in median time to wound healing (p=0.9) or postoperative analgesia use (p=0.5). Furthermore, no difference was found in the median time taken to return to normal activity (p=0.8), though this time was longer in the NPWT group for all-but-one outcome. There were no changes in pre- and postoperative self-reported health ratings in either group (p>0.9).

Conclusions

This was an interim analysis of a trial with ongoing recruitment. There were no statistical differences in any outcome between the CP and NWPT groups in our underpowered cohort. Based on our current findings, continuation of this RCT is feasible and necessary to reveal any significant differences.

Emily Feng-Gu

Looking forward or looking back: Individual responsibility in healthcare and mobile health technology

A/Prof Justin Oakley – The Bioethics Centre at Monash University
Prof Julian Savulescu – The Uehiro Centre for Practical Ethics at the University of Oxford
Dr Hannah Maslen – The Uehiro Centre for Practical Ethics at the University of Oxford
Dr Rebecca Brown – The Uehiro Centre for Practical Ethics at the University of Oxford

Tell us a bit about yourself. For example tell us what year you're in, why you chose your project and what you learned and gained from the Honours project and year. If you wish, you can also include advice for future students and if you are happy to be contacted by future students.

I completed my BMedSc(Hons) after my fourth year of medical school. I decided to take a research year to expand my horizons and have a break from clinical medicine before diving into busy fifth year and internship. I was lucky enough to be one of six students undertaking their BMedSc(Hons) projects at the University of Oxford. I was able to learn about bioethics, conduct empirical research in a fascinating area, and get involved in the fantastic student life in Oxford. It was an extremely enjoyable and challenging year, and I could not recommend it enough.

If you have any questions about the Oxford bioethics program or the BMedSc(Hons) program, feel free to contact me at ejfen2@student.monash.edu

ABSTRACT

Background

As the prevalence of chronic, lifestyle-related diseases continues to grow, the focus of many health campaigns has shifted towards individual responsibility for ill health. There is some evidence to suggest that individuals' role in disease may become a more common healthcare rationing criterion. With developments in lifestyle-tracking technology, it may soon be possible to monitor many behaviours which result in lifestyle-related diseases. Much of the debate regarding individual responsibility in healthcare focuses on retrospective (or backward-looking) responsibility. Prospective responsibility is an alternative framework for if responsibility is to become a healthcare rationing criterion. Public attitudes towards prospective, lifestyle contract models of responsibility, and towards using mobile health technology to assess responsibility for disease, have not previously been studied.

Method

An online survey was conducted on members of the UK general public using the crowdsourcing platform, Prolific (n=81). Participants were invited to respond to a series of statements on responsibility in healthcare, both retrospective and prospective, and on using mobile health technology to assess responsibility for lifestyle and ill health. IBM SPSS Statistics version 25 for Windows was used to conduct the statistical analysis. A p-value was considered statistically significant at $p<0.05$. Findings from the survey informed the ethical analysis and provided empirical evidence to support the overall argument that prospective responsibility is preferable to retrospective responsibility in the context of healthcare rationing.

Results

Findings included that participants disagreed significantly more with the notion of intrinsic desert ($M=1.9877$, $SD=1.14558$) than of extrinsic social benefit ($M=2.5802$, $SD=1.30254$) as a justifiable rationale for holding people responsible for past behaviours ($t(80)=-6.400$, $p<0.001$). There was greater support for lowering healthcare priority on the grounds of multiple failed lifestyle contracts than either non-specific patient responsibility ($MD=0.716$, $SE=0.137$, $p<0.001$) or a single failed lifestyle contract ($MD=0.568$, $SE=0.111$, $p<0.001$). Furthermore, participants approved more of using mHealth technology to monitor adherence to a lifestyle contract ($M=3.2593$, $SD=1.37639$) than of determining whether past behaviour contributed to illness ($M=3.0123$, $SD=1.21957$), $t(80)=-1.958$).

Conclusions

Prospective responsibility is preferable to retrospective responsibility in the context of healthcare rationing. A reasonably achievable lifestyle contract model is less vulnerable to many of the objections commonly used against retrospective responsibility in healthcare. Our study found evidence that the public supports consequentialist allocations of scarce healthcare over retributivist frameworks, and that they believe good intentions have some moral worth. They also preferred lowering healthcare priority after multiple violated lifestyle contracts over non-specific responsibility. These views are better aligned with a prospective model of responsibility. Furthermore, developments in mHealth technology are likely to produce specific and accurate monitors that can reduce the time and personnel required to support the prospective model.

Charlie Fink

Factors affecting vitamin D status in infants

Dr Justin Brown, Department of Paediatric Endocrinology and Diabetes, Monash Children's Hospital
Prof. Katie Allen, Murdoch Children's Research Institute, Royal Children's Hospital
Dr Rachel Peters, Murdoch Children's Research Institute
Dr Jennifer Koplin, Murdoch Children's Research Institute

My name is Charlie: I chose my project through my supervisor, which I would recommend. I met Prof Allen, who's working on several projects, and chose vitamin D in HealthNuts because I am interested in common problems in medicine. Katie also was a great choice of supervisor because she was very keen to set out the year as a way of learning skills (e.g., academic writing, data analysis, epidemiology).

My advice to future students would be a) pick a supervisor who you can easily get along with, and b) try to make clear goals about what you want to learn (there'll always be more; you don't know what you don't know), rather than what you want to achieve. Everyone is lovely in research-land, they have lots of time to show people around, but also things move more slowly there, so plan ahead and try to give as much time as possible for every step of your project. Everyone's always on leave, and everything takes longer than expected.

A BMedSc(Hons) is a great experience, one in which you can learn a lot about research in a short period of time, and a great way to dip your toes in the water.

ABSTRACT

Background

Vitamin D is a micronutrient essential for normal growth and development in infancy, the first two years of life. Recognised for its effect in calcium and phosphate metabolism and skeletal mineralisation, there is also emerging evidence that vitamin D may be important for other body systems. Large RCTs in progress, such as the Vitality trial, are assessing the non-osseous benefits that vitamin D may have.

Despite the importance of vitamin D, the factors which determine vitamin D status in infancy remain incompletely understood. Although some associations between vitamin D status and formula intake and UV exposure have been observed, many more relationships have yet to be fully understood, such as ethnicity and socioeconomic status. The published studies vary widely in the ages and the factors assessed; only one study has investigated 1-year olds alone, and none have investigated 2-year olds alone. Additionally, no studies have used paired samples to assess how the determinants of vitamin D status may change over time.

The purpose of this study is to assess the factors determining vitamin D status at 1 year of age, at 2 years of age, and the factors which affect the change between these two ages.

Methods

Vitamin D deficiency in this study is defined as less than 50 nmol/L of serum 25-hydroxyvitamin D. It uses vitamin D measurements from the HealthNuts study, which was a population-representative, longitudinal study in Melbourne between 2007-2011, with the aim of assessing the prevalence and potential risk factors of food allergy, including vitamin D deficiency. This study includes 851 1-year olds and 125 2-year olds.

Results

At 1 year of age, the factors which affected risk of vitamin D deficiency were formula intake (aOR = 0.21 for fully-formula feeding vs. exclusive breastfeeding), UV exposure (aOR = 0.08 and aOR = 0.01 for highest vs. lowest quintile of ambient and personal UV exposure respectively), ethnicity (aOR = 1.68 for Asians vs. Caucasians), socioeconomic status (aOR = 0.42 for highest vs. lowest quintile), and gestational age at birth (aOR = 0.54 for post-term vs. term birth).

At 2 years of age, Asian ethnicity and UV exposure both had stronger associations with vitamin D status than at 1 year of age (aOR = 3.40 for Asian vs. Caucasian ethnicity; aOR = 0.01 for highest vs. lowest quintile of ambient UV radiation); and the relationship with formula intake was seen to be weaker.

In the change between these ages, risk factors for developing a new deficiency were formula intake (aOR = 10.64 for exclusive formula feeding vs. exclusive breastfeeding) and Asian ethnicity (aOR = 3.76 for Asian vs. Caucasian ethnicity), while increased UV exposure remained protective (aOR = 0.26 for increasing ambient UV radiation).

Conclusions

Regarding the factors affecting vitamin D status at 1 year of age, the findings of this study supports current evidence. With 2-year olds, and the use of paired samples to explore the factors affecting the change in vitamin D status between 1 and 2 years of age, the study is entirely novel. The findings of these analyses suggest new avenues for research and could point to children at risk of developing vitamin D deficiency in the first two years of life.

Hansen Yonathan Firdaus

The impact of musculoskeletal disorders on productivity in Australia

School of Public Health and Preventive Medicine

I'm Hansen Yonathan Firdaus, a year 4 medical student from Indonesia. I was given the opportunity to study overseas in Monash University. It was a fun and challenging year. My thesis was titled the impacts of musculoskeletal disorders on productivity in Australia. Through this research I've learnt how to effectively write a thesis and to present the idea to other people. My advice to future students is to start early and not panic in the last month before the submission date.

ABSTRACT

Background

Musculoskeletal disorders (MSD) have a major impact on the population's health and productivity, leading to a substantial economic burden. The recently published productivity-adjusted life year (PALY) is a new measure to estimate the productivity impact attributable to a disease or condition at a population level. To date, no studies have examined the productivity impact of two of the most prevalent MSDs low back pain and osteoarthritis using PALYs.

Aims

This study aims to investigate the burden of low back pain and osteoarthritis with regards to quality-adjusted life years (QALYs) lost, PALYs lost, and the economic cost of productivity loss in Australia.

Methods

Life table modelling was employed to hypothetically simulate the experiences of the 2016 Australian working-age population. The sample comprised Australians aged 20 to 69 years, who were followed up to 70 years of age or death. Separate life tables were constructed for those with the MSD under study (low back pain and osteoarthritis) based on prevalence data. Mortality rates, utility and productivity indices were applied. The life tables were then duplicated, assuming the population did not have the conditions of interest, and the utility and productivity indices were updated accordingly. QALYs and PALYs were summed for each life table. The difference in total QALYs and PALYs between each MSD, and assuming the MSD under study did not exist, provided the health and productivity impact of each MSD. The economic cost of this productivity loss was estimated by multiplying each PALY lost to the gross domestic product (GDP) per equivalent full-time worker (EFT).

Results

Our modelling shows that in those aged 20 to 69 years, followed up to 70 years of age, low back pain reduces the total number of QALYs by 18.3% and PALYs by 0.8%, compared to if low back pain did not exist. While osteoarthritis reduces QALYs by 10.8% and PALYs by 9.2%, compared to if osteoarthritis did not exist. The economic burden of low back pain and osteoarthritis on workforce participation over the remaining working lifetime of Australians currently living with these MSDs is estimated to be $ 34.8 billion and $ 147.8 billion in lost GDP, respectively. When considering additional work impairments of absenteeism and presenteeism, low back pain reduces PALYs by 17.8% and osteoarthritis by 17.5%, resulting in $ 652.7 billion lost GDP due to low back pain and $ 232.0 billion lost GDP due to osteoarthritis.

Conclusions

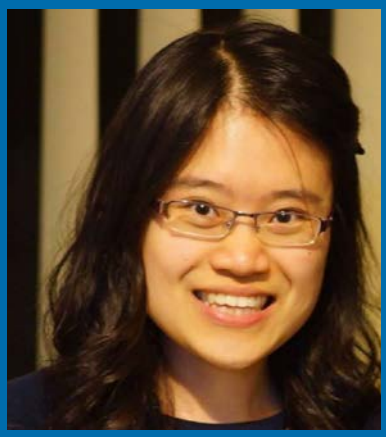
MSDs such as low back pain and osteoarthritis are associated with reduced quality of life and work productivity, which can be quantified as a reduction in QALYs and PALYs. This study provides an indication of the size of the economic loss to society conferred by these conditions and illustrates the potential increase in GDP if these conditions are to be better managed and prevented in the long run. Results found in this study will allow cost-benefit analysis on the management and prevention strategies implemented.

Maylyn Goh

Identifying and addressing osteoporosis knowledge gaps in women with Premature Ovarian Insufficiency (POI) and Early Menopause (EM)

A/Prof Amanda Vincent & A/Prof Jacqueline Boyle

Monash Centre for Health Research and Implementation,
Monash University, Clayton, Victoria, Australia



I decided to undertake a BMedSci (Honours) year after finishing 3rd year. Before entering into the Honours program, I did not know much at all about research. However, my experience this year has given me an insight into what research entails. From learning how to perform data analysis, to recruiting and conducting interviews, I have managed to develop a wide range of skills throughout the year. Furthermore, as I was involved in a translational research in which we developed a factsheet/Infographic that will be made freely available to the general community, it is truly rewarding to have a final end product after all the hard work this year! For me, pursuing an Honours year also opened up various valuable opportunities such as networking and presenting at conferences.

ABSTRACT

Background

Premature Ovarian Insufficiency (POI) and Early Menopause (EM), menopause before age 40 and 45 years respectively, affects up to 10% of women. The prevalence of POI/EM is expected to rise as increasing numbers of women develop iatrogenic POI/EM. POI/EM is associated with an increased risk of osteoporosis, a condition with significant adverse impacts upon one's quality of life. Many women with POI/EM have unmet information needs, which may lead to sub-optimal health-related behaviours and outcomes. Even though osteoporosis is a major concern for women with POI/EM, little is known about women's knowledge, beliefs, information needs and behaviours regarding osteoporosis.

Study's Aims

I. To evaluate women with POI/EM's current understanding and practices regarding bone health.

II. To assess current online consumer resources regarding POI/EM and bone health.

III. To co-design a bone health factsheet for women with POI/EM.

Method

This mixed-method study involved two phases: (I) An initial needs-analysis which informed (II) The development of an acceptable factsheet.

The needs-analysis compromised: (A) A quantitative survey of women, recruited from the community and hospital with a self-reported diagnosis of POI/EM, assessing demographics, medical history, calcium intake, exercise, factsheet information needs, osteoporosis knowledge (OKAT), beliefs and self-efficacy (validated scales) and (B) An assessment of the quality and readability of current online consumer resources related to POI/EM and bone health.

Using the results of the needs-analysis, a bone health factsheet was developed and refined, using semi-structured interviews involving women with POI/EM. Data analysis involved descriptive statistics, logistic regression (SPSS) and thematic analysis (NVivo) of interview transcripts.

Results

Needs-Analysis

The median age of survey respondents (n=316) was 54 years (IQR: 47-63) and 75.7% had a post-school qualification. Median age of menopause was 40 years (IQR: 38-43) and iatrogenic POI/EM affected 55.6% of women. According to current guidelines, most women reported inadequate dietary calcium intake (98.7%) and exercise (65%). Osteoporosis was diagnosed in 19.3% of women. The median OKAT score was 8 (IQR: 6-10)/19 and main areas of knowledge gaps were related to osteoporosis risk factors, treatment options and post-menopause bone loss. OKAT, adjusted for age and education, predicted calcium intake [OR 1.126 (CI 1.035-1.225); p=0.006] and screening [OR1.186 (CI1.077-1.305); p=0.001]. All factsheet topics were considered Very Important/Essential to include (>75% of women).

Significant shortcomings exist in current resources regarding POI/EM and bone health. Quality assessment, using the DISCERN tool, demonstrated that 54% of resources were of a moderate quality or lower (Score ≤3). None of the assessed resources had a readability consistent with current recommendations (Grade 8 or lower).

Development of factsheet

Two rounds of interviews were conducted (n=10 each). The five main themes that emerged included: content, design, perceived usefulness, emotional responses and clinical considerations.

Conclusions

This is the first Australian study to identify women with POI/EM's knowledge, beliefs, information needs and health-behaviours regarding osteoporosis. The co-designed factsheet addresses women's information needs and may facilitate discussions with health professionals and self-care of condition. Further investigations exploring the effectiveness of the factsheet in improving women's knowledge, health-related behaviours and health professionals interaction is needed

Christopher Hardy

Trends in condomless anal sex and drug and alcohol usage amongst Men who have Sex with Men in Melbourne, Australia; A retrospective case analysis from 2011 to 2017

Dr Eric P.F. Chow[1,2], Prof Christopher K Fairley[1,2]

1. Melbourne Sexual Health Centre, Alfred Health, Carlton, VIC 3053, Australia
2. Central Clinical School, Monash University, Melbourne, VIC 3004, Australia

Hey there! My name is Chris, and I decided to undertake BMedSc(Hons) project after completing my fourth year of the MBBS degree. I have always been incredibly interested in sexual and LGBTQIA+ health, so I thought a project at MSHC would be perfect for me.

This year has been challenging; a lot of blood, sweat, and (mostly) tears have gone into writing the literature review, the thesis, and my article. But, it has also been an incredible year that has allowed me to explore another aspect of medicine whilst also making some incredible friends and contacts.

Working with a large dataset, using statistical analysis software, and learning how to get things published have been skills that I will no doubt be using further on in my career. A huge thanks to Dr Eric Chow and Prof Kit Fairley for their patience with me, and thank you to MSHC for welcoming me in with open arms!

If you have any questions or queries please email me: cahar25@student.monash.edu.

ABSTRACT

Background

The rates of STI infection have been rising for a decade in Men who have Sex with Men. The aim of this paper is to see if trends in sexual risk factors have been increasing over the same period to determine if they may potentially explain the increase in STI infection.

Method

Data from clinical consultations at Melbourne Sexual Health Centre (MSHC) from January 1st 2011 to December 31st 2017 were reviewed. Only those who completed CASI were included in the analysis. Logistic regression analysis using generalised estimating equations was conducted to explore the risk factors associated with condomless anal sex during drug use, alcohol use, and with health issues. Risk factors included number of casual sexual partners, overseas birth, PrEP use, a positive HIV status, and having a regular sexual partner.

Results

There were 134 614 consultations in MSM in the study period of which 22, 255 were included for analysis. The number of consultations with MSM reporting condomless anal sex with casual sexual partners in the past 12 months increased from 1686 in 2011 to 5635 in 2017. Condomless anal sex during and/or after drug use increased significantly by 5% per year (adjusted odds ratio [AOR] 1.05; 95%CI 1.03-1.08, p<0.001). Condomless anal sex during and/or after alcohol use and with health issues showed no change.

Conclusions

The finding of increases in condomless anal sex over time has been previously described but the finding of increases in drug use among men practicing condomless anal sex is new. Given drug use increases other activities such as group sex it may explain some of the rises in STIs. Further research is needed in this area to clarify further risk factors, and continual surveillance of MSM will be required to monitor their sexual health into the future.

Alexander Herdyanto

Cardial Procedural Outcomes During the Festive Season

Dr Alice Owen PhD , BSc (Hons), Dr Diem Dinh PhD, BAppSc (Hons)
School of Public Health Preventive Medicine Monash University

I'm a 4th year medical student in University of Indonesia. The reason why I chose my project is because there are a lack of studies exploring differences in cardiac procedural outcomes during holiday period compared to non-holiday period, especially in southern hemisphere. Throughout this Honours year, I learned a lot how to keep the good relationship with all Honours students and supervisors. I gained more confident in group discussion as well as presentation from this project. For future students, my suggestion is to always keep contact and manage good relationship with your supervisors. Ask for directions whenever in doubt or feel confused within your thesis journey. Good luck and God bless! Cheers

ABSTRACT

Background

Previous studies have suggested that there are seasonal impacts on CVD outcomes. In northern hemisphere where Christmas time falls in winter, an analysis by Phillips and colleagues found that deaths from heart disease increased in the winter season, but that there were also spikes in cardiac mortality around Christmas and New Year. Relatively fewer studies have been conducted in the Southern Hemisphere (where Christmas and New year occur during summer). This study by Knight and colleagues looked at out of hospital cardiac death and found that even though there was lower mortality during the summer season, there appeared to be a small increase over the Christmas New year holiday period relative to surrounding time periods. The aim of this study was to use VCOR data to determine whether there are differences in PCI outcomes for patients having procedures during the Christmas-New Year holiday period compared to another non-holiday summer period.

Method

Data obtained from the Victorian Cardiac Outcomes Registry, or VCOR. VCOR was established in 2013, and the aim of the registry is to improve quality of care for patients. The study examines PCIs performed during the period 2013-2017. The festive season period was defined as 24th December to 1st January and non-festive defined as 8th November to 17th November and 20th February to 28th February. Temperature data obtained for day of procedure from the Bureau of Meteorology.

Categorical variable (gender, history of diabetes, CABG, PCI, peripheral vascular disease, cerebrovascular disease, public/private hospital, and number of stents) analysed by chi-square, while continuous variable such as age and BMI were analyzed by t-test. Multivariate logistic regression modelling with backward step was used to examine predictors outcomes between Christmas/New-Year's Holiday and the selected non-holiday periods.

Results

The majority of patients were male, with no difference in proportions of males and females between time periods. here were significant differences in 30-day mortality and major cardiac and cerebrovascular events (MACCE) between the festive and non-festive season periods. Moreover, analyses identified some risk factors that may contribute to 30-day mortality. Age, ventricular function, myocardial infarction status and temperature were significantly associated with 30 day mortality. This was also seen in MACCE that age, ventricular function, sick on-hospital cardiogenic shock, and maximum daily temperature were associated significantly towards MACCE outcomes.

Conclusions

In summary, there are differences in 30-day mortality and MACCE outcomes between festive and non-festive season periods. Analyses suggest that patients having PCI in the holiday period have poorer pre-procedural ventricular function. In addition, Regression analyses indicate that festive season itself is not a significant predictor of outcome, but patient age and maximum daily temperature are associated with adverse outcomes post-PCI.

Frisky Maulida Hidayat

Dispensing trends and medication use behaviour of SGLT2 inhibitors versus other glucose-lowering drugs in older adults: The Australian perspective.

Supervisor: Dr Ken Lee Chin
CCRE Therapeutics, Department of Epidemiology and Preventive Medicine

Co-supervisor: Professor Danny Liew
CCRE Therapeutics, Department of Epidemiology and Preventive Medicine

I enrolled in this course in year 2018 as a part of a double-degree programme from Universitas Indonesia. I honestly never thought I'd enjoy a year-long research project. I developed an interest in science at a young age, but never really thought I'd become a medical student. I was always more of an astrophysics enthusiast. But doing research at School of Public Health and Preventive Medicine has proven me that research, even though not particularly on my childhood dream subject, can be fun an interesting.

ABSTRACT

Background

The therapeutic landscape in diabetes has changed rapidly in recent years. Whether or not dispensing patterns of glucose-lowering drugs (GLD) in Australia are in accord with recently published data is unclear. The present study sought (i) to compare the dispensing patterns of sodium-glucose cotransporter-2 (SGLT2) inhibitors versus other GLD and its associated costs from the Australian perspective; and (ii) to evaluate adherence and persistence of use in patients who received GLD.

Methods

A retrospective cohort study was performed using the Australian Pharmaceutical Benefits Scheme (PBS) databases, covering a 10% random sample of the Australian population. The yearly prevalence and incidence use of GLD was assessed by descriptive statistics. Adherence was assessed using proportion of days covered (PDC) and GLD discontinuation was defined as the first ≥90 days without GLD coverage.

Results

Data from a total of 175,125 patients who received GLD were analysed. In the time period 2013-2016, metformin (84%) and sulfonylurea (33%) were the most commonly dispensed GLD, while SGLT2 inhibitors were dispensed to 3% of the patients. Patients were most commonly initiated with metformin (77%). The incidence of patients newly initiated with SGLT2 inhibitors increased 24-fold from 0.8 per 1,000 in 2014 to 19.3 per 1,000 in 2016, while the incidence for metformin initiation decreased from 774.1 per 1,000 to 750.9 per 1,000 during the same period. In 2016, 18% of patients were initiated with a GLD that was inconsistent with contemporary diabetes guidelines. In 2006, the Australian government subsidised a total of AUD $1.2 million on GLD, largely attributed to metformin (52%) and sulfonylureas (41%). By 2016, the cost increased by AUD $480 million/year to AUD $6 million and is projected to reach AUD $8.5 million by 2020. Only 58.8% of the patients were considered adherent using metformin (PDC≥80). A total of 55.2% of patients dispensed with SGLT2i were considered adherent.

Conclusion

Despite decreasing trends from 2012 to 2016, metformin remained the most commonly dispensed GLD during the study period. 18% of the patients were not initiated with first-line therapy as recommended by contemporary guidelines. Annual costs of glucose-lowering drugs are expected to continue rising.

Ryan Hirsch

The SITAR study: SIRT versus DEB-TACE identifying good prognostic indicators

Supervisor: Prof Amanda Nicoll: EHCS Monash University and Eastern Health
Co-Supervisor: Dr Rohit Sawhney: Eastern Health

Wanting an exciting project I picked Gastroenterology, it takes guts. A lot of HCC treatments are in vein, so I thought Aorta pick a trans-arterial therapy. Most treatments only fixed things superficially, they're portal veineers. It was hard work, but I still found time to liver little. I learnt a lot and became more driven, I used to not care if I got As, Bs or Cs, hepatitis clinic changed that. Sometimes it can be bile and make you want to NASH your teeth, but in the end I had a Gall. Not being humerus, it really de-liver-ed a great experience. It takes time and patients, but it is definitely worth it.

ABSTRACT

Background

The treatment of Hepatocellular Carcinoma (HCC) is generally guided by the Barcelona Clinic Liver Cancer (BCLC) staging system. However, this is a guide and with the constant evolution of non-curative therapies many cases have treatments other than those recommended. Indeed, despite not being part of the BCLC algorithm the use of selective internal radiation therapy (SIRT) is increasing, however there is limited data that can be used to discern which patients would be the best candidates for SIRT. We aimed to catalogue the use of SIRT within Victoria and identify which characteristics were associated with superior response within the SIRT cohort, as well as determine specific groups that may be more suited to SIRT or Dr g Eluting Bead Trans-arterial Chemoembolisation (DEB-TACE).

Methods

A retrospective multicentre study, with the SIRT cohort consisting of patients from five major liver centres within Victoria, and the DEB-TACE cohort consisting of patients from a single site. Participants were identified by a search of each site's HCC database and were supplemented by electronic patient records. The endpoints used were overall survival from the time of diagnosis and from time of treatment, time to progression and radiological response.

Results

The SIRT cohort had significantly more advanced tumour burden, despite this there was no significant difference in overall survival or time to progression between the two cohorts either from first DEB-TACE or SIRT or from diagnosis. Subgroup analysis conducted on covariates considered pertinent demonstrated patient characteristics more suited to each treatment modality.

Conclusion

This research is the first to catalogue the experience of using SIRT in HCC in an Australian population, and the largest study to compare SIRT and DEB-TACE. This study suggests there may be subgroups of patients with HCC that are more suited to DEB-TACE or SIRT and highlights the need for further research to establish the optimal roles for these treatments

Chi Hsuan (Kellie) Hu

Smell perception in Motor Neurone Disease

Dr Phyllis Chua[1,2] & Dr Susan Mathers[1,2,3]

1. Department of Neurology, Calvary Health Care Bethlehem, Parkdale
2. Monash University, Clayton
3. Monash Health, Clayton

I completed my project at Calvary Health Care Bethlehem – the statewide centre for Motor Neurone Disease patient care. I have an interest in neurology and chose to undertake a clinical project to develop my patient communication skills and grasp a good under-standing of research. Under the guidance of my supervisors, I was allowed to conduct my research independently and could therefore experience all the major aspects of a clinical study within a year. I was heavily involved in participant recruitment, participant assessments, data entry, and data analysis.

I've had a fantastic year, and I got to work with many wonderful patients, volunteers, and clinicians at Calvary Bethlehem. I've gained valuable knowledge on Motor Neurone Disease and research, which will definitely benefit me in the future. My advice to future students conducting a clinical project is to not be too discouraged if you don't reach the desired participant numbers. It's a tough year with quite a short timeframe, so just try your best and enjoy yourself. The honours year is all about learning in the process. If you have an interest in neurology, I highly recommend a project at Calvary Bethlehem. I'd be more than happy to be contacted: chhu2@student.monash.edu.

ABSTRACT

Background

The discovery of hyposmia as a common feature of Parkinson's Disease (PD) and Alzheimer's Disease (AD), has generated increasing interest in the area of olfactory dysfunction (OD) in neurodegenerative disorders. It's early presentation in PD and AD has led to the proposal of olfactory testing as a potential diagnostic tool for these disorders.

It has been established that people with Motor Neurone Disease (MND) can suffer from non-motor problems. OD has been observed through anecdotal evidence and small sample studies, with some suggesting possible correlations with bulbar, frontotemporal, and respiratory impairment. However, the evidence remains conflicting and there's a paucity of studies assessing correlations with clinical sub-types, important clinical parameters and the diagnostic utility of smell impairment.

Method

This is a cross-sectional study (still in progress) at Calvary Health Care Bethlehem that aimed to examine the prevalence of smell abnormalities in the MND population, and determine whether they correlated with clinical phenotype, stage of disease, disease severity, cognitive impairment and respiratory decline. Furthermore, it aimed to assess the clinical usefulness of the smell test in differentiating MND patients from a healthy control group.

We have thus far, analysed olfactory performance in 60 MND patients and 20 age and gender-matched controls. All participants were screened for sinonasal problems, questioned for self-perceived smell and taste changes and impacts on QOL, and assessed with a cognitive test and a smell test. Additional MND patient data was collected on clinical phenotype, disease stage and severity, behavioural dysfunction, disease duration and respiratory function. We performed non-parametric statistics and receiver operating characteristic (ROC) curve analyses.

Preliminary Results

Findings show 31.7% of MND participants displayed smell abnormalities. Median B-SIT scores were mildly but significantly lower than controls (MND=9/12 vs. Controls=11/12, $p<0.05$). Median B-SIT scores didn't differ between bulbar and limb-onset phenotypes. Olfactory or gustatory changes was self-reported by 63.2% of MND patients that demonstrated abnormal smell performance. Half of those that self-reported changes reported an impact on quality of life (QOL). There was no notable correlation between olfactory performance, and frontotemporal changes, disease duration, disease stage, severity nor respiratory decline. The sensitivity of the B-SIT in identifying MND was 0.32. ROC analysis additionally showed poor diagnostic accuracy (area under curve=0.58).

Conclusions

OD was significantly more common in MND patients, but impairment appeared to be only mild thus far. This suggests that olfactory structures may be involved in the MND disease process. Our findings so far do not support smell testing as a useful clinical biomarker, nor a method of early screening. The lack of correlation between OD and other clinical parameters further deducts from its potential clinical utility.

Our findings suggest OD can contribute to poorer QOL in MND patients, which highlights an area that should be addressed by clinicians in practice. We aim to study more patients and controls to validate our findings. Further larger sample studies, longitudinal studies and pathological studies would assist our understanding of OD in MND and its relationship with clinical variables and the underlying neuropathology.

Mourushi Isa

Is physical examination accurate in the detection of specific sonographic characteristics of Achilles tendon xanthoma in Familial Hypercholesterolemia patients?

Main supervisor: Prof. James Cameron. Director, Monash Cardiovascular Research Centre; Associate Director, MonashHEART
Co-supervisor: Dr Sam Mirzaee. Cardiologist, MonashHEART.

I decided to undertake a BMedSc (honours) year after completing fourth year. I have an interest in cardiology and was keen to take part in a clinical project. After discussing this project with my supervisors, I found the concept very intriguing and hence decided to be involved.

For my project, we aimed to explore whether ultrasound has any potential role in the diagnosis of xanthoma in patients with Familial Hypercholesterolaemia. A steep learning curve was involved while undertaking this project and I believe this is the case for most BMedSc students. It can appear daunting at the start, but you will have a much deeper understanding of research by the end of the year! Honours year provides a unique opportunity to know more about scientific research and learn how to effectively deliver your findings to an audience. It is definitely not a year off!

I had a very rewarding and enjoyable year at MonashHEART. I was lucky to be surrounded by people who were supportive throughout the year and would like to thank my supervisors Professor James Cameron and Dr Sam Mirzaee.

Please feel free to contact me if you have questions (mnisa1@student.monash.edu).

ABSTRACT

Background

Familial Hypercholesterolaemia (FH) is an inherited disorder that predisposes patients to increased cardiovascular risk. Achilles tendon (AT) xanthoma represents lipid deposition in the AT and is a pathognomonic feature of FH. It is associated with increased risk of premature cardiovascular disease.

The role of imaging in the detection of xanthoma has been explored and ultrasound has been deemed to be superior to X-ray, computed tomography (CT) and Magnetic Resonance Imaging (MRI). However, there is limited data regarding the accuracy of physical examination in the detection of xanthoma, compared to ultrasound. Scarcity of data also exists regarding the frequency of xanthoma in the Australian FH population.

Method

Between March 2017 and June 2018, 42 patients with possible, probable or definite FH according to the Dutch Lipid Clinic Network Score from a lipid clinic based at MonashHeart (Melbourne, Australia) were included in the study. The baseline demographics, medication and pathology results were obtained from medical records, pathology services and phone calls to GP clinics.

The physical examinations were performed by the same examiner with expertise in lipidology. The patients were considered to have xanthoma on physical examination if the tendon felt thicker than normal subjectively or nodular lesions could be palpated. The ultrasound imaging were performed at Monash Imaging and analysed from the database by an expert radiographer. Xanthoma was considered to be present if the tendon was thicker than normal or if discrete hypoechoic lesions could be observed.

Statistical analysis was performed on Microsoft Excel, version 16.16.1 and Stata/MP 14.0 2015 for Mac (StataCor, College Station, TX). Distribution for variables was determined by the Skewness-Kurtosis test. Categorical variables are reported as number (n) and percentages (%). Continuous variables are expressed as mean ± standard deviation (normal distribution) or median and Interquartile Range (IQR) (skewed). p value <0.05 was considered significant.

Results

Mean age was 47.7 years, mean Low Density Lipoprotein Cholesterol (LDL-C) was 4.76mmol/L and 47.6% of the subjects were male. The frequency of xanthoma was 73.8% by ultrasound and the median antero-posterior diameter was 5.15mm (IQR 4.7mm-5.7mm). Physical examination had a sensitivity of 38% (95% Confidence Interval (CI) 24.7% to 52.8%) and a specificity of 73.5% (95% CI 55.6% to 87.1%) in xanthoma detection. No single factor demonstrated significant association with xanthoma. There was a trend of association of Arcus Cornealis with the presence of xanthoma (OR=4.5, 95% CI, p=0.18). No association between age and xanthoma was observed.

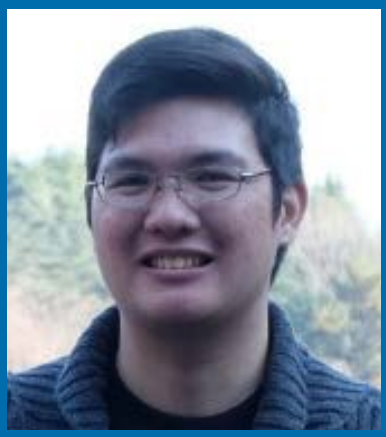
Conclusions

The frequency of xanthoma in our FH population was 73.8%. Ultrasound, used in conjunction to physical examination increased the accuracy of xanthoma detection. No association between xanthoma and age was observed. We observed a trend of association between xanthoma and Arcus Cornealis.

Pradipta Kiswandono

Physiology of Gastro-Oesophageal Reflux Disease Following Sleeve Gastrectomy

Mr Paul Burton – Department of Surgery



My name is Pradipta, I am a fourth-year medical student from the University of Indonesia. Taking the Honours course in Monash was one of the best decision I made in recent years. I chose this project because of my interest in the field of surgery, and it has given me a whole new experience on how clinical research works.

Department of Surgery has provided me with a really supportive environment to engage and expand my ability to think critically, communicate properly, and do a proper clinical research. Moreover, I got to meet various amazing people, made new friends, and get to explore a new country that I would never get the chance had I not chose come here.

ABSTRACT

Background

Sleeve gastrectomy is currently the most commonly performed bariatric surgery used to treat morbid obesity. Gastro-oesophageal reflux disease (GORD), is an important issue following sleeve gastrectomy due to its prevalence, adverse effects on quality of life and potential role as a driver of Barrett's oesophagus and oesophageal carcinoma. GORD is a major cause of re-operation following sleeve gastrectomy. Following the gastric sleeve procedure, there are contrasting views regarding the occurrence of gastro-oesophageal reflux disease, with the majority of reports suggesting sleeve gastrectomy promotes GORD, while another view proposes that sleeve gastrectomy can alleviate GORD symptoms. Despite multiple investigations from various studies, the physiology of gastro-oesophageal reflux disease following sleeve gastrectomy procedure remains poorly understood.

In this study we sought to determine: 1) the expected pattern of gastro-oesophageal reflux following sleeve gastrectomy, using nuclear scintigraphy.2) The expected symptoms of reflux and associated gastrointestinal symptoms following sleeve gastrectomy. 3) To describe how reflux symptoms and nuclear scintigraphic appearance of reflux change over the first two years following sleeve gastrectomy. 4) To define how the pattern of gastro-oesophageal reflux differs in patients suffering severe adverse symptoms.

Method

Sleeve gastrectomy patients with minimal symptoms from The Alfred hospital were recruited into the study. They were classified into different cohorts base on their following months after surgery. Early(0-4 months), Intermediate(5-15 months), and Established(>15 months) Pattern of emptying, gastric emptying half-time, quality of transit, and oesophageal transit property data were taken using nuclear scintigraphy study. Series of questionnaires were used to assess patient's reported reflux symptoms, dysphagia, Quality of Life, and depression.

Seventeen "optimal patients" with minimal symptoms and have matched nuclear scintigraphy and questionnaires were selected from the whole cohort. Another separate cohort of patients with significant reflux symptoms following the surgery will be recruited as a comparison to the asymptomatic group.

Results

We obtained a total of 30 patients for the asymptomatic group, 17 optimal patients, and 7 patients with significant reflux symptoms that has done nuclear scintigraphy scans. Majority of the patients had reflux, with 67% and 76% from the asymptomatic group and the optimal group were detected to had reflux.

We found that there was a significant increase of gastric content retained in the oesophagus and sleeve at the end of nuclear scintigraphy in patients with significant reflux(p-value: 0.048 and 0.0445). This event could indicate the association of impaired gastric clearing with severe reflux symptoms

We observed that there is no significant decrease in quality of life in sleeve gastrectomy patients in comparison to community norms. However, there is a significant decrease in physical function in established group patients compared to early and intermediate group(p-value: 0.0357 and 0.0160).

Conclusions

We identified that around the time of a meal, reflux appears to be expected following gastric sleeve procedure. There are potentially three patterns of GORD following sleeve gastrectomy that is associated with altered gastric anatomy and physiology. Further delineating these patterns and linking them specifically with symptoms will be an important future research endeavour.

Putri Nurra Kusumawardhany

Prostate Cancer Pattern of Presentation and Treatment in Jakarta and Victoria

Associate Professor Sue Evans – Head of Prostate Cancer Outcomes Registry
Fanny Sampurno – Prostate Cancer Outcomes Registry
Professor Rainy Umbas – Faculty of Medicine, Universitas Indonesia

I'm currently in my fourth year of medical school and commenced my honours year in School of Public Health and Preventive Medicine under the supervision of A/Prof Sue Evans and Fanny Sampurno from Prostate Cancer Outcomes Registry – Victoria and Prof. Rainy Umbas, a consultant urologist from the Faculty of Medicine, Universitas Indonesia.

I had a very enjoyable time during my honours year and it has given me a fresh perspective on the importance of research towards the future of science, especially on how it can help physicians to have a deeper understanding on how to treat the patients effectively. I have gained an enormous amount of new knowledge and skills this year, which benefitted greatly from my supervisors and the PCOR-Vic team for their constant support and generosity of time.

This has been an unforgettable year. I would encourage anyone to take on Honours year to step outside their comfort zone and to develop research skills, which I believe will be very beneficial for the future healthcare careers!

pkus0003@student.monash.edu
dindahkm@hotmail.com

ABSTRACT

Background

Prostate cancer (PCa) is the fourth most common cancer in Indonesia and the most common non-skin cancer in Australia. Although the number of PCa incidence rate is higher in Australia, but the five-year mortality rate in Indonesia is nearly as high as the Australian rate. This study aims in gaining understanding regarding the pattern of treatment and presentation of men with PCa in Jakarta, Indonesia, the timeliness to treatment as well as the factors affecting the choice of treatment and compared it to Victorian men with PCa.

Method

Data were extracted from two databases; Prostate Cancer Outcomes Registry – Victoria and database from Department of Urology, Cipto Mangunkusumo National Central General Hospital in Jakarta. Descriptive, univariate and multivariate logistic regression analyses were used.

Results

This cohort consisted of 448 men from Jakarta and 16,738 men from Victoria diagnosed with PCa. The mean age at diagnosis of men in our Jakarta cohort was 67.0 years of age and in Victoria was 66.4 years. Our study found that most men in the Jakarta cohort were diagnosed with metastatic risk disease (51%). Whereas most men in Victoria were diagnosed with intermediate risk disease (45%). Over half of men in Jakarta (65%) were diagnosed with PSA level >20 ng/mL and on the contrary, most men in Victoria were diagnosed with PSA level 4.01-10.00 ng/mL (54%). In Jakarta, most men were diagnosed with Gleason score of 8-10 (53%) while in Victoria, most men were diagnosed with a Gleason score of 7 (46%).

In terms of treatment, men in Jakarta were nearly six times and 1.5 times fold more likely to receive ADT or radiotherapy and more than 50% less likely to receive AS/WW or surgery compared to Victorian men. We also found that patients with localised PCa who were diagnosed at the age of 75 years and over were 20 times more likely to receive ADT as monotherapy and less likely to receive surgery compared to patients who were diagnosed in younger age across the entire cohort.

Compared to men being managed in Victoria, more men with low risk disease in Jakarta received surgery (41% vs 46%, $p<0.001$) and less men received AS or WW (28% vs 47%, $p<0.001$). Moreover, men in the high-risk group in Jakarta were more than twice as likely to receive ADT compared to Victorian men in this same risk group (28% vs 13%, $p<0.001$). For men with metastatic disease, our findings found that these men in Jakarta were 100 times more likely to receive ADT compared to localised PCa (OR 111.75, $p<0.01$). In Victoria, metastatic PCa patients were 23 times fold more likely to receive ADT compared to localised PCa (OR 23.07, $p<0.01$). Men with high and very high-risk disease in Jakarta received more timely treatment compared to men in Victoria (14 days vs 27 days, $p<0.001$)

Conclusions

To our knowledge, this was the first study that directly compares pattern of diagnosis and treatment for PCa between Indonesia and the developed country of Australia. The results of this study can be used to support the development of updated comprehensive treatment guidelines in Indonesia. Moreover, to provide an indication of the importance of developing a national PCa registry and contributing to a Global PCa registry.

Vivien Lai

Systemic Treatments for Alopecia Areata: The Efficacy of Cyclosporin

Prof. Rodney Sinclair, Sinclair Dermatology;
Prof. Douglas Gin, Alfred Hospital;
Dr Gang Chen, Monash Centre for Health Economics

I decided to pursue a Bachelor of Medical Science (Honours) following 5th year medicine. Having always had an interest in furthering medical knowledge, I desired a greater, more enriching experience in research prior to beginning work as a junior doctor. This year, I had the exciting project of conducting a clinical trial at Sinclair Dermatology Clinical Trials Centre, in a disease area that has often been overlooked. I am greatly appreciative of the skills, friendships, insights and inspiration I have gained and I look forward to continuing to build on these in the years to come. I would like to thank my supervisors, Prof. Sinclair, Prof. Gin, Dr Chen for all their support this year!

ABSTRACT

Background

Alopecia areata (AA) is a T-cell mediated autoimmune disease of the hair follicle resulting in acute or chronic patches of non-scarring hair loss, which may progress to loss of total scalp hair (alopecia totalis, AT), or universal loss of hair over the entire body (alopecia univeralis, AU). Systemic treatment for extensive disease has been poorly investigated. Despite widespread use of steroid-sparing agents, particularly cyclosporin, in the treatment of moderate to severe AA, there are no randomised, placebo-controlled trials evaluating its efficacy. Case series indicate the response rate to cyclosporin is in the range of 33% - 55%.

Aims

To evaluate the efficacy of cyclosporin compared to placebo at 3 months in patients aged 18 to 65 years with moderate to severe AA.

Methods

A double-blind, randomised, placebo-controlled trial was conducted. Adults aged 18 to 65 years of age with moderate to severe AA were randomised in a 1:1 ratio to receive 3 months of cyclosporin (4mg/kg/day) or matching placebo. The study was powered to detect a 50% reduction in SALT score in 50% of participants. Blinded assessments were conducted monthly and included: physical examination, blood biochemistry, photography, quality of life measurements and efficacy evaluation using Severity of Alopecia Tool (SALT) score, eyelash and eyebrow assessment scales. A per protocol interim analysis was performed for participants completing 3 months of treatment.

Results

28 participants (cyclosporin: 13; placebo: 15) were analysed. At baseline, the mean SALT score was 79.4% and approximately half of participants in each group had AT or AU. The mean duration of current AA episode was 6.5 years. While the cyclosporin group had a greater mean change in SALT score (-10.3% versus -2.6%; p=0.59) and greater proportion of participants achieving at least a 50% reduction of SALT score (23.1% versus 6.7%; p=0.216) compared to placebo at 3 months, this did not achieve statistical significance. Only the proportion of participants achieving a 1 grade improvement in eyebrow assessment scale was significantly different between cyclosporin and placebo (23.1% versus 0.0%; p=0.049). Quality of life assessment did not show any statistically significant change for each group at the end of treatment compared to baseline.

Conclusion

This is the first randomised, placebo-controlled, prospective clinical trial investigating the effectiveness of 4mg/kg/day cyclosporin monotherapy in the treatment of moderate to severe AA for 3 months. Interim results of 28 participants did not reveal a statistically significant difference between cyclosporin and placebo in reduction of scalp hair loss at 3 months of treatment. The trend for continued response over time suggests that trials employing a larger sample size and longer treatment duration may allow detection of lower response rates. These results suggest that any potential benefit associated with cyclosporin treatment is likely to be slower in onset than other inflammatory skin diseases, such as psoriasis and atopic dermatitis. These results may be interpreted for a cohort of patients with moderate to severe, long-standing AA and will guide clinicians in their choice of second-line agents for this patient cohort.

Yael Lefkovits

Factors improving outcomes of the artificial pancreas during pregnancy in women with type 1 diabetes

Dr Zoe Stewart, Professor Helen Murphy, Professor Euan Wallace
Department of Obstetrics and Gynaecology, School of Clinical Sciences, Monash University
Wolfson College, University of Cambridge

I'm extremely grateful that I had the opportunity to complete a BmedSci. I was fortunate enough to have completed my project in Cambridge, UK. It's been an incredible adventure and exposed me to a wide depth of scientific knowledge and a wealth of passionate individuals. I believe the ability to think critically has been the most valuable skill I've learn this year. I've also been fortunate to have had exceptionally supportive supervisors and believe this to be a key component to a successful year. I would be happy to discuss my project. Feel free to contact me at yrlef1@student.monash.edu

ABSTRACT

Background

Even with myriad advances in diabetes technology, the majority of pregnant women with type 1 diabetes struggle to meet the recommended glycaemic targets during pregnancy. Maternal and neonatal outcomes remain suboptimal with one in two pregnancies being complicated by pre-term delivery, large-for-gestational-age infants and neonatal intensive-care admissions. Outside of pregnancy, the novel approach of a closed-loop insulin delivery advice (artificial pancreas) has been shown to improve glycemic control. To date, our group has performed two studies assessing its efficacy in type 1 diabetes during pregnancy; one overnight study (Closed-Loop in Pregnancy 03) and one day-and-night study (CLIP 24/7). These randomised-crossover trials compared the closed-loop device to sensor-augmented pump therapy (SAP) – the women completed 4 weeks of closed-loop (intervention) and SAP (control) in random orders. The efficacy and safety of the device during pregnancy was demonstrated, but with a high degree of variability in glycaemic responses.

Method

This study aimed to assess factors that predict women's glycaemic and psychosocial response to the closed-loop technology. This pre-specified secondary analysis examined data from CLIP 03 and 24/7. The combined dataset (n=32) includes women from Cambridge, Norwich and Ipswich, UK. Our primary endpoint examined factors predictive of a positive composite outcome of biomedical and psychosocial response. A positive psychosocial response was defined as an improvement in the participants' attitude to the technology from their baseline qualitative interview to their follow-up interview. The effects of multiple variables on the biomedical and psychosocial efficacy of closed-loop was examined using a range of qualitative and quantitative outcomes.

Result

Overall, 28 women (87.5%) experienced a positive composite outcome with 22 women experiencing a biomedical response and 13 women experiencing a positive psychosocial response to the technology. Women with a lower baseline HbA1c had a more significant biomedical improvement (p=0.014) and women with a higher baseline HbA1c had a more significant psychosocial response with the device (p=0.018). Baseline demographic factors such as age, body-mass index, duration of diabetes, location of treatment and previous usage of insulin pumps or multiple-daily injections, had no effect on the biomedical or psychosocial efficacy.

Conclusion

For women with strong peri-conceptual glycaemic control, the closed-loop device may enable them to achieve an even more stringent level of glycaemic control. In contrast, the women with a higher baseline HbA1c may derive more psychosocial benefit from the technology as the device may provide a way to mitigate the burden of type 1 diabetes. It is important that clinicians paint a detailed and accurate picture of the capabilities of the technology to properly manage women's expectations prior to its use. We eagerly await the results of the upcoming, large, randomised trial assessing the closed-loop device in type 1 diabetes pregnancies before any robust conclusions can be made.

Eva Matthews Staindl

Investigating if ibuprofen could improve antenatal respiratory function in preterm infants

A/Prof Graeme Polglase – The Ritchie Centre, Hudson Institute of Medical Research
Dr Vanesa Stojanovska – The Ritchie Centre, Hudson Institute of Medical Research

I was interested in finding out a bit more about research and what it entails, and figured after 4th year and all the exams was a good time to explore that. This year has offered valuable insight into the world of research and provided a good skills framework to pursue research interests in the future. I chose to do my project in perinatal care/obstetrics & gynaecology as it was an area of interest and the project was something hands on rather than just sifting through data. That was really engaging and interesting however offers little flexibility and means a there's always lots to do.

ABSTRACT

Background

Preterm infants are amongst the most vulnerable members of our society and despite major advances in respiratory support methods, they suffer from high rates of respiratory insufficiency – a major cause of morbidity and mortality. Current management of respiratory insufficiency includes respiratory support at birth with injurious ventilation methods, and postnatal stimulation of breathing using caffeine. These methods largely ignore the neural control of respiration – found in the brainstem respiratory centres, which are vital for sufficient breathing.

Inflammation, which affects a large proportion of preterm infants in utero, is known to affect these brainstem respiratory centres, and also affects fetal breathing movements. In particular, inflammatory mediator prostaglandin E2 (PGE2) has been shown to reduce fetal breathing and has an inhibitory effect on the brainstem. Intrauterine inflammation can be reliably induced using lipopolysaccharide (LPS). COX-inhibitors such as ibuprofen are known to reduce inflammation and PGE2 levels, as well as stimulating fetal breathing movements (FBMs), however these concepts have never been studied simultaneously.

Aims

Our aims were to assess the effects of LPS-induced inflammation on ovine FBMs and brainstem PGE2 levels, and to determine if antenatal ibuprofen could decrease localised PGE2 expression in the brainstem and stimulate FBMs.

Methods

Pregnant ewes at 120 days gestation underwent surgery to instrument the maternal vein, uterus and the fetal veins, arteries, and trachea to allow for monitoring of FBMs and the delivery of LPS/saline/ibuprofen. On days 1-3 of the experiment, fetuses received intravenous LPS (escalating doses: 300ng, 600ng, 1.2ug) or saline. On days 4-5 saline or ibuprofen 5mg/kg twice daily was delivered. Throughout the experiment, FBMs were continuously monitored, and fetal blood and plasma were collected for analysis. At the conclusion of the experiment, both ewe and fetus were euthanized and fetal cerebrospinal fluid and brainstems were collected for analysis.

Results

Incidence of FBMs was reduced by up to 63% following LPS administration on day 1 which was sustained for 6 hours then returned to baseline. There was a reduced response in FBMs on day 2, and no significant difference across groups on day 3. Lactate, partial pressure of oxygen, oxygen saturations, and partial pressure of carbon dioxide followed the same pattern of decreasing responses to LPS over the 3 days of LPS. Whilst the ibuprofen group had limited animal numbers, ibuprofen appeared to transiently stimulate FBMs. Preliminary tissue analysis indicated that animals that received LPS + saline (compared to saline controls and LPS + ibuprofen animals) had: increased PGE2 immunoreactivity in brainstem respiratory centres, increased cytokines and cell death markers in the medulla oblongata, and increased PGE2 levels in the cerebrospinal fluid.

Conclusion

LPS significantly reduced FBMs however the effect was transient – we suspect the fetuses developed a tolerance to LPS. This theory was supported by blood gas data that showed a similar pattern of response and recovery. Tissue analysis appears to support the theory that PGE2 plays a role in the respiratory inhibition observed however further analysis of more animals and of plasma PGE2 and cytokines will help to provide a clearer picture.

Fadhil Muhammad

A Retrospective Study of the Effect of Nivolumab on Overall Survival in Non-small Cell Lung Cancer

John Zalcberg – Cancer Research Program division of SPHPM Monash University
Rob Stirling – Allergy, Asthma & Clinical Immunology Clinic of Alfred Hospital

Hi everyone! My name is Fadhil Muhammad and I am from Indonesia. This honour program is part of my study program from Universitas Indonesia and I finished my pre-clinical years before underwent this honour degree.

Well, it was an outstanding experience to do research which I interested on, cancer. The friendly environment and clinical type of research were the reasons why I chose this research. My research was drafted by myself from scratch with the help of my supervisors and other staffs during my honour years.

There were countless benefits of taking the honour degree, but I could simplify for the newcomers into 3 things: critical thinking in how we appraise the problem and come up with an idea of research, we learn a specific topic of research, and we get a chance to form up our own research from draft. Those advantages were worth for one-year degree program.

If I may suggest to newcomers, spend a year to learn and make a good quality research needs hard-work and good time management but enjoy the whole process. If you have further queries about honour degree or my research, feel free to contact me through email: dr.fadhilm@gmail.com

ABSTRACT

Background

Most of lung cancer patient is not detected until the disease is advanced. In 2006 Australian data, Advanced Non-Small cell lung cancer (NSCLC) patients had very poor survival, which was 7.8 months. This number was associated with the therapies for advanced patients, which was standard chemotherapy, EGFR inhibitor, and ALK inhibitor. In 2014, there was a new drug called nivolumab which showed the survival benefit in clinical trials studies (Trials 017 and 057). The median survival of trial study (057) was 12.2 months, which was 4.4 months longer than the previous data. Although the trial result showed a promising result of this treatment, the real-world study of nivolumab is limited.

The objective was to assess the impact of nivolumab use in stage III and IV NSCLC in an Australian hospital and evaluate the impact of nivolumab on overall survival.

Method

This study was a retrospective, observational and single-site study that used medical records as primary data and survival analysis as an illustration of the survival benefit of nivolumab. Two survival analyses were conducted to confirm the aim of this study. The first survival analysis was to illustrate the survival differences among nivolumab, chemotherapy and no anti-tumour therapy groups, whereas the second survival analysis was to validate the survival benefit of nivolumab as second-line therapy. Lastly, the regression model was generated based on prognostic factors of NSCLC patients to confirm the survival result of second survival analysis.

Results

Data collection was finished. Three hundred and forty patients were included. The first survival analysis showed that patients with nivolumab (21. 2 months) had longer survival than chemotherapy patients (13.5 months) and no anti-tumour medication patients (4.6 months). Then, the second survival analysis showed that patients with second-line nivolumab had the median survival of 19.8 months, whereas the median survival of patient treated with second-line chemotherapy was 10.1 months. The confirmation of the second survival result was by analysing factors including age, sex, smoking status, tumour types, sites of metastases, mutation status (EGFR, ALK), PDL1 result, surgery, radiotherapy, and targeted therapy using Cox regression method. Among all factors, the adenocarcinoma of Tumour types played a significant role in patient survival, which was showed by significant p-value (0.027) and significant hazard ratio (0.08)

Conclusions

Despite the low number of patients and higher treatment effect showed in this study, it was revealed that this real-world study supported the survival benefit of nivolumab of the previous clinical trials studies (Trials 017 and 057). This study also can become the reference to the clinician who seeks the evidence of nivolumab use in real-world patients. With the limitations and strength of this study, future directions for real-world nivolumab study should include exploration of the adverse event of therapy and complications occurred due to the treatment. Also required is an investigation of quality of life between nivolumab and chemotherapy patients.

Ari Mushin

Predictors of Cardiovascular Disease in HIV

Professor Jennifer Hoy, Director of HIV medicine, Department of Infectious Diseases, the Alfred Hospital and Monash University
Doctor Anna Hearps, Deputy Program Director, Healthy Ageing (Expansion Program), Burnet Institute

I decided to do a BMedSc(Hons) year after finishing 3rd year. I was lucky enough to find a project in the field I find interesting; Infectious Diseases and in particular, HIV. Through this project I have had the opportunity to work with both the clinical and lab teams at the Alfred Hospital and the Burnett Institute, covering a wide range of research techniques and clinical applications. I learnt more than I could have hoped, not just about the particulars of my project, but about the process of developing, implementing, revaluating and refining research projects. I also had a fantastic time in the Infectious Diseases department, which id full of great people and learning opportunities.

The full scope of my research wasn't completed by the end of the BMedSc(Hons) course so I am still working with the team on continuing the research, which is fantastic and will hopefully allow me to stay engaged with this part of the medical world throughout the rest of my medical degree.

Feel free to email me at mushinari@gmail.com with any questions about the project or BMedSc(Hons) in general; I am happy to talk and provide any insight I can.

ABSTRACT

Background

People Living with HIV in the developed world have seen increased lifespan since the introduction of antiretroviral therapy. As the life expectancy has increased, an increase in serious non-AIDS events including cardiovascular disease has been identified. It is not known whether this increased risk is due to HIV infection and the changes it causes, exposure to antiretroviral therapy, traditional risk factors, or a combination of these.

Method

A retrospective case control study was designed. HIV patients with a diagnosis of CVD were identified from the Victorian HIV Database as cases and matched by age and gender to HIV patients without a diagnosis of CVD as controls. Data on the history of the HIV infection (including duration of known infection, contemporary and nadir CD4 counts, CD8 counts and viral loads) and the antiretroviral therapy used to treat HIV (including length of exposure to ART, current regimen, and previous drugs used) was collected, as were data on traditional risk factors (including blood pressure, lipid profile, and current prescriptions).

Results

172 cases and 344 age- and sex-matched controls were identified. Analysis of traditional risk factors revealed that

- History of hypertension (but not current systolic or diastolic blood pressure) was associated with CVD
- High density lipoprotein levels were associated with lower rates of CVD, and triglyceride levels were associated with higher rates of CVD
- Current smoking and history of smoking were both associated with CVD
- Diabetes was associated with CVD
- Prescriptions for hypertension, dyslipidaemia, and anticoagulation were all associated with CVD

The analysis of HIV factors revealed no statistically significant associations.

The analysis of ART factors showed an association between NNRTI use with lower rates of CVD, current use of abacavir and dolutegravir with higher rates of CVD, and historical use of lamivudine with lower rates of CVD.

Conclusions

This study showed a risk factor profile different to that which might be expected. While the elevated risk of CVD may be explained by higher rates of traditional risk factors, further research is warranted to determine the physiological changes caused by ART that may modify the risk of CVD.

Cameron Naidu

Developing a Model to Elucidate Dendritic Cells in Colorectal Carcinomas

Professor Eva Segelov
Dr Maja Green
Translational Oncology Research Group at MHTP

In 2018 I undertook a Bachelor of Medical Science (Honours) degree after completing my fourth year of medical school. I hoped to learn about the processes of how research goes from the translational stage to eventually being implemented into clinical practice. I find the breakthroughs in oncology research to be fascinating and was excited to see how things function at the cutting edge of medical research.

The Translational Oncology Research Group proved to be a great group, allowing me to experience all aspects of the research process, from establishing a project to conducting and analysing the results myself. I would highly recommend future students consider them for honours projects in the future.

ABSTRACT

Background

Dendritic cells (DCs) interact with both innate and adaptive immune systems, functioning as a crucial mediator of the natural anti-tumour response. Recently, it has been found that DCs up-regulate the immune checkpoint programmed cell death protein 1 (PD-1) in response to inflammatory stimuli as well as potentially in the tumour microenvironment itself, the same immune checkpoint targeted by anti-PD-1 immunotherapeutic medications. Additionally, it appears as though certain DC functions, specifically production of the cytokine interferon (IFN)-λ may be regulated by this checkpoint. Despite this, minimal research has been conducted on how these crucial cells are affected by these immunotherapies. Mismatch repair-deficient (MMR-D) colorectal carcinomas (CRCs) are known to be more responsive to anti-PD-1 immunotherapies than mismatch repair-proficient (MMR-P). However, in searching for explanations as to why this is the case, the role of dendritic cells has been largely overlooked.

We aimed to identify the presence and abundance of DC subsets infiltrating MMR-D and MMR-P CRC tumour microenvironments as well as their expression of the PD-1 immune checkpoint and the anti-cancer cytokine IFN-λ. Hypothesising that MMR-D tumours would exhibit increased cDC1 dendritic cells, PD-1 and IFN-λ compared with the MMR-P cancers. Ancillary, we aimed to assess the effect of anti-PD-1 therapy over time on the expression of IFN-λ within serum samples of melanoma patients, hypothesising that circulating levels would increase throughout treatment.

Method

Antibodies directed towards PD-1, IFN-λ and human leukocyte antigen-DR isotype (HLA-DR) were optimized through immunohistochemistry (IHC) on MMR-D and MMR-P CRC tumours. Subsequently, preliminary series staining MMR-D and MMR-P CRCs for HLA-DR and IFN-λ infiltration were performed and analysed for comparison. Immunofluorescence (IF) was performed on these antibodies and a number of additional antibodies to distinguish the distinct dendritic cell subsets.

Results

Antibodies directed towards PD-1, IFN-λ and HLA-DR were identified and optimized for future use in IHC and IF for IFN-λ and HLA-DR. Comparative series of MMR-D and MMR-P CRCs revealed average percentage tumour area staining of 11.49% and 11.50% for HLA-DR ($p=0.34$) and 1.01% and 0.38% ($p=0.29$) for IFN-λ.

Conclusions

This study was an important first step in assessing the role of DCs in anti-PD-1 immunotherapies. Preliminary findings from this work suggest MMR-D and MMR-P CRCs exhibit distinct patterns of IFN-λ expression prior to treatment. However, further antibody optimization and immunofluorescence must be performed to assess DC infiltration. Testing of larger sample sizes is necessary in order to draw distinct conclusions. Circulating levels of IFN-λ must also be assessed throughout treatment.

Tim Nasteka

Atrial Fibrillation at a Victorian tertiary metropolitan hospital

Professor Danny Liew
School of public Health and preventive Medicine
Chair of Clinical Outcomes Research Monash University
Head of the Division of Clinical Epidemiology Monash University
Co-Director of the Centre of Cardiovascular Research and Education (CCRET)
Consultant physician at the Alfred Hospital in Clinical Pharmacology and General Medicine.

I started my BMedSci after finishing my fourth year of studies last year and will be entering my fifth and (hopefully) final year next year. I did not start the year in this project and was able to be involved due to the generosity of Professor Liew and the staff at the School of Public Health and Preventive Medicine. The project however was incredibly interesting, and I had a fantastic year overall.

Being part of the BMedSci programme allowed me to learn general research skills, data analysis, how to use statistical tools and software, and what being a 'clinician scientist' is all about; giving ideas on future career pathways. I would heartily recommend those considering a BMedSci to be involved in one; while it can be challenging and hectic, it is ultimately rewarding.

My advice to prospective students is to speak up as early as possible if there are issues, that things will always take twice as long as you expect, and while everything may not go to plan there can still be a good outcome. I'm also happy to be contacted at tanas3@student.monash.edu.

ABSTRACT

Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia and a significant cause of morbidity and mortality. The pathophysiology, outcomes and classification remain disputed, and while hospital data and epidemiological information exist for the condition, there are many gaps in understanding, particularly in an Australian context.

Method

This study was a retrospective cohort study, utilising administrative data from The Alfred Hospital collected from 1 January 2013 to 30 June 2018. The primary analyses used inpatient admissions as the units of measure. Descriptive analyses were undertaken of patient characteristics (sex, age, Charlson comorbidity index), burden of care (length of stay and costs), and outcomes (readmissions, complications, and mortality). Central tendency and variance of numerical data were described using medians and interquartile ranges (IQR), given the strong positive skew of data. Categorical data were described by percentages. In 'associative analyses', the positive skew of outcome data meant that negative binomial regression was used for non-binary outcomes, while logistical regression was used for binary outcomes. Secondary analyses were performed using individual patients as the units of measure.

Results

There were 10,251 admissions of interest in the study period, involving 7,387 unique patients. A higher percentage of admissions were for men (56.63%), with the median (IQR) age at admission being 75 (65, 84) years, and the median (IQR) and mean (standard deviation (SD)) Charlson comorbidity index score being 1 (0, 2) and 1.37 (1.93), respectively. The median (IQR) LOS was 4 (1, 9) days, with a median (IQR) cost of AUD $6,258 ($3,331, $11,884). All admissions involved at least one in-hospital complication, with the median (IQR) number of complications being 9 (5, 15). Of the admissions, 11.65% resulted in death, and 7.14% of admissions involved readmissions for AF within 30 days of discharge. A higher Charlson comorbidity index score was predictive of longer LOS, higher costs, a higher number of in-hospital complications and in-hospital death, while being male was predictive of higher costs, a higher number of in-hospital complications and in-hospital death. Increasing age was predictive of longer LOS, lower costs, a higher number of in-hospital complications and in-hospital death.

The results of the secondary analyses (based on individual patients) were similar to those of the primary analyses. Among the study patients, 75.96% only had a single admission during the study period, 6.00% had a readmission for AF of any classification within 30 days of whom 92.43% readmitted with a primary diagnosis of AF; 18.43% within a year, with 94.00% readmitted with a primary diagnosis of AF. Analyses of longitudinal outcome data found that 16.43% of the cohort died (as an Alfred Hospital inpatient) during the study period. From the first day of the index admission, the one-month, one-year and three-year mortality rates were 5.18%, 12.57% and 19.67%, respectively.

Conclusions

AF imposes a large, and growing, burden of hospitalised care in Australia, with high risk of morbidity and mortality. The consistent association of Charlson comorbidity scores with burden of care and outcomes highlights the importance of recognising comorbidities in this patient population.

Henry Pan

What is the Role of Novel Hybrid 68Ga-PSMA PET/MRI Imaging in the Diagnosis and Localisation of Prostate Cancer? – The SAMURAI Study

Associate Professor Jeremy Grummet
Alfred Health Department of Urology, Monash University Department of Surgery/Central Clinical School

Professor Mark Frydenberg
Monash Health Department of Urology, Monash University Department of Surgery/Southern Clinical School

I wanted to take a year prior to graduating to do some sort of research. Clinical research has always interested me, and I had heard great things from other BMedSc students. It's important for future clinicians to know the ins and outs of research, and what better way than to take on a project of my own! I've learnt a huge amount about my topic and urology in general and furthered my data crunching and research skills. More importantly, I've made new friends, broadened my knowledge base and made new industry connections.

My project also allowed me to see into the world of both public and private urological practice at the Australian Urology Associates and The Alfred Department of Urology, and has given me the opportunity to present at conferences and be involved in clinical practice. A BMedSc year has its highs (pressing submit on the thesis) and lows (the weeks preceding pressing submit on the thesis), but has definitely been a truly worthwhile year.

It takes a team to get a newbie through this year, so thanks everyone who has helped me successfully complete my thesis. A special thanks to my supervisor, A/Prof Jeremy Grummet, for a great year!

ABSTRACT

Background

Imaging has played an increasingly dominant role in the diagnosis and localisation of prostate cancers. Prostate Specific Membrane Antigen (PSMA) ligands in PET imaging show superior results compared to traditional prostate cancer imaging techniques. These have mostly been studied in the context of recurrent staging of prostate cancers. Simultaneous PSMA PET/MRI is an emerging modality yielding strong initial results in the localisation of primary prostate cancers.

Objectives: To compare the diagnostic accuracy of multiparametric MRI, PSMA PET/MRI and PSMA PET/CT to whole-mount histopathology for localisation of primary prostate cancer.

1. Localisation and characterisation of significant primary prostate cancers on PSMA PET/MRI compared to PSMA PET/CT and multiparametric MRI.

2. Compare the accuracy of these modalities to whole-mount prostate histopathology specimens.

Method

A prospective database for patients who underwent mpMRI in our group urology practice since 2013 was used. 13 patients underwent mpMRI, 68Ga-PSMA PET/CT, 68Ga-PSMA PET/MRI and subsequent radical prostatectomy with whole-mount histopathology. Imaging was reported based on PIRADS sector maps, with results analysed by dividing the prostate into 12-sectors. The histopathology was matched to imaging with the 12-sector prostate map. Diagnostic performance of each modality was assessed using sensitivity, specificity, positive and negative predictive value, positive and negative likelihood ratio and accuracy. Receiver Operating Characteristics analysis was used to compare modalities. Significant cancer defined as greater than or equal to Gleason 3+4=7 (Grade Group 2).

Results

Analysis was based on 156 sectors from 13 patients. Whole-mount histopathology reveals significant cancer in all 13 patients, with positive tumour detection in 59 of 156 sectors (37.8%).

mpMRI detected lesions in 36 sectors, of which 31 were true positives, and no lesion in 120 sectors, of which 92 were true negatives. 68Ga-PSMA PET/CT demonstrated avidity in 32 sectors, of which 25 were true positives, and no avidity in 124 sectors, of which 90 were true negatives. 68Ga-PSMA PET/MRI demonstrated avidity in 36 sectors, of which 32 were true positives and no avidity in 120 sectors, of which 93 were true negatives. The overall accuracies were 71%, 63% and 75% respectively.

mpMRI, 68Ga-PSMA PET/CT and 68Ga-PSMA PET/MRI each conferred a sensitivity and specificity of 50.85%/94.85%, 42.37%/92.78% and 54.25%/95.88% respectively.

Conclusions

In this pilot study involving high selected patients undergoing prostate mpMRI, 68Ga-PSMA PET/CT, 68Ga-PSMA PET/MRI and subsequent radical prostatectomy with whole-mount histopathology, 68Ga-PSMA PET/MRI outperformed both mpMRI and 68Ga-PSMA PET/CT in accurately detecting and localising significant primary prostate cancer. As a diagnostic technique, pelvic PSMA PET/MRI is an emerging modality, and as such requires further investigation and cost-effectiveness analysis. Expansion into whole-body 68Ga-PSMA PET/MRI imaging could lead to an all-in-one diagnostic and staging modality for prostate cancer.

Laura Panozzo

Communication and Implementation of Advance Care Planning in Regional Victoria.

Dr Bernadette Ward – Monash School of Rural Health
Ms Pam Harvey – Monash School of Rural Health
Dr Dennis O'Connor – Monash School of Rural Health
Dr Jason Fletcher – Bendigo Health

Relocating to Bendigo to complete my BMedSc(Hons) project was a big leap faith – and it most certainly paid off. The support from all staff at the School of Rural Health was sensational. In particular, I would like to extend my gratitude to my academic supervisors, Dr Bernadette Ward and Ms Pam Harvey. The scope of this project was not feasible in a metropolitan setting; it was fantastic to have the opportunity to interact with both the ICU and all general practices in the local area. This year has reignited my passion for high-quality, regional healthcare while engaging my interest in continuing with research in the future. I would strongly recommend that any future student who is considering a BMedSc(Hons) project consider completing a project with the School of Rural Health.

ABSTRACT

Background

Advance Care Planning (ACP) is a process that can empower competent individuals to make decisions regarding their future medical care. An Advance Care Plan (Plan) is a written declaration of these wishes which can be referenced by health practitioners so that medical care is provided in alignment with that individual's preferences and values. The prevalence of Plans in Australia is low, and it is unclear how these ACP documents are communicated from their recommended point of uptake in general practice to a hospital service. The content of Plans and whether preferences are implemented when an individual loses decision-making capacity has had very limited research. The aim of this project was to measure the prevalence, communication and implementation of ACP documents for decedents aged 75 years and over in a regional setting in 2016 – 2017.

Method

Three consecutive retrospective decedent medical record audits with feedback were conducted. These assessed the uptake (prevalence), communication and implementation of ACP alerts and documents for decedents aged 75 years and over who died in the study hospital between 1 January 2016 and 31 December 2017. For the purposes of this study, an ACP document could include: a Plan; a Refusal of Treatment Certificate; an Enduring Power of Attorney (Medical Treatment); or an Enduring Power of Guardianship. The prevalence of ACP alerts and documents for hospital records was determined, with the content and implementation of those with a Plan assessed. General practice records for those with no in-hospital alerts were examined for evidence of uncommunicated ACP documents. Data was analysed using descriptive statistics, including Chi square (categorical/categorical) and Mann-Whitney U tests (categorical/non-parametric continuous). Feedback was presented to the study hospital and participating general practices.

Results

Of the 536 decedent hospital records audited, the majority did not have any ACP alerts (n=110; 79.5%) or documents (n=96; 82.1%). Only 9.7% (n=52) of hospital decedent records contained a Plan.

Of those with no hospital record ACP alert, 14.6% of decedent general practice records with a GP in the immediate surrounding local government area contained at least one ACP document that was created, but not communicated, to the study hospital. This included four Plans.

The content of the Plans that were available in hospital records were divided in their preference for (44.2%) or against (50.0%) life-prolonging treatment. In some cases, Plan preferences were not implemented. This included cases where a Plan explicitly preferenced against a treatment and it was given, including intubation, surgery, antibiotics and medication.

Conclusions

The use of ACP to ensure a patient's preferences and values are respected is currently hindered by low Plan prevalence, inconsistent communication of documents from general practice to a hospital service and variable Plan implementation. By refining medical record systems and proposing methods of consistent communication, existing ACP documents can be identified and referenced during end-of-life care. Future work should include identifying populations that could benefit most from having a Plan, such as those who are socially isolated and do not have a substitute decision-maker.

Jessica Paynter

A multicentre comparison of the contemporary management of Dupuytren's disease.

Associate Professor David Hunter-Smith
Professor David Warren
Department of Plastic and Reconstructive Surgery, Peninsula Clinical School.
Central Clinical School, Monash University.

I chose to undertake a BMedSc in order to gain a taste of medical research and to experience another side of clinical medicine, particularly in the field of surgery which I am interested in. I found this year incredibly challenging and motivating. I believe that I have developed a wide range of skills critical to both medicine and research. As I completed a clinical project alongside research my year included a lot of patient and teaching interaction within the surgical department. I am incredibly grateful to both my supervisors, and the Peninsula Health Surgical department for the teaching and learning experiences I gained.

For those students considering a BMedSc I would recommend choosing a supportive supervisor in a field that you are interested in. I am happy to be contacted for further questions via japay1.

ABSTRACT

Background

Collagenase Clostridium Histolyticum (CCH) is a novel treatment for Dupuytren's disease (DD) within Australia. However, the delivery of CCH as a therapeutic is believed to be variable within the public sector. The effectiveness and safety of CCH for treating DD has not been assessed or documented within the Australian public health sector, nor the Victorian population itself.

Method

This ongoing multicentre, observational comparative study included a consecutive cohort of adult patients with DD being treated with CCH within the Victorian public health system. The exclusion criteria varied according to each individual clinic. Assessment occurred at three times-points; injection, manipulation and follow-up. Injection was day one across all clinics, yet the manipulation and follow-up time-point varied and formed a part of this investigation. Assessment of the therapeutic effect of CCH was made objectively using the Total Passive Extension Deficit (TPED), clinical success and clinical improvement. Patient perception of CCH effectiveness was subjectively assessed using three Patient Reported Outcome Measures (PROMs); Unite Rheumatologiquedes Affections de la Main (URAM), Southampton and the Canadian Occupation Performance Measure Patient Set Questionnaire (PSFS). Analysis was undertaken using median values, analysis of variance and mixed effects logistic regression to determine if CCH outcomes were affected by clinic design.

Results

Qualitative analysis

The delivery of CCH is variable across all Victorian public health clinics. Differences are observed at injection, manipulation and follow-up of people with DD. At injection the adoption of anaesthetic, assessment of disease severity, technique and monitoring differs across all clinics. Manipulation is variable by time frame (two to seven days), location (outpatients or theatre) and anaesthetic use itself. Follow-up is different across all clinics via both length and time.

Quantitative analysis

Seven public clinics were observed across this project; 30 clinics at Frankston Hospital, two at Dandenong Hospital, three at Austin Hospital, two at Maroondah Hospital and one at Northern, Box Hill and Geelong Hospital. Currently only patient data for Frankston and Dandenong Hospital is available for analysis. 209 and 36 patients respectively at Peninsula Health (PH) and Monash Health (MH) were treated with CCH. Clinical success was achieved in 42% of the Frankston and 35% of the Dandenong cohort. Clinical improvement was achieved in 78% of the Frankston and 86% of the Dandenong cohort. A statistically significant reduction in all three PROMs was observed at both the Frankston and Dandenong cohorts. A two way repeated measures for effectiveness (clinical success, clinical improvement, TPED and PROMs) across both centres found nil statistical significant difference between the two cohort's results. CCH clinic design does not impact upon outcomes.

Conclusions

The delivery of CCH is variable across public hospital clinics in Victoria. CCH clinic design does not impact upon the effectiveness of CCH at first review. CCH is effective and safe for treating people with DD in Victoria, Australia. CCH results in improved patient reported functional outcomes. Furthermore, it has led to reduced contracture degree, as reported by the outcomes of clinical success, clinical improvement and TPED.

Holly Pertile

Regularity Learning in Schizophrenia and Psychosis

Professor Suresh Sundram,
Department of Psychiatry, School of Clinical Sciences, Monash University, Clayton, VIC, Australia;
Monash Medical Centre, Monash Health, Clayton, VIC, Australia

Associate Professor Olivia Carter,
School of Psychological Sciences, University of Melbourne,
Parkville, VIC, Australia

I chose to undertake a Bachelor of Medical Science following my fourth year of Medicine to experience a different side of the medical profession. I have always been interested in psychiatry, in particular improving outcomes and quality of life for those experiencing mental illness. This project not only allowed me to contribute to research that may help to improve these outcomes, but also provided me with valuable clinical experience on a psychiatric ward. I learned important techniques in data collection and analysis that have given me a good foundation for future research practice. In all, I found this to be a highly enjoyable and rewarding year, which I would definitely recommend to future students!

ABSTRACT

Background

Schizophrenia is a disabling psychiatric illness, characterised by delusions and hallucinations. These symptoms may cause significant distress and impaired functioning in affected individuals, however their pathology is not well understood. Recent theories in computational psychiatry have proposed that these symptoms may arise from an impaired ability to store, and use knowledge of regularities in the sensory environment to influence current perception. However, no previous study has specifically examined 'regularity learning' in schizophrenia. Moreover, the relationship between regularity learning and psychotic symptoms remains poorly defined. We therefore aimed to examine whether regularity learning is impaired in schizophrenia, and if this impairment is associated with the severity of psychotic symptoms. In addition, we aimed to examine if regularity learning deficits are associated with the occurrence of 'psychotic-like' experiences in healthy individuals and across other psychiatric diagnoses.

Methods

44 psychiatric inpatients (22 schizophrenia spectrum disorder, 22 non-psychotic controls) and 22 healthy controls were administered an auditory regularity learning task. Psychotic-like traits were assessed for all participants. Psychotic symptom profiles of inpatients were also scored.

Results

Participants with a schizophrenia spectrum disorder made significantly more errors in regularity learning than healthy controls. Regularity learning errors were positively associated with the severity of positive 'psychotic-like' traits occurring in all study participants.

Conclusions

These results suggest that regularity learning is impaired in schizophrenia. In addition, they suggest that regularity learning deficits may be involved in the pathology of psychotic symptoms, such as delusions and hallucinations. This finding was not specific to schizophrenia, and may point to a similar mechanism underlying psychotic experiences at both the subclinical and clinical level. However, larger trials are necessary to better define this relationship.

Sai Ponnaganti

How does age of trauma exposure influence the relationship between early life adversity and dissociation?

Professor Jayashri Kulkarni – Monash-Alfred Psychiatry Research Centre, Monash University
Dr Caroline Gurvich – Monash-Alfred Psychiatry Research Centre, Monash University
Dr Natalie Thomas – Monash-Alfred Psychiatry Research Centre, Monash University

I chose to undertake my Bachelor of Medical Science (Honours) at the Monash-Alfred Psychiatry Research Centre with the Women's Mental Health Team after completing 4th year. Psychiatry has always been a field that has fascinated me and after completing my mental health rotation at The Alfred, the impacts and consequences of childhood trauma stood out as an area of interest that I wanted to learn more about. My project was clinical and allowed me to practice skills such as history taking and phlebotomy which I greatly enjoyed.

While there were ups and downs over the course of the year, I can confidently say that I have developed several skills that I had not experienced during medicine, such as designing a clinical study, writing a research paper, and learning to conduct statistical analyses. I also want to stress the importance of choosing a lab and supervisor who you feel comfortable with! It absolutely defines how great your year will be, and I was fortunate enough to work with an amazing team.

It has overall been a very rewarding year, and I wholeheartedly recommend undertaking a BMedSc(Hons) to anyone considering one! Don't hesitate to contact me if you have any questions (spon13@student.monash.edu).

ABSTRACT

Background

Borderline Personality Disorder (BPD); a diagnosis now recognised to be on a stress-trauma spectrum along with complex Post-Traumatic Stress Disorder (cPTSD) is a condition which has debilitating effects on everyday quality of life, and for which there are few effective treatment options. This is in part attributable to the heterogeneity of the condition, with many different symptoms leading to the same diagnosis. Dissociation is often associated with BPD, and better understanding of key symptoms, and the development of BPD helps to better define the condition and consequently improves treatment outcomes. Early life trauma is thought to play a significant role in the development of dissociation, and this study explores this relationship; specifically the age at which early life trauma was experienced and the type of trauma experienced.

Aims/Hypotheses:

The aims for this study were to a) determine whether the age of an individual at the time of trauma affects the severity of dissociation as an outcome, b) identify whether the type of trauma affects the severity of dissociation as an outcome, and c) conduct an exploratory analysis to ascertain if there are specific age groups within each category of trauma which affect the severity of dissociation as an outcome. It was hypothesised that the results would show differences in long term outcomes different types of trauma experienced and between trauma experienced at different ages.

Method

Twenty-five participants were recruited, all of whom had experienced early life trauma as determined by the Maltreatment and Chronology of Exposure (MACE) scale, and dissociative symptoms as recorded using the Dissociative Experiences Scale (DES). These participants also completed the Life-Experiences Checklist (LEC-5) to determine whether the participants felt that they had experienced trauma to compare with their MACE scores. Dissociation scores (DES) were then compared across different age groups, and different trauma types to test if there were any significant factors of trauma exposure that were influencing dissociative outcomes. Statistical analyses were conducted using Generalised Linear Models (GLMs) and Mann-Whitney U tests to test for significance.

Results

We found that early life trauma occurring between 6-18 years, was significantly associated with the development of dissociative symptoms in adulthood. Moreover, the trauma categories of parental verbal and physical abuse, emotional neglect and peer emotional abuse were also significantly associated with dissociation. The exploratory analysis considering the age that each trauma type is experienced, suggested that experiencing parental physical abuse between 6-10 years and peer emotional abuse between 11-18 years was significantly associated with dissociation.

Conclusions

The findings from this study support the existing literature, in that there is a link between early life trauma and the development of dissociation, and that the age that trauma is experienced as well as the type of trauma experienced both have a significant impact. It is important to understand the roles that these factors have in the aetiology of dissociation, a symptom of BPD and cPTSD, allowing us to better characterise the diagnoses and more effectively treat patients with these diagnoses.

Kirby Qin

Extended Peripheral Intravenous Catheters in Paediatric Surgery: A Randomised Controlled Trial (The EPIC Trial)

Mr Maurizio Pacilli, Mr Ram Nataraja.
Department of Paediatric Surgery, Monash Children's Hospital.
School of Clinical Sciences at Monash Health,
Monash University.

I was fortunate enough to work with the wonderful Department of Paediatric Surgery at Monash Children's Hospital. Although I do not have my sights set on a career in paediatric surgery, I chose this project to gain greater exposure to surgical research and because I enjoy working with children. My illustrious supervisors, Maurizio and Ram, have provided me with plenty of opportunities to involve myself in all fields of research.

This is a phenomenal department, but be prepared for a busy year! Maurizio and Ram are constantly coming up with new research projects and also encourage you to develop your own ideas. I highly recommend this department to anyone interested in paediatrics and/or surgery.

Don't hesitate to contact me if you want to have a chat: kirbyqin@gmail.com

ABSTRACT

Background

In paediatric surgery, many children require multiple days of intravenous (IV) therapy after an operation. Intravenous therapy is generally administered through a peripheral intravenous catheter (PIVC). PIVCs are widely used and readily available, however, there is growing evidence to suggest that they are inappropriate for more than 48 hours of therapy. As a result, a longer, more durable catheter has been developed: the long peripheral catheter (LPC). They are 6-15cm long compared to PIVCs which are 2-6cm. Randomised controlled trials (RCTs) have shown LPCs to have superior outcomes compared to PIVCs in adults. Paediatric research is limited to observational studies which have shown that LPCs are safe and well-tolerated.

The aim of this study was to determine if LPCs would demonstrate improved duration of action, reduced failure rates, reduced postoperative IV cannulations and increased patient satisfaction.

Methods

This was an open-label RCT involving paediatric surgical patients requiring >48 hours of postoperative IV access. Participants were randomised to receive either a standard PIVC or an 8cm 22G LPC, inserted intraoperatively under general anaesthesia. The allocated catheter was used to deliver IV therapy on the inpatient ward. Throughout their admission, participants were monitored daily to assess catheter function. If the allocated catheter failed on the ward, participants were subsequently treated with PIVCs. In addition, cost-effectiveness analysis was performed and parental satisfaction was assessed by means of a questionnaire. Parametric data is presented as median [range] and non-parametric data is presented as mean ± standard deviation.

Results

Although recruitment is still ongoing, 50 patients are documented in this interim analysis – 26 in the PIVC group and 24 in the LPC group. Gender, age, weight and emergency status were similar between groups. The median duration of IV therapy was 5.1 days [2.1-16.1]. The mean duration of PIVCs and LPCs was 3.8 ± 1.9 days and 4.3 ± 1.4 days respectively (p=0.38). Patients in the PIVC group received a median of 2 [1-4] catheters compared to 1 [1-3] in the LPC group (p=0.005). Furthermore, patients with LPCs were more likely to complete postoperative treatment with a single catheter (70.8% vs. 38.5%, p=0.02). The rate of catheter failure was higher for PIVCs than for LPCs (65.4% vs. 29.2%, RR 2.2, p=0.01; 170 vs. 71.1 failures per 1000 catheter-days). Infiltration was the most common complication; 34.6% of PIVCs infiltrated compared to 4.7% of LPCs (RR 8.3, p=0.007). Parental satisfaction was higher for LPCs for all domains, although only 'Pain and discomfort due to IV access' (p=0.007) and 'Overall satisfaction' (p=0.02) were significant. The average cost of insertion (including theatre costs) was $97.50 AUD for PIVCs and $263.00 AUD for LPCs.

Conclusions

In children receiving surgery, intraoperative insertion of LPCs is a feasible and effective procedure. Preliminary results indicate superior outcomes in the LPC group. LPCs succeeded in reducing postoperative IV cannulations and the incidence of catheter failure. Patients also indicated a clear preference for the LPC.

Camilla Sophi Ramadhanti

The Role of Nox5 in the Akita Mouse Model of Diabetic Nephropathy

Prof Karin Jandeleit-Dahm
Dr Jay C Jha

Hi, my name is Camilla. I'm in my fourth year of medical school in Universitas Indonesia, and Honours year has been a new experience for me. Because I had such little lab work experiences before, having a lab-based research was quite challenging for me. But at the end I'm glad because I developed skills I needed for my future career. Also, I was really thankful because I met such interesting people who are in Honours program as well as having a supportive working environment in Department of Diabetes. For future Honours student, you will not regret taking Honours year because I think that's where you can really push yourself to overcome obstacles. Haha cheers!

ABSTRACT

Background

Diabetic nephropathy (DN) is one of the most common diabetic complication and the leading cause of end stage renal disease worldwide. DN development and progression is contributed by metabolic and hemodynamic changes, which inevitably increase the production of reactive oxygen species (ROS). NADPH oxidase is the major source of ROS in the kidney, with several Nox isoforms have been identified for their role in the progression of DN. Based on recent evidences, Nox5 expression is found to be upregulated in diabetes, suggesting its possible role in DN. However, Nox5 is expressed in humans, but not in rodents. Therefore, there is a paucity of data regarding its role in DN.

Aim

To investigate the role of Nox5 in the development and progression of DN using endothelial cell specific (using VEcadherin promoter) Nox5 transgenic Akita mice in the absence or presence of diabetes.

Method

Nox5 transgenic Akita mouse with Ins2 gene mutation was used to create spontaneous T1DM. After 10 weeks, urine and blood sample were collected for metabolic data and renal function measurement. Kidney tissues were collected and assessed for renal structural injury as well as gene and protein expression of pro inflammatory, pro fibrotic, and oxidative stress parameters.

Result & Conclusion

Metabolic parameters showed a decrease in body weight, elevated blood glucose and glycated haemoglobin, an increase in food and water intake as well as urine output in diabetic mice groups compared to the respective control groups, with no difference observed among the diabetic groups when subjected to Nox5 expression. Significant increase in albuminuria and expression of pro fibrotic and pro inflammatory genes (collagen III, fibronectin, ά-SMA) were observed in VEcad+Nox5+ groups compared to VEcad+Nox5- in the presence of diabetes. Nox5 expression selectively in endothelial cells worsen the renal function and upregulated the expression of pro-inflammatory and pro-fibrotic genes in the renal cortex of diabetic mice.

Greasha Rathnasekara

Contraceptive counselling in areas of high teenage pregnancy: a qualitative study of General Practitioner insights

Primary: Professor Danielle Mazza, Department of General Practice, School of Primary and Allied Health Care, Faculty of Medicine, Nursing and Health Sciences, Monash University

Secondary: Dr Cathy Watson, Department of General Practice, School of Primary and Allied Health Care, Faculty of Medicine, Nursing and Health Sciences, Monash University

I decided to undertake a BMedSc(Hons) after my fourth year and was fortunate enough to be able to complete my project at the Monash University Department of General Practice. I chose my project because it provided the opportunity to combine my interests of women's health and general practice.

During the year I have gained new skills in developing and carrying out qualitative research, a process much more complex than I had originally anticipated. It has been an enriching experience learning about the research process, and hear directly from GPs about their clinical practice and experiences.

The Department of General Practice has been a fantastic place to complete my project and I've had an influx of support since the beginning of the year. I would highly recommend anyone thinking about doing a BMedSc to do so, and qualitative research is interesting and manageable within the Honours year.

ABSTRACT

Background

Teenage pregnancy is associated with negative outcomes for both mother and child. While the rates of teenage pregnancy in Australia have declined, there are still areas of relative high-risk in Victoria. Effective contraception can prevent unintended pregnancies and general practitioners (GPs) are the first-line providers of prescription contraceptives. In high-risk areas for teenage pregnancy, GPs may face additional barriers accessing and providing contraceptive counselling to teenage women. The aim of this study is to explore GP insights into the provision of contraceptive counselling and to determine if GPs perceive any additional challenges when providing contraceptive counselling in the context of a high-risk area for teenage pregnancy.

Method

A qualitative study design was utilised for this project using a constructivist grounded theory approach. Semi-structured, in-depth telephone interviews were conducted with 18 GPs purposively sampled from high-risk local government areas as defined by the Victorian Women's Health Atlas. Interviews were transcribed verbatim and imported to NVivo 11 for management. An inductive and iterative data analysis approach was used to develop themes.

Results

We identified three major themes from the interviews. Firstly, GPs believed they provided best-standard care when delivering contraceptive counselling to teenagers; however, many did not offer all contraceptive options which may have impacted a teenager's ability to make an informed, empowered contraceptive choice. Secondly, most GPs recognised that the teenagers in their area were a vulnerable group and required targeted contraceptive counselling that also addressed wider social issues. There were additional challenges reported in engaging this group in contraceptive counselling as teenage women in high-risk areas were perceived to have a higher acceptability of teenage pregnancy. We found some GPs had limited understanding of the high-risk for teenage pregnancy in their local government area. Thirdly, GPs reported multiple structural and patient barriers to delivering contraceptive counselling. However there were also multiple GP biases, which can affect the delivery of best-standard contraceptive care and in particular, the recommendation of long-acting reversible contraceptives as a first-line option.

Conclusions

Our study explores GPs' insights into providing contraceptive counselling within high-risk regions for teenage pregnancy. GPs reported additional challenges at a patient and structural level and their own biases and misperceptions, which can be targeted with interventions to improve the standard of contraceptive counselling and potentially reduce teenage pregnancies. Our findings also suggest there is limited knowledge of the high-risk for teenage pregnancy amongst GPs in high-risk areas. Educating GPs to improve awareness of the high-risk for teenage pregnancy may improve the delivery of counselling and help target vulnerable teenagers.

Aisha Emilirosy Roekman

A Qualitative Analysis on the Perceived Barriers and Enablers to Falls Prevention Implementation in the Acute Hospital Setting

Dr Darshini Ayton

Health Service Research Unit, Division of Health Services,
Department of Epidemiology and Preventive Medicine,
Monash University, Melbourne, Australia.

It was my fourth year as a medical student of the University of Indonesia, where we need to take one-year research abroad, I chose Monash University. I chose this project because it is a common problem both in Indonesia and Australia, and many countries have tried developing their program implementation to solve this problem. Yet, even the largest falls prevention trial in the world, failed to prevent this incidence. Therefore, I decided to find out the factors that may involve in program failure. Throughout the Honours year, I gained a lot of knowledge regarding how to conduct a qualitative analysis, since this method is rarely used in Indonesia. I also had the best opportunity to work with my research team, where they created a supportive environment, constant support, and trained me to be a better researcher. Furthermore, I had the opportunity to present my project at an International (bio)Medical student congress, which I was fortunate to attend and gained new insights on amazing research that has been done around the world. I can say this one-year would be a life-changing experience for all the prospective students. If you have further questions regarding this Honours program, do not be hesitant to contact me (aishaeroekman@gmail.com)

ABSTRACT

Background

Studies examining the effectiveness of falls prevention programs have been the focus of research attention as falls remain the most common adverse event in the hospital setting. However, there is limited research exploring the barriers and enablers to the implementation of falls prevention programs. 6-PACK was a nurse-led falls prevention program implemented in six hospitals in Australia. The 6-PACK RCT was the world's largest falls prevention falls prevention trial. Unfortunately, the trial results demonstrated that 6-PACK did not reduce in-hospital falls. To understand the contextual factors impacting on the trial results, this study collected qualitative data from senior hospital staff and nurses post-implementation of the 6-PACK program.

Aim

To explore the perceived barriers, enablers, and sustainability factors to implementation of the 6-PACK program.

Method

Seven focus groups with nurses and 13 interviews with hospital senior staff. Data analysis was guided by the COM-B framework. This framework includes capability, opportunity, and motivation factors that interact to create behaviour change.

Results

Small hospital rooms, belief that falls were inevitable, privacy issues during bathroom supervision, insufficient staffing levels, lack of resources to implement 6-PACK strategies, ineffectiveness of 6-PACK facilities, and staff juggling multiple projects were identified as barriers to 6-PACK implementation. Enabling factors included one-on-one education during ward round, senior staff leadership and support, nurses' positive attitudes towards 6-PACK, provision of audit-feedback-reminder, and staff held accountable for program implementation. In order to sustain the program, the hospitals must continue ward-champion role as project leader, introduce 6-PACK to future nursing staff, provide on-going audit and feedback, encourage staff involvement in 6-PACK implementation, and adopt 6-PACK for hospital-wide implementation.

Conclusions

This study identifies the perceived barriers, enablers, and sustainability factors to falls prevention program implementation from the perspective of hospital staff. These results can be used in the design future falls prevention programs and implementation strategies.

Antonia Rowson

Single-cell RNA Sequencing to Understand Inflammatory Disease Mechanisms

Prof Alex Hewitt,
Department of Clinical Genetics, Centre for Eye Research Australia, East Melbourne, Victoria;
Menzies Institute, Hobart, Tasmania

A/Prof Christine Chen,
Department of Surgery, Monash Medical Centre, Clayton, Victoria

I wanted to gain more specialist ophthalmology exposure than I'd had as part of clinical medical placements, so I decided to do my honours year at the Royal Victorian Eye and Ear Hospital. I saw a lot of rare genetic conditions affecting the eye during my time there, as I'd hoped I would. I also got to spend a lot of time in Hobart, staying there for about two months this year as part of my research, and getting to know that lovely (if cold!) city. While my hours in Hobart were fairly long, my time in Melbourne was really flexible and I had a really relaxed year; if you are comfortable dictating your own project and having a more laid-back supervisor, I can definitely recommend my supervisor Alex. Honours year is both liberating and challenging, but regardless of what you do in it you can be sure of two things; you won't get as much done as you initially expect, and you will learn a lot of new skills.

ABSTRACT

Background

The pathophysiology driving inflammatory diseases such as giant cell arteritis (GCA) is incompletely understood, preventing the development of targeted therapies. As such, glucocorticoids and other non-specific anti-inflammatory medications are the principal treatments for many inflammatory conditions, with a host of subsequent adverse effects. Single-cell RNA sequencing (scRNA-seq) provides a means of characterising the activity levels of every gene within a cell. Hence, scRNA-seq offers an unparalleled means of asserting the specific contribution of each gene to a pathological cellular state, instead of merely documenting correlations between specific alleles and disease states. We aimed to compare the gene expression profiles of individuals with systemic inflammatory disease with individuals of non-inflammatory phenotype via scRNA-seq in a Caucasian population.

Methods

1,010 participants provided demographic data on sex, age, gender, smoking status, and ethnicity, and gave a peripheral blood sample. After initial scRNA-seq preparation and assessment of cell count and viability, samples were outsourced for further genomic and scRNA-seq analysis; this analysis is still ongoing. Meanwhile, data was retrieved from medical records available for 550 participants regarding health status and medications. A sub-group of 45 individuals with systemic inflammatory disease was identified, and demographic details of this group were compared with the rest of the cohort. A temporal artery tissue sample was taken from one patient with GCA, in addition to a blood sample, and enzyme dissociation of this temporal artery tissue was attempted as an initial step in comparative analysis of cells from the temporal artery and peripheral blood cells.

Results

Of the non-inflammatory cohort of participants, mean age was 63.55 years, and 42.90% were male. Of the inflammatory sub-group, mean age was 70.84 years, and 35.56% were male. Age was statistically significant between the two groups ($p = 0.0036$), and conformed to a normal distribution. There was no significant difference between groups with regard to sex ($p = 0.3583$) or smoking status ($p = 0.3945$). Following scRNA-seq preparation, peripheral blood mononuclear cell samples of the non-inflammatory cohort yielded on average 3.452 x 106 cells each, with a mean 91.86% of cells viable. Mean cell count of the inflammatory group was 3.703 x 106 , with average viability of 91.82%. Neither cohort was significantly different by these two outcomes ($p = 0.6306$ for cell count, $p = 0.7920$ for viability). Temporal arterial tissue dissociation was unsuccessful, with a cell count of 1.23 x 105 and 0% viability.

Conclusion

As genomic and scRNA-seq data is as yet unavailable, we are currently unable to assess the aims of our study. However, consideration of demographic data allows us to posit the validity of the awaited study results. Based upon normal distribution of age and relative similarity with other demographic factors of the Australian population generally, the study cohort is likely a fairly representative sample from which to draw conclusions about normal cellular gene expression, and the similarity between the inflammatory and non-inflammatory subgroups, except as regards mean age, also suggest a fair basis for comparison.

Saskia Rowson

Improving the prediction and diagnosis of pre-eclampsia: validation of a novel biomarker assay

Dr Kirsten Palmer[a,b], Professor Euan Wallace[a,b]

a Department of Obstetrics and Gynaecology, Monash Medical Centre, Clayton, Victoria.

b The Ritchie Centre, Hudson Institute of Medical Research, Clayton, Victoria.

I completed fourth year in 2017, and thought a BMedSci would be a good change of pace from clinical medicine. I chose an Obstetric clinical/lab project mainly because of how much I enjoyed O&G last year.

It's been a fantastic year, but if you do something lab-based it can be a very different skill set, so you've got to be prepared to learn new things and work quite hard, depending on the demands of the project. That said, the Ritchie Centre is a great place to do a lab-based project, because there are lots of other students working there who will help and support you. Also, if you don't know something in the lab, Googling it works more often than not from personal experience.

Your supervisor and team are very important, and I was incredibly lucky in mine. If you're unsure whether or not you want to do one, my advice would be to go for it.

ABSTRACT

Background

Pre-eclampsia is a heterogeneous clinical syndrome of pregnancy with a high maternal and fetal morbidity and mortality. Recent gains in our understanding of the pathophysiology of pre-eclampsia indicate that the pathogenesis of disease is complex and multifactorial. However, a common feature of the various pathogenetic streams is the tendency towards an anti-angiogenic imbalance, with resultant endothelial dysfunction causing the clinical manifestation of disease. Currently, there is a limited clinical capacity to predict pre-eclampsia. This anti-angiogenic imbalance provides plausible targets for pre-eclampsia prediction and diagnosis. For this reason, technologies to accurately measure recently-characterised serum biomarkers, soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF), are becoming increasingly commercially available. However, the ability to refine these biomarker tests further may be possible with sFlt-1 e15a, a placental-specific variant of sFlt-1 that is as yet untested in a large population.

Aim

To establish the test capabilities of serum biomarkers sFlt-1, PlGF, sFlt-1 e15a and their ratios in the prediction and diagnosis of pre-eclampsia.

Methods

I recruited pregnant women in two cohorts: longitudinal and diagnostic. The former accrued 4-5 blood collections across pregnancy at specific gestational windows, while the latter gave a single blood collection at the time of clinical investigation for suspected pre-eclampsia. These samples were collected and stored at -80°C until processing. To analyse the serum sFlt-1 and PlGF levels, I utilised automated BRAHMS Kryptor compact PLUS immunoassay technology. To analyse the levels of serum sFlt-1 e15a, I performed enzyme-linked immunosorbent assays (ELISAs) using an sFlt-1 e15a antibody developed in-house.

Results

In the longitudinal cohort, sFlt-1, total sFlt-1:PlGF and sFlt-1 e15a all showed significant differences between those who would develop pre-eclampsia and those who would not at particular gestational windows. However, our analyses were limited by low numbers of pre-eclamptic women in this group and lack of severe disease. In the diagnostic cohort, there were significant differences in levels of sFlt-1, PlGF, total sFlt-1:PlGF, sFlt-1 e15a and sFlt-1 e15a:PlGF in those with pre-eclampsia compared to those without. sFlt-1 e15a in particular discriminated well in this group, with a positive likelihood ratio of pre-eclampsia of 7.88 for those with an sFlt-1 e15a greater than 803.704 ng/mL.

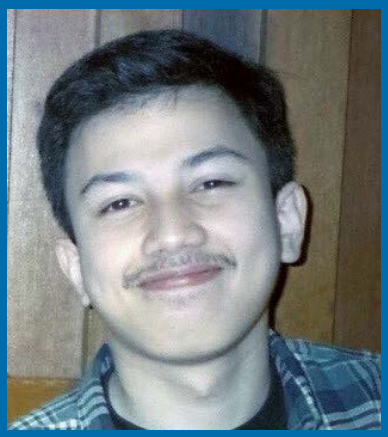
Conclusion

Serum biomarkers are an emerging force in the prediction and diagnosis of pre-eclampsia. It appears that automated platforms, such as the Kryptor, offer a reliable aid to pre-eclampsia detection. Our research suggests that sFlt-1 e15a could improve even further on existing commercialised biomarkers, especially in a diagnostic capacity for early-onset pre-eclampsia. Its ability to predict disease requires further investigation, but nevertheless sFlt-1 e15a offers exciting potential.

Wildan Iman Santoso

Comorbidities of Chronic Heart Failure in Australians Managed in the Primary Care Setting

Dr Alice J Owen, Dr Tom Hird and Dr Enayet Chowdhury, CCRET, SPHPM



Hi, I am Wildan Iman Santoso, 4th year medical student in Faculty of Medicine University of Indonesia. I had my honours project in Centre of Cardiovascular Research and Education in Therapeutics, School of Public Health and Preventive Medicine under supervision of Dr Alice J Owen, Dr Tom Hird and Dr Enayet Chowdhury. I enjoy this BMedSci year because I got a lot of new experience and new knowledge which I think will be very useful for my clinical year in Indonesia. Don't worry doing research will be hard at the beginning, but it will be easier when you keep working on it.

ABSTRACT

Background

Heart Failure (HF) is a complex clinical syndrome characterized by the reduced ability of the heart to pump blood to complete the needs of the body. In this study we will focus on chronic heart failure and defined HF as chronic heart failure. HF is associated with multiple comorbidities that leads to or may affect the development of HF and the patients' outcome. Moreover, comorbidities also appear as an important determinant of health care cost. Although there are a number of studies on the prevalence and incidence of HF, however relatively few studies have described data on common comorbidities in HF patients, particularly in the Australian primary health care setting.

Method

This study used a cross-sectional study design. Data was obtained clinical practice software of n=676 GPs from across all states and territories of Australia pertaining to their patients with HF treated in the period 2011-2016. De-identified patient information regarding age, sex, risk factors and comorbidities was obtained for patients recorded as having HF.

Results

This study found that hypertension is the most common comorbidity (33.1%) among nine selected comorbidities (i.e. hypertension, arthritis, diabetes, hyperlipidaemia, renal disease, depression, chronic obstructive pulmonary disease (COPD), anaemia, and chronic pain) and most common across all age groups in 7093 HF patients ranging in age from 18-115 years. Significant gender difference were found for arthritis, diabetes, renal disease, COPD, depression and chronic pain ($p<0.01$). Further, significant differences between age groups were observed for proportions of patients with arthritis, renal disease and COPD. We also found that hypertension and arthritis is the most common comorbidity pairs in our study. Increasing number of GP visits were observed with comorbidity burden ranging from an annual average of 17 visits for those with two comorbidities up to an annual average of 24 visits for more than five comorbidities.

Conclusions

Management strategy for HF patients with comorbidities in Australian primary setting should be considered particularly for HF patients with hypertension and HF patients with hypertension and arthritis.

Eugene Alfathan Satryo

IDENTIFICATION OF PREDICTORS OF CRITICAL BLEEDING IN CARDIOTHORACIC SURGERY PATIENTS AND VARIATIONS IN PATIENT BLOOD MANAGEMENT

Australian and New Zealand Massive Transfusion Registry and Australia and New Zealand Society of Cardiac and Thoracic Surgeons Cardiac Surgery Database Data Linkage

Dr Rosemary Sparrow[1], Assoc. Prof. Erica Wood[1]
Dr Lavinia Tran[2], Dr Jenni Williams-Spence[2], Prof. Christopher Reid[2]
Transfusion Research Unit[1], Centre of Cardiovascular Research and Education in Therapeutics[2]

My name is Eugene and I am currently a 4th year medical student given the opportunity to do research abroad here in Monash University. I'm doing my research with the Transfusion Research Unit and Centre of Cardiovascular Research and Education in Therapeutics. My research project is about prediction of critical bleeding in cardiothoracic surgery and I chose that specific project because emergency medicine is interesting and I have prior experience with biostatistics.

I have learned many things during my time in the School of Public Health and Preventive Medicine, such as the proper process in making predictive models and new skills and knowledge in research and biostatistics in general (which will no doubt be useful in the future), and other things such as being aware of medical issues and subjects from the weekly available talks and presentations at the Alfred and SPHPM.

Melbourne is also a very nice place to live in. Everything is convenient and the people are very friendly. Tips include making sure to space out your time appropriately so you can have fun and relax in the busy year, and don't forget to set deadlines for yourself that can be accountable (which gives you the extra drive to get your work done).

ABSTRACT

Introduction

One Australian dies every 12 minutes due to cardiovascular disease (CVD). Cardiothoracic surgery (CTS) is a common intervention for treating serious CVD. Critical bleeding (CB), which necessitates massive transfusion (MT), is one of many risks of CTS. A study on prediction of CB/MT, using the MT definition of ≥5 RBC units transfused in any 4 hours, with an Australian CTS cohort has not been done. The aims of the project were to identify: 1) patient or procedure variables that can predict CB in CTS, and 2) variations indicative of differences between hospitals in perioperative patient blood management (PBM) and transfusion strategies by conducting a data linkage with the ANZ-MTR and ANZSCTS databases.

Methods

Inclusion criteria for the total cohort were: patient ≥18 years of age at time of CTS, underwent CTS indicated by ACHI procedure codes, data came from hospitals participating in both ANZ-MTR and ANZSCTS databases. Test cohort (MT patients) were CTS patients listed in ANZ-MTR (received MT). Control cohort (non-MT patients) were CTS patients not listed in the ANZ-MTR, but from the same sites and same timeframe. Final MT cohort consisted of 565 CB/MT cases from 11 sites between January 2011 to December 2017; and final non-MT with 29,010 cases. Initial variables were chosen based on statistical significance of univariate analysis (significant at $p<0.001$). The final model used binomial logistic regression. The model was adjusted for site and year of procedure. Statistical significance for categorical variables was determined by the Chi-Square test and the Mann Whitney U test for continuous variables. P-value <0.001 was considered statistically significant for difference between sites and $p<0.05$ for difference between cohorts within sites.

Results

Patient-related factors predisposing to CB were: lower Body Surface Area (OR 0.38); infective endocarditis at presentation (OR 2.96); worse heart failure, classified as NYHA class IV (OR 1.78); Increased number of diseased vessels (OR 1.24); lower renal function based on eGFR (OR 0.986) (all $p<0.001$).

Procedural factors included in the model were having aortic procedures (OR 2.83, $p<0.001$); using Cardiopulmonary Bypass (CPB) (OR 2.52, $p=0.003$), and having more complex procedures (i.e. Valve surgery, Valve+CABG surgery, and Other CTS) (OR 2.4, 2.11, 2.15 respectively, $p<0.001$) and any increased urgency of procedure (reflecting patient status and readiness of the surgery team), (OR 2.100(urgent), 2.888(emergency), 8.455(salvage); $p<0.001$).

Variation between sites was significant for all variables included in the model with indication of significant differences within the sites between MT and non-MT cohorts.

Conclusions

Patient and procedural factors can predict for CB/MT for the population used in this study; patient characteristics and comorbidities appear to be the most important factors that affect rate of CB/MT; mostly impacting complexity and length of procedure and not many of them are modifiable by the surgeon. Variation was apparent between sites, but insufficient data was available to assess differences, if any, in PBM and transfusion strategies. Aims of this project were achieved; but variation due to perioperative blood management could only be partly proven and will require more detailed PBM-related data to be made available.

Sameer Sharma

Treatment Initiation Decisions in Newly Diagnosed Epilepsy

Professor Patrick Kwan and Dr Zhibin Chen
Department of Neurosciences, Central Clinical School, Monash University, Alfred Hospital, VIC;
Department of Medicine, The University of Melbourne, Royal Melbourne Hospital, VIC;
School of Public Health and Preventive Medicine, Monash University, VIC;

In medical school, I was always interested in neurology, but never had the time or incentive to delve into its details. Doing a BMedSc (Hons) after 4th year was my opportunity to spend time formally developing research skills, but also to try to gain expertise in a topic of personal interest and work towards analysing problems greater than the patient in front of me.

Apart from looking into treatment decisions in newly diagnosed epilepsy patients, I also involved myself in research assessing their prognosis and pharmacotherapeutic options, as well smaller projects in neuropsychiatry and neurosurgery. I have a richer appreciation of the breadth of research opportunities, and their utility in optimising our clinical acumen and skills as well as future career prospects. I also gained many research skills, particularly revolving around clinical- or data-based projects and their design. I've additionally grew in my understanding of practical biostatistics, while simultaneously maintained my clinical learning via ward rounds and outpatient clinics.

A BMedSc (Hons) is an investment that can be rewarding, but really does require an interest in the field, research in general, and the perseverance to work on the same project for most of a year.

ABSTRACT

Background

Epilepsy is a serious chronic neurological disease characterised by an enduring predisposition to seizures. Up to 90% of people with epilepsy living in resource-poor countries do not receive antiepileptic drug (AED) therapy. This phenomenon is described as the "treatment gap" and is generally attributed to socioeconomic reasons. However, there has been scant study of this phenomenon in resource-rich specialised setting and the reasons for patients not receiving treatment is not well understood.

The objective of this thesis is firstly to evaluate the scale of untreated epilepsy in a cohort with newly diagnosed epilepsy. Secondly, to examine the risk factors associated with not being treated with AEDs at diagnosis, and finally, understand the individual reasons why patients did not commence with treatment.

Method

Adult patients seen at hospital-based First Seizure and Neurology Clinics for evaluation and management of seizures between 1 May 1999 and 31 May 2016 were screened. Patients with epilepsy diagnosed by the managing neurologist were identified and had their medical records reviewed. Reasons for not being treated and eventually commencing therapy if applicable were captured. Factors that influenced the likelihood of treatment initiation were statistically assessed via penalised logistic regression models.

Results

Of 1317 patients presenting with one or more unprovoked seizures, 611 were diagnosed with epilepsy (61% male; median age at diagnosis: 40 years [IQR: 24-57]). 421 (69%) commenced AEDs at diagnosis. During follow-up (median 5.6 years, IQR: 1.8-8.9), 118 (19%) subsequently commenced AEDs, while 72 (12%) remained untreated by the end of follow-up.

Patients treated at diagnosis were older (OR=1.02, 95% CI: 1.01-1.03) and had lower socio-economic status (OR=0.42 95% CI: 0.18-0.98) compared to those who commenced treatment at diagnosis. An epileptogenic lesion on neuroimaging (OR=1.95 95% CI: 1.16-3.27) and a greater number of seizures prior to diagnosis (OR=2.63 95% CI: 1.39-4.97) were associated with treatment initiation at diagnosis. Among the 427 patients who had more than one pre-diagnosis seizure, those having at least one seizure per year were more likely to be treated compared to those with less than one seizure per year (OR=5.15, 95% CI: 2.53-10.47). Epilepsy type, seizure type, the sleep/awake status when seizures occurred, and epileptiform electroencephalogram were not associated with treatment initiation.

At diagnosis, 101 (17%) patients were not offered treatment, and 89 (15%) declined treatment. The most common reasons for patients not being offered treatment were having had only a single seizure (30% of 101), pending further investigations (29%), and presence of seizure precipitants (22%). The most common reasons for patients declining therapy were unconvinced of the necessity of treatment (48% of 89), unconvinced of the diagnosis (17%), and presence of seizure precipitants (13%).

Conclusions

More than 30% of adult patients with newly diagnosed epilepsy had delayed or no AED treatment initiation. Decision making in this patient population is complex and influenced by physician-, patient-, and disease-related factors. Further study is needed to understand the variables contributing to the non-treatment of patients with epilepsy when AEDs are available, and the clinical and health economic consequences of this.

Nishat Siddique

The role of Grhl3 in oesophageal barrier function

Dr Smitha Rose Georgy, Professor Stephen Jane
Department of Medicine, Alfred Hospital, Monash University

Like most people, I undertook a BMedSc(Hons) after 4th year, mainly because I hadn't done any research up until that point and was eager to see what it was like. I also thought it presented a unique opportunity to try lab-based research.

This year was full of ups and downs for me. Getting used to lab work and trying to master various techniques was definitely a challenge at the start of the year, but an enjoyable one. I learnt a huge variety of skills throughout the course of this year and I think it has enabled me to be more confident when approaching research in my future career. I have a particular soft spot for science research now, as I think it is where the most exciting discoveries are made.

Doing a BMedSc(Hons) definitely wasn't a year off for me, but it has been a very interesting break from medicine, and I think I have developed a much deeper understanding of the molecular basis of diseases. I've also made a lot of valuable friends and colleagues along the way, who I'm sure I'll keep in touch with for years to come. All in all, it was a stressful but fun year which I am glad I signed up for.

ABSTRACT

Background

Barrett's oesophagus (BO) is a metaplasia of the oesophageal epithelium and has been strongly linked to development of adenocarcinoma. It is a response to epithelial damage from gastro-oesophageal reflux. Barrier defects resulting from this unfavourable environment predispose the oesophagus to inflammation, metaplasia and dysplasia. However, the underlying genetic drivers of this condition remain unclear. As such, there is a lack of diagnostic biomarkers for Barrett's oesophagus. Grainyhead-like 3 (Grhl3) is a transcription factor from an ancient gene family which is crucial for the development of epithelial barriers. Grhl3 loss is associated with defective barriers in utero and predisposition to tumorigenesis in postnatal life. Our study is the first to investigate the role of Grhl3 in postnatal oesophageal epithelium.

Methods

Using conditional knockout mice, $Grhl3^{\Delta/-}$ L2-cre/+, we studied the effect of Grhl3 deletion in mice ranging from 6 to 12 months of age. We developed a novel barrier permeability experimental model, which involved the injection of fluorescent dye into the oesophageal lumen. Oesophagi were later imaged in cross-section to view the depth of barrier penetration. Furthermore, we examined the squamocolumnar junction in these mice with Haematoxylin and Eosin, Alcian Blue and proliferation markers to identify any metaplastic changes. Lastly, we reviewed the regulation of a series of putative barrier genes using immunohistochemistry and qPCR.

Results

Though Grhl3 does not cause an increase in oesophageal paracellular permeability, it likely causes abnormalities in the keratinised layer. Conditional knockout (CKO) mice are more likely to have an expanded gastric cardia region, which may be a precursor to metaplasia. Additionally, several putative barrier genes were significantly downregulated in the oesophageal epithelium of CKO mice, including Hrnr, Vstm5, Sprr2k with Krt10 being significantly upregulated.

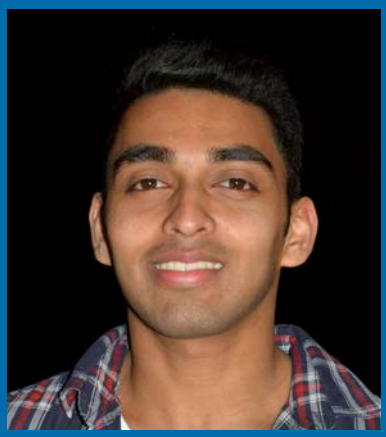
Conclusion

Despite intact barrier function, Grhl3 loss likely causes abnormalities of the stratum corneum, consistent with other literature. Grhl3 also may lead to impaired wound-healing in the adult oesophagus and increased metaplastic potential. Future research with similar experiments should be conducted in a reflux model to instigate barrier defects and see if there is impaired tissue repair in CKO mice. This will enable us to further understand the role that Grhl3 has in this tissue and increase knowledge of the pathogenesis of oesophageal metaplasia. One day, Grhl3 may serve as a diagnostic biomarker to improve diagnostic certainty in the context of Barrett's oesophagus.

Leon Siriwardhana

Control of respiration in children with sleep disordered breathing

Professor Rosemary Horne[1,2], Dr Lisa Walter[1,2]
[1] The Ritchie Centre, Hudson Institute of Medical Research
[2] Department of paediatrics, Monash University



I chose to undertake a BMedSc(Hons) after completing my fourth year of medicine. I have always been intrigued by sleep and decided to combine this with my interest in paediatrics to undertake my honours year at The Ritchie Centre. This year offered me an incredible opportunity to gain valuable insight into the world of research and I thoroughly enjoyed my project, especially attending overnight sleep studies and learning about sleep in children.

I was privileged to benefit from the guidance and mentorship of two highly experienced supervisors; Professor Rosemary Horne and Dr Lisa Walter. Under their patient and dedicated tutelage, I was able to develop a range of highly transferrable skills that will no doubt benefit in my future career. I would highly encourage anyone with an interest in research to consider a BMedSc(Hons).

ABSTRACT

Background

Sleep disordered breathing (SDB) is a common sleep disorder in children. It represents a spectrum of severity from primary snoring to obstructive sleep apnoea (OSA) and has been associated with a number of long-term cardiovascular and neurocognitive sequela. SDB in children is caused by an anatomically compromised airway, usually as a result of adenotonsillar hypertrophy. However, there is significant variance in the degree of anatomical susceptibility to airway collapse among children with SDB, suggesting non-anatomical factors may contribute to its development. Instability of the ventilatory control system (high loop gain (LG)) has been postulated as a possible pathophysiological mechanism in adults with OSA. This study aimed to explore the role of ventilatory control instability in children with SDB.

Methods

One hundred and ten children (3-18 years) with SBD and 36 non-snoring controls were studied retrospectively. All children had undergone polysomnography at the Melbourne Children's Sleep Centre and the scored polysomnography data were obtained for the selected children. Ventilatory control instability was assessed using LG, a measure of the sensitivity of the negative feedback loop that control ventilation. LG was calculated using standard polysomnography data by first identifying spontaneous sighs that occured in periods of non-rapid eye movement (NREM) sleep using the nasal pressure trace. A standard model of ventilatory control (gain, time-constant, delay) was then fitted to the post-sigh ventilatory pattern to calculate LG. SDB children were grouped according their obstructive apnoea-hypopnoea index (OAHI): primary snoring (<1 event/h), mild OSA (1-5 events/h) and moderate/severe OSA (>5 events/h). Control children all had an OAHI <1 event/h and no history of snoring.

Results

Groups were matched for age, sex and BMI Z-score. There was no significant difference in LG between the control and SDB severity groups. LG showed no significant relationship to the severity of SDB, although an unexpected downward trend in LG was observed across the groups. A large variance in LG was also observed in all groups. Demographic characteristics and anthropometric measures including age, sex, BMI Z-score, neck circumference, waist circumference, neck-to-waist ratio all showed no significant correlations with LG. However, LG was significantly higher in children with a Mallamapti score (estimate of oropharyngeal patency) of class I compared with classes III/IV (median LG [range]: 0.37[0.27, 0.44] vs. 0.28[0.24, 0.33]; p=0.028). LG was also higher in children with smaller tonsil size (tonsil grade 0/1) compared with children with larger tonsils (tonsil grade 4) (0.32[0.25, 0.44] vs. 0.25[0.20, 0.42]; p=0.009).

Conclusion

This study found no direct relationship between ventilatory control instability measured using LG and SDB in children. This suggests that different mechanisms of ventilatory control are involved in the pathophysiology of SDB in children compared with adults. LG as a tool to conceptualize the stability of the ventilatory control system is still evolving. Further research is needed obtain a more comprehensive understanding of the role of ventilatory control in the pathophysiology of SDB in children and its therapeutic implications.

Caitlin Smart

The Influence of Tissue-type Plasminogen Activator on Synaptic Plasticity in the Auditory Cortex

Prof Alexander Thiele – Institute of Neuroscience, Newcastle University, UK
Prof Robert Medcalf – Australian Centre for Blood Diseases, Monash University, AUS

I was on 3rd year placement in Mildura, when I first contacted my soon-to-be supervisor, Rob, about an interesting project in Melbourne. The project seemed like a good fit, until I learnt of a similar project, this time in the brain, at Newcastle University in the UK.

Of course, my interest in the complexity of the brain, as well as my love of travel and leaving my comfort zone meant that by the end of 2017, my bags were packed, and I was off to the heart of Geordie-land, Newcastle upon Tyne in the North East of England (with a stop in Uganda and Spain along the way).

From the moment I set foot in England everything was new, I'd never lived in a place where snow was more common than sunshine, I'd never done any research in my life, I hadn't even held a mouse before, let alone collected data from its brain.

Hence, 2018 has been a huge year of personal and professional growth, I learnt an incredible amount, not only about my project, but about research and academia, and of course the UK! I had a wonderful year, and I would do it again in a heartbeat!

ABSTRACT

Background

The serine protease tissue-type plasminogen activator (tPA) is known for its classical role as a clot busting enzyme in the bloodstream. This role has extended to the brain where tPA is the only thrombolytic agent approved for use in humans, during ischaemic stroke. Many further functions of tPA in the brain – both beneficial and detrimental – have been discovered in recent years, including a role in synaptic plasticity. tPA is suspected to facilitate synaptic plasticity through plasminogen-dependent (plasmin-mediated brain-derived neurotrophic factor activation) and independently through its actions on N-methyl-D-aspartate receptor and low-density lipoprotein-receptor related protein – exact mechanisms are unknown. The influence on tPA on synaptic plasticity has been demonstrated in vitro in the hippocampus, and in vivo in the visual cortex. Here we investigated its role in synaptic plasticity in the mouse auditory cortex. Synaptic plasticity is lifelong in the auditory cortex and experience-dependent plasticity has been evoked by the application of other synaptic modulators, such as noradrenaline and acetylcholine in the past. These studies have demonstrated changes in the best frequency of neurons, the frequency that elicits the biggest response, and neuronal bandwidth, the range of frequencies to which the neurons respond.

Aim

To determine if exogenous tPA can influence the tuning of neurons in the auditory cortex, when paired with an auditory stimulus.

Methods

Intracranial injection of exogenous tPA or control substance into the auditory cortex under anaesthesia was paired with the presentation of a single-frequency auditory stimulus – conditioned frequency – in awake mice, to assess if tPA or choice of conditioned frequency being higher (higher pairing) or lower (lower pairing) than the neurons best frequency could influence the tuning of neurons, which would be indicative of synaptic plasticity. Electrophysiological recordings were used to determine the tuning of neurons before and after conditioning, to demonstrate changes in neuronal response, including best frequency and neuronal bandwidth.

Results

tPA application under higher pairing significantly influenced the tuning of neurons, causing a best frequency shift away from the conditioned frequency ($p<0.001$), whilst the inverse effect of a shift towards the conditioned frequency was produced in the tPA lower pairing condition ($p=0.024$). tPA also significantly influenced the strength of the response to the post-conditioning best frequency, relative to the pre-conditioning best frequency, but only in the higher pairing condition ($p=0.002$). Changes in the tuning of neurons were also attributed to pairing choice in control conditions, namely when higher pairing was employed. However, these results showed the opposite pattern as the tPA condition, with significant best frequency shifts towards the conditioned frequency.

Conclusions

The known synaptic modulator tPA is capable of producing changes in the tuning of neurons of the auditory cortex, indicative of synaptic plasticity that have not previously been described. These changes appear to be stimulus-dependent, as tPA application produced opposite effects dependent on whether the frequency chosen for conditioning was higher or lower than the best frequency of the neurons. This effect has not been previously described, and the mechanism by which tPA produced these effects is unclear.

Zheng Song

Personalised approach to the treatment of subfertility: a cohort study

Ben Mol
Beverley Vollenhoven
Monash Health Department of Obstetrics and Gynaecology

I decided to do a BmedSc(Hons) after my 4th year of medical school as I was keen to get a taste of research and a deeper understanding of how it contributes to clinical medicine. It was a very interesting and unexpected year with a lot of opportunities for personal growth and self-discoveries. I was really lucky to have encountered people from my clinical school who were extremely understanding and patient and kept me engaged and motivated even in times when things were not going smoothly. I will always be grateful to these people and this year will definitely be one that I will remember for the rest of my life.

Please feel free to contact me if you have any questions. Email: zson23@student.monash.edu

ABSTRACT

Background

The use of in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI) has increased significantly over the last decade in Australia and worldwide and its indications have expanded to include nearly all types of subfertility. We aim to determine whether patients' diagnostic categories and a simple prognostic algorithm could be used to discriminate between couples that would benefit from immediate ART and couples in whom ART could be delayed.

Methods

We performed a retrospective cohort study of couples consulting an Adelaide fertility clinic in the year 2012. We included heterosexual couples seeking conception with their own gametes. Couples who returned for treatment after a previously successful treatment, couples who were referred for treatment following diagnostic testing at another fertility clinic and couples seeking preimplantation screening and diagnosis were excluded.

Couples were classified into groups according to diagnosis and their likelihood of natural conception based on female age, duration of infertility, previous pregnancies, semen motility and whether they were referred to the clinic by a gynaecologist or a general practitioner. Kaplan Meier Survival Curves were constructed for each group showing the cumulative pregnancy and live birth rates with treatment effect as well as after censored at the start of fertility treatment.

Results

We studied 513 couples. There were 60 couples with an absolute indication for In Vitro Fertilisation (IVF)/intracytoplasmic sperm injection (ICSI). There were 117 couples with anovulation, for whom assisted reproductive treatment (ART) is likely to be required but treatments less invasive than IVF/ICSI may suffice. In 59 couples, the woman was aged 39 years and above. Out of the remaining couples, 33 were excluded, as their prognosis could not be calculated due to missing data. Out of the couples for whom prognosis of spontaneous pregnancy was calculated, 87 had a good prognosis (more than 40% chance of achieving a spontaneous pregnancy leading to live birth within the next 12 months), 70 had moderate prognosis (30-40% inclusively) and 87 had poor prognosis (below 30%). Fertility treatments were highly beneficial for couples with an absolute indication for IVF, couples where the woman was older and couples with a poor prognosis. However, the value of fertility treatments was limited in couples with a good prognosis. The value of IVF/ICSI was similar to that of less invasive treatments, such as ovulation induction, for couples with anovulation.

Conclusion

Individual diagnostic and demographic characteristics of couples could be used to personalise fertility treatment decisions and optimise the use of assisted reproductive treatment without compromising pregnancy chances.

Sophie Suke

Life Found in the Red Sea? Are endometrial stem/progenitor cells detectable in menstrual blood using a single novel marker?

Professor Caroline Gargett of the Ritchie Centre, and
Dr Jemma Evans of the Hudson Institute of Medical Research

When I was little, I wanted to spend my life researching dragons and breed a loyal legion of fire-breathing monstrosities with which I could conquer the playground. Then I found out dragons weren't real and settled for studying medicine. Many years passed but the thirst to delve into the world of research remained unquenched, and after completing my fourth year of medicine, I was itching to try my hand at something different. A BMedSc(Hons) seemed like the perfect opportunity.

I jumped headfirst into the unknown by exploring the baseline characteristics of menstruation, a topic in serious need of thorough investigation and almost limitless clinical potential from gynaecological prognostic/diagnostic testing (e.g. endometriosis) to a non-invasive source of adult stem cells. Having no prior lab work experience, I sure learnt a lot this year including optimising tissue processing protocols, performing intricate flow cytometry analyses, and improving my critical thinking and investigative skills to gain a better understanding of medical research

This year has been unexpectedly delightful, especially when learn about all the fantastic new developments being performed across multiple research centres by my fellow students. For any potential BMedSc students wanting more of my ramblings, feel free to message me at sgsu1@student.monash.edu

ABSTRACT

Background

Menstrual blood is an untapped, naturally occurring resource that may reflect female reproductive health and be a potential source of adult stem cells. In this project I aimed to characterise the baseline variation of endometrial stem/progenitor cell shedding in menstrual blood across menstrual cycles and between regularly menstruating women. Novel endometrial stem/progenitor cell surface markers, SUSD2 and N-cadherin, were used to identify endometrial mesenchymal stem cells and endometrial epithelial progenitor cells, respectively.

Method

Seven menstrual blood samples were collected from three women with regular menstrual cycles. Samples were processed through a combination of mechanical shearing and enzymatic digestion. Red blood cells were removed via Ficoll Paque density gradient separation and application of a red blood cell lysis buffer. Both fluorescence activated cell sorting and CD45 magnetic bead sorting were trialed to enriched samples for CD45 endometrial cells before samples were analysed by flow cytometry and cultured to assess clonogenicity. Menstrual blood processing was optimised to generate a reproducible protocol, including performing mechanical shearing and enzymatic digestion to break down blood clots, mucus, and tissue fragments, red blood cell removal via an ammonium chloride-based lysis buffer, and CD45 magnetic bead sorting to remove leukocytes before culturing and flow cytometry.

Results

Performing either CD45 magnetic bead sorting or FACS yielded a higher cloning efficiency of the single cell suspension than culturing all menstrual blood-derived cells (3.87% vs. 0.60% and 17.8% vs. 1.27%, respectively), however CD45 magnetic bead sorting proved more practical than FACS. Between 1.0% and 7.1% of $CD45^-$ cells in each menstrual blood sample were $SUSD2^+$ cells with a median value of 5.4%. The percentage of $SUSD2^+$ cells appears to vary between cycles and women, although this was not statistically significant. N-cadherin+ cells were detected in 5 of 7 samples with varying degrees of certainty. The median percentage of $N\text{-cadherin}^+$ cells was 0.06% (range of 0% - 3.0%) with no significant variation between cycles or participants (p=0.4). While the clonogenicity of menstrual blood-derived cells was inversely associated with the percentage of $SUSD2^+$ cells found in each sample (R2=0.3427, p=0.4146), more samples are required to draw this conclusion.

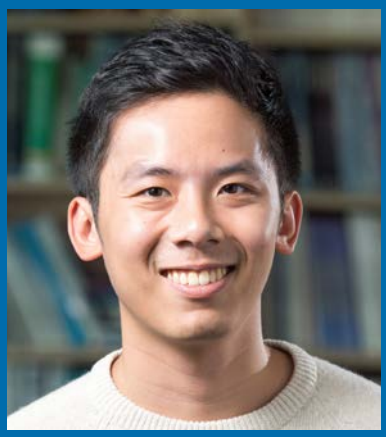
Conclusions

$SUSD2^+$ cells are detectible in menstrual blood and may vary between participants and cycles. Identifying $SUSD2^+$ cells may aid in the detection and isolation of endometrial mesenchymal stem cells in menstrual blood. This research could lead to the development of non-invasive prognostic tests, using menstrual blood to assess for obstetric and gynaecological conditions like endometriosis and female infertility.

Jed Tan

Does sildenafil citrate reduce damage to the developing fetal grey matter and hippocampus in fetal growth restriction

Supervisor: Dr Beth Allison
Co-supervisor: A/Prof Suzanne Miller
Institute Affiliations: The Ritchie Centre, Hudson Institute of Medical Research; Southern Clinical School



I decided to undertake a lab-based BMedSc(Hons) in feto-maternal medicine after my fourth year. Our women's health rotation kindled my interest in this field and prompted me to pursue a project with The Ritchie Centre. The successful undertaking of my project would not have been possible without my amazing supervisors and lab group who patiently guided me throughout the year.

Naturally a lab-based BMedSc(Hons) project is not an easy task. The steep learning curves and self-directed learning by trial-and-error are some of the main challenges I faced. My word of advice is to first, find a well-established project and supervisors that are willing to guide you. Secondly, although there are times when you encounter obstacles and self-doubt, you are not alone! Never give up and don't be afraid to seek help from your colleagues. Lastly, one year flies by really quickly so take initiative and work hard, but always remember to take a break!

I really enjoyed my Honours. I believe it's definitely character building and prepares you well for the future. Should you do a BMedSc? Yes. Absolutely!

I'm more than happy to talk about my project or lab-based research in general on wjtan31@student.monash.edu.

ABSTRACT

Background

Fetal growth restriction (FGR) is when the growing fetus fails to meet its genetically predetermined growth potential. Of the plethora of FGR-related perinatal and postnatal complications, postnatal neurocognitive deficits may extend well into long term. Abnormal fetal neurodevelopment has been identified as the potential cause of these deficits in FGR infants. A serious global health problem with no definitive treatment and a varied aetiology, placental insufficiency has been singled out as one of the most common causes and a target for treatment. Thus over the past decade, much focus has turned to sildenafil citrate (SC) to alleviate placental insufficiency, thereby attenuating the deleterious effects of FGR.

Method

This study aimed to assess if SC improves neuronal and cerebrovascular development in an ovine model of FGR. I assessed the effects of FGR on neuronal and cerebrovascular development within key regions of the brain identified as vulnerable to FGR-related damage. The abnormalities in the hippocampus, PVWM and CGM are associated with poor postnatal neurocognitive outcomes. I assessed the effects of FGR and SC on fetal weight, brain weight and 'brain sparing'. I assessed gross histopathology using H&E staining, and neuronal development by quantifying the density of NeuN+ neurons. I then assessed markers of cellular damage through quantifying amounts of 8OHdG, GFAP and caspase-3. I assessed cerebrovasculature by investigating blood-brain barrier (BBB) integrity (albumin) and endothelial cells (GLUT1). Lastly I cross-referenced alterations in GLUT1 expressions, with fetal glucose delivery to isolate the cause.

Results

SC reduced fetal weight and brain weight, and increased brain:body ratio. In hippocampal subregion CA3, there was significantly (p=0.02) reduced neuronal number (NeuN) in FGR lambs (27.4 0.7 cells) compared to AG controls (41.5 3.5 cells) which were not attenuated by SC. Increased percentage area of oxidative stress (8OHdG+ cells) caused by growth restriction was tended to be attenuated by SC in the CGM. In the PVWM, FGR had significant increments on the number of cells demonstrating apoptotic cell death (caspase-3) (p=0.0157), total area (p=0.002) and percentage area (p=0.0019). Although attenuated by SC, this did not reach significance. In the PVWM and CGM, FGR caused increased albumin extravasation compared to AG controls. Albumin extravasation in FGRSC was notably more severe compared to FGR lambs. No significant differences were noted in GLUT1 and GFAP across groups.

Conclusions

Based on fetal weights, FGR and 'brain sparing' may be exacerbated, not alleviated by SC. SC is associated with compromised BBB integrity and abnormal neuronal development which were not rescued by SC therapy. Although the mechanisms are unclear, my findings suggest that SC may modulate mechanisms in neuronal and cerebrovascular development, leading to regional differences between the hippocampus, PVWM and CGM. Given the recent updates in the STRIDER trial, future research into the mechanisms underlying the SC-related effects on neurodevelopment may help steer future investigations into the treatment of FGR-related neuropathology.

Ribka Hillary Tjahjana

The Association between Alcohol and Tobacco with Depression among a Cohort of Healthy Older Australians

Dr Rosanne Freak-Poli. BSc, BHealthSc, PhD
Dr Suzanne Orchard. BSc (Hons), PhD
Dr S. Fiona Barker. B.Sc Env (Hons), PhD.
School of Public Health and Preventive Medicine, Monash University

Hi, I'm Ribka! This year is my fourth year of studying medicine in Universitas Indonesia. The reason why I chose this project for my Honours year is because it has been my passion to study something that is beyond my competence. At first, doing epidemiological study was hard and confusing for me. However, after I did this project, my knowledge about statistical analysis, critical thinking, how to present the data, as well as my writing skill were increased significantly. Moreover, the environment that surrounds me was giving major contribution in my study. I really feel the support and encouragement from my supervisors and colleagues through feedbacks that they gave during my research period. For future students, don't be afraid to try something new because there will be something great waiting for you at the end and you will be proud of yourself just like I am.

ABSTRACT

Background

According to recent data from the World Health Organization (WHO), smoking was responsible for 7.2 million deaths in 2017 and high-risk drinking has caused 3.3 million deaths up to 2015. These behaviours can produce physical and mental health disorder, including depression. In Australia, 50% of younger adults (aged 18-24 years old) are associated with high-risk drinking and there is an association between smoking, high-risk drinking, and depression. This pattern has not been described in older populations and there is no adequate research in this area, despite the proportion of older adults within the Australian population increasing over time.

Aims

The main aim is to examine the cross-sectional relationship between tobacco smoking, high-risk drinking, and high depressive symptoms among a cohort of healthy older Australians.

Methods

From the ASPREE Study, 19,114 participants aged 65 years and older, have met the inclusion and exclusion criteria were recruited. In this study, they were required to fill in the questions regarding their smoking status, drinking status, and mental health status (screened by CES-D 10). Univariate and multinomial logistic regression were stratified by sex, adjusted for age (years) and conducted in SPSS software (Version 20). Given multiple testing within the ASPREE cohort for secondary aims, the threshold of significance is $p<0.001$.

Results

Male participants were more likely to smoke tobacco (Males: 4.6% versus Females: 3.3%, $p<0.001$) and drink alcohol at high-risk levels (Males: 17.8% versus Females: 3.2%, $p<0.001$), compared to females, they were more likely to be indicated as depressed (Males: 7.6% versus Females: 11.6%, $p<0.001$). Among both males and females, being a current smoker increased the likelihood of being a high-risk drinker (Males: 19% and Females: 7%, $p<0.001$) and the combination of either being a high-risk drinker or indicated as depressed was associated with being a current smoker (Males: 3% and Females: 2%, $p<0.001$). And being either a current smoker or high-risk drinker was associated with high depressive symptoms (Males: 55% and Females: 69%, $p<0.001$). For males, having one risk factor (either smoking or high depressive symptoms) increased the chance of being a high-risk drinker by 5% (OR: 1.05, $p<0.001$).

Conclusion

Among a large cohort of healthy older adults, smoking, high-risk drinking, and high depressive symptoms were associated cross-sectionally. These findings have significant implications for understanding of how older adults deal with challenging life events (losing family members, retirement, and illnesses) that may contribute to smoking, high-risk drinking and high depressive symptoms. These findings highlight that interventions should address these health concerns in combination.

Nupoor Tomar

Prenatal, postnatal antibiotics, birth weight and childhood obesity

Professor David Burgner[1,3,4], A/Professor Lars Henning Pedersen[5] and Dr Jessica Miller[1]

[1] Murdoch Childrens' Research Institute, Royal Childrens' Hospital
[2] Hudson's Institute Monash Hospital
[3] Department of Paediatrics, Monash Health
[4] Monash University
[5] Aarhus University & Aarhus University Hospital, Obstetrics and Gynaecology, Denmark

Taking a BMedSc(Hons) and completing it in Aarhus, Denmark has been the best decision I have made! The research was exciting and presented me with a new way of looking at medicine to what we get the chance to do in our course. I never thought that I could enjoy statics, coding and epidemiology so much! I was very well supported by all my supervisors and was welcomed by Lars in Aarhus so that I always had someone to help me through any issues that arose. I am really thankful for all the meetings, emails and advice! Aarhus itself was an incredible city with such a diverse group of students and activities. I was lucky to get enough time to immerse myself in the Danish culture while completing a stimulating research project. I encourage anyone with doubts about undertaking a BMedSc(Hons)—I definitely hesitated about both doing research and going overseas for this year—to just take the plunge! Feel free to contact me via email (nupoor.tomar@gmail.com) with any questions about a BMedSc(Hons) in epidemiology, overseas or just life in general!

ABSTRACT

Background

Antibiotic exposure in early childhood has been linked to childhood obesity. It is unknown whether antibiotic exposure in pregnancy is associated with higher birth weight and whether this relationship differs by exposure timing, mode of delivery, child sex, maternal body-mass-index (BMI) and postnatal antibiotic exposure. We therefore investigated the association between caesarean section and antibiotic exposure during pregnancy and postnatally to 18 months of age with birth weight and childhood BMI.

Method

This longitudinal cohort study of 48 025 and 30 542 mother-child dyads used data from the Danish Birth Registry and Danish National Birth Cohort. Exposures were caesarean section and antibiotic use from conception to 18 months of age. Primary outcomes were birth weight and BMI z-score at 5 months, 12 months and 7-years of age. We controlled for maternal parity, age, smoking, BMI, socio-economic status (parental education or job title), and child gestational age and breastfeeding. We conducted linear regression for analysis, and stratified analyses by maternal BMI, mode of delivery and sex. Data analyses were conducted with STATA (StataCorp version 13., College Station, TX, USA).

Results

Prenatal antibiotic use was associated with a 19.31g higher birth weight in boys (95%CI: 5.16–28.48g). The effect size was largest when comparing trimester 1 or 2 exposure in boys with overweight mothers to unexposed boys in this sub-group (+58.85g, 95%CI: 22.05–95.65g). The relationship between postnatal antibiotic exposure from 0-6 months and childhood BMI z-score was less clear and differences between sexes were minor and inconsistent. Additive prenatal and postnatal antibiotic exposure from 0-18 months was associated with higher BMI z-score in girls at 7 years of age (adjusted +0.061, 95%CI: 0.00–0.12). Caesarean section was not associated with a consistent pattern or direction of BMI difference from infancy to mid-childhood.

Conclusions

Prenatal antibiotics were associated with higher birth weight in boys, especially in those born to overweight mothers exposed to antibiotics earlier in pregnancy. The relationship between postnatal or prenatal antibiotics and childhood BMI was small and less consistent. Mechanisms for the association may relate to epigenetics or the gut microbiome, while sex-differences could be explained by placental differences in female versus male fetuses. Judicious use of antibiotics in pregnancy and early childhood, particularly in high-risk groups may reduce the risk of high birth weight, which is predictive of later obesity.

Dunya Tomic

Prevalence, Epidemiology and Clinical Characteristics of Non-Alcoholic Fatty Liver Disease in Rural Victoria

Professor Stuart Roberts and A/Prof William Kemp,
Department of Gastroenterology,
Alfred Health

I'm Dee and I decided to do a BMedSc after fourth year, having involved myself in numerous research opportunities during my clinical years. Liver disease is a particular interest area of mine and through contacting clinicians I knew, I managed to involve myself in the first Australian study of non-alcoholic fatty liver disease, something I never thought would be possible as a medical student. My project was based at the Alfred Hospital with the Gastroenterology Department and was a sub-study of the wider government Crossroads study on undiagnosed chronic disease in rural Victoria. It involved reviewing the literature on the area (which I have been lucky enough to be published for in an international journal), data collection and analysis, and result interpretation, which showed a high prevalence of non-alcoholic fatty liver in our community. This year has been by far the best year I've had at university and I would highly recommend for anyone considering it to pursue a BMedSc. The year has given me fundamental skills in research and communication and has helped me see the field of medicine from a different and broader perspective, which will certainly be beneficial going into internship and working as a clinician.

ABSTRACT

Background

Non-alcoholic fatty liver disease (NAFLD) is a major health issue expected to rise in parallel with obesity and the metabolic syndrome. Epidemiological data regarding NAFLD mostly comes from the United States and Europe, with prevalence estimated at 20-30%; no significant Australian data has been recorded. A possible diagnostic approach to suspected NAFLD includes ultrasonography, vibration-controlled transient elastography (FibroScan®), and liver biopsy. Major complications of NAFLD include liver cirrhosis and cardiovascular disease.

Treatment may include lifestyle changes and medications such as vitamin E. This research aimed to determine the prevalence of NAFLD in the Goulburn Valley region of Victoria, to measure severity of disease in NAFLD cases using liver stiffness measurement (LSM) on FibroScan, and to determine any association between NAFLD and metabolic factors. Additionally, it aimed to assess the utility of FibroScan as a screening tool in the general population to identify those at risk of liver disease.

Method

This research was conducted through the Crossroads study on undiagnosed chronic disease in rural Victoria, a cross-sectional epidemiological study of four towns in Victoria's Goulburn Valley. The study participants completed household demographic surveys, and a smaller cohort was randomly selected for blood testing and FibroScan assessment. Those found to have elevated ALT levels in absence of significant alcohol consumption were determined as having NAFLD. All data was incorporated into an Excel database and calculations including Wilcoxon rank-sum and chi-square tests were conducted to explore overall cohort demographics, NAFLD prevalence, characteristics of the NAFLD group in comparison to those with normal ALT levels, and severity of liver disease.

Results

The overall cohort was found to have a high prevalence of metabolic risk factors including obesity, diabetes and dyslipidaemia, with 25.6% of the total group being affected by metabolic syndrome. The prevalence of NAFLD was found to be 13% on the basis of ALT levels, and 63.3% using controlled attenuation parameter through FibroScan. NAFLD was associated with metabolic risk factors including obesity and diabetes, and a significant relationship was found between NAFLD and metabolic syndrome ($p < 0.001$). Significant associations ($p < 0.05$) were also found between NAFLD and weight, BMI, liver enzymes (ALT, AST, GGT), lipids (total cholesterol, triglycerides, HDL- and LDL-cholesterol) and markers of diabetes (fasting and 2-hour glucose, HbA1c). Those with NAFLD had significantly higher liver stiffness on FibroScan compared to those with normal ALT ($p < 0.001$).

Conclusions

This study provided the first insight into the issue of NAFLD in the Australian domain, and the results closely resemble similar international studies, indicating a substantial burden of disease. It confirmed the significance of metabolic syndrome as a risk factor for NAFLD, and as a major issue in the rural Australian community. Greater severity of liver disease was found in those with NAFLD, and the feasibility of large-scale screening for liver disease using FibroScan was demonstrated. There is potential for a follow-up study across major metropolitan Australian cities to further explore the issue of NAFLD and study the effects of rural living status on NAFLD and metabolic disease.

Aimy Tran

Epidemiology of adenotonsillectomy in Victoria and risk factors for postoperative complications

Associate Professor Gillian Nixon[1, 2, 3], Professor Danny Liew[4] and Professor Rosemary Horne[1, 3]

[1] Department of Paediatrics, School of Clinical Sciences, Monash University
[2] Melbourne Children's Sleep Centre, Monash Children's Hospital
[3] The Ritchie Centre, Hudson Institute of Medical Research
[4] Centre of Cardiovascular Research and Education in Therapeutics, School of Public Health and Preventive Medicine, Monash University

I undertook my BMedSc(Hons) following fourth year in the Department of Paediatrics at Monash Children's Hospital. After having learnt the fundamentals of medicine, I wanted to explore the science that underpins clinical practice. I have an interest in paediatrics and respiratory medicine, and decided to undergo a paediatric quality improvement project involving adenotonsillectomy.

Under the supervision of my very supportive supervisors, I had the opportunity to develop my research skills in creating good methodology, scientific writing, public speaking, manipulating datasets and analysing data. As well as improving skills, this Honours year allowed me to be involved in many events and create professional networks. I had the chance to attend a conference and was invited to be a member of the Victorian Government's Expert Working Group towards improving adenotonsillectomy provision in Victoria.

I would highly recommend the BMedSc(Hons) to any prospective student seeking to learn new skills and meet experts in medical fields. I'm more than happy to be contacted for any questions: atra44@student.monash.edu

ABSTRACT

Background

Tonsillectomy, adenoidectomy and adenotonsillectomy (collectively referred to as adenotonsillectomy) are the most common paediatric procedures performed in Australia. Factors driving differences in adenotonsillectomy procedural volume and postoperative complications across Victoria are unclear. We aimed to describe the epidemiology of adenotonsillectomy in Victoria and identify predictors for haemorrhage, respiratory compromise, dehydration and length of hospital stay.

Method

The Department of Health and Human Services provided administrative data of people aged 0-19 years having tonsillectomy, adenoidectomy or adenotonsillectomy between 1 June 2010 and 30 June 2015 in Victoria. A linked dataset contained readmission data within 30 days of surgery. We conducted a cross sectional study to describe the epidemiology of adenotonsillectomy, and a retrospective cohort study, using stepwise multivariable regression, to identify risk factors for haemorrhage, respiratory compromise, dehydration and length of hospital stay.

Results

Over the 5-year period, 59,008 patients had 61,281 procedures. Most procedures involved children aged under 10 years (0-4y 38%; 5-9y 36%; 10-14y 14%; 15-19y 12%), the two least socioeconomically disadvantaged quintiles (48%), and were for the indications of obstructive sleep apnoea (47%) and tonsillitis (47%). Rates of adenotonsillectomy by geographical area were highest in regional Victoria and lowest in metropolitan areas. The strongest driver for procedure rate were rural hospitals, compared to metropolitan (coefficient 187.87; 95% CI 185.28-190.47; p<0.001). Other risk factors included tonsillitis diagnosis, decreasing age, and tonsillectomy or adenotonsillectomy procedures compared to adenoidectomy alone.

Of the procedures, 1,660 resulted in haemorrhage (3% total procedures; 50% readmissions), 479 in dehydration (0.78% procedures; 14% readmissions) and 93 in respiratory compromise (0.15% procedures; 3% readmissions). Increasing age was the strongest predictor for haemorrhage (adjusted odds ratio [OR], 1.90; 95% CI, 1.81-2.00, p<0.001). In contrast, youngest age was the strongest predictor for respiratory compromise (OR, 1.37; 95% CI, 1.09-1.72; p=0.008). Having a tonsillectomy/adenotonsillectomy (compared to adenoidectomy alone) was the strongest driver for dehydration (OR 1.60; 95% CI, 1.38-1.86; p<0.001) and longer length of hospital stay (OR 4.40; 95% CI, 4.20-4.61; p<0.001).

Conclusions

This study described the contemporary epidemiology of paediatric tonsillectomy, adenoidectomy and adenotonsillectomy in Victoria, as well as investigated predictors for complications and length of hospital stay. There are demographic and geographic variations in adenotonsillectomy and in postoperative complications for children across the state. These findings will inform evidence-based state-wide recommendations for service provision, access to healthcare and peri- and post-operative care.

Luke Chenkan Wang

Preventing postoperative middle ear ventilation tube complications in children with topical ciprofloxacin: a randomised controlled trial

Dr Debra Phyland
(Department of Surgery Monash University, Department of ENT – Head and Neck Surgery Monash Health)

Mr Charles Giddings
(Department of ENT – Head and Neck Surgery Monash Health)

I decided to undertake a BMedSc(Honours) project after my fourth year of Medicine. I chose my project because I had an interest in Otolaryngology and Paediatrics and wanted to develop my skills as a researcher. Through the year I've learn how to thoroughly conduct scientific research, apply for research ethics, collect data and perform statistical analysis, while juggling the logistical concerns of a multi-site clinical trial. The learning curve was steep but well worth its reward. I've also had the opportunity to work with an amazing group of supportive people in the ENT department at Monash Health and gained valuable clinical experiences, from general outpatient clinics to assisting in complex head and neck operations.

ABSTRACT

Background

The insertion of middle ear ventilation tubes is one of the most common surgeries performed in the paediatric population in Australia. The main indications for ventilation tube insertion are recurrent acute otitis media and chronic otitis media with effusion. Insertion of the ventilation tube usually leads to prompt quality of life improvements and resolution of symptoms. However, these benefits can be hindered by the presence of postoperative complications such as ventilation tube otorrhoea and blockage. The use of ciprofloxacin antibiotic ear drops to prevent these outcomes is commonplace despite a lack high quality evidence supporting its use. Studies which investigate the quality of life benefit of using antibiotic ear drops are also lacking.

Method

An assessor-blinded randomised controlled trial of 360 paediatric patients undergoing bilateral grommet surgery was designed. Patients were randomised in a 1:1 ratio to receive either ciprofloxacin ear drops during surgery and for 5 days postoperatively or to receive no drops. Baseline and intraoperative characteristics were recorded for each patient. Patients were assessed at 6 weeks postoperatively for ventilation tube otorrhoea and blockage. A validated parent-reported disease-specific outcome measure Otitis Media Outcome 22 (OMO-22) score was used to assess disease severity preoperatively and at 6 weeks postoperatively.

Results

To date, 81 patients were recruited with 35 patients completing follow-up. 19 patients were allocated to treatment while 16 patients were allocated to control.

There was no statistically significant difference in the incidence of ventilation tube otorrhoea between the two groups. The incidence of the treatment group was 18.4% while the incidence of the control group was 6.3% (OR=3.387, 95% CI 0.651 – 17.631, p=0.166).

There was no statistically significant difference in the incidence of ventilation tube blockage between the two groups. The incidence of the treatment group was 13.2% while the incidence of the control group was 9.4% (OR=1.464, 95% CI 0.322 – 6.669, p=0.719).

There was no statistically significant difference in preoperative OMO-22 scores between the two groups (Mann-Whitney U, p=0.528). The median preoperative OMO-22 score for the treatment group was 45 and for the control group was 48.

There was no statistically significant difference in postoperative OMO-22 scores between the two groups (Mann-Whitney U, p=0.941). The median postoperative score for the treatment group was 14 and for the control group was 14.5. The median score improvement was 51.1% for the treatment group and 66.6% in the control group. This difference was statistically insignificant (Mann-Whitney U, p=0.057).

Conclusions

Our current findings suggest that the use of ciprofloxacin ear drops does not decrease the incidence of ventilation tube otorrhoea and blockage compared to control. Furthermore, the use of ciprofloxacin ear drops does not increase the quality of life benefit compared to control. At this preliminary stage, we lack the statistical power to detect small differences between treatment and control groups in the primary outcomes of ventilation tube otorrhoea and blockage, nor the secondary outcome of quality of life improvement. Further recruitment is required for this study to make definitive recommendations regarding the use of ciprofloxacin ear drops in the prevention of postoperative complications.

Sebastian Wrobel

The Impact of Preoperative Factors on Knee Pain and Function After Total Knee Arthroplasty For Osteoarthritis.

Associate Professor Anita Wluka, Professor Flavia Cicuttini,
School of Public Health and Preventative Medicine,
Department of Epidemiology and Preventative Medicine,
The Alfred Hospital.

Hello everyone! After completing my fourth year of medicine I decided to undertake a BMedSc to try something new and explore the research side of medicine. Now, I personally did not find it greatly appealing to study in a lab for the majority of my year so decided to take on a project requiring data collection from a database. After hearing numerous accounts that having a great supervisor is paramount to keeping your sanity throughout the year, I too can vouch for this. I could not have overcome the frustrating setbacks throughout the year, in addition to moments where I had no idea what I was doing (believe me it happens), without the feedback and guidance of my supportive supervisor.

One of the most valuable insights I have taken away from the year is that no matter what your project finds, there is an appreciation for your work and its contribution to future research and medical practice. Overall, the BMedSc was very rewarding and I would recommend it to anyone interested in research or willing to take that leap of faith in trying something new. I am happy to be contacted by email sfwro1@student.monash.edu to share my experience.

ABSTRACT

Background

The growing prevalence of knee osteoarthritis places a large burden on the healthcare system. Correspondingly, the rates of total knee arthroplasty (TKA) have risen substantially, offered as an effective management option in advanced osteoarthritis. Despite the suggested effectiveness of joint replacement, 10-34% of recipients remain in a painful and functionally limiting state postoperatively. Thus it is important to determine preoperative factors that may identify those at increased risk of poor outcome.

Aims

To examine the association between preoperative factors and poor postoperative outcome at 12 months following TKA, and to determine the associations between preoperative factors and knee pain and function at 12 months following TKA in a public hospital population.

Method

A retrospective cohort study assessed all patients undergoing primary TKA for a primary diagnosis of osteoarthritis, referred into the Alfred Hospital Osteoarthritis Hip and Knee Service between 1st January 2013 and 31st December 2015. Data was collected prospectively. Parametric and non-parametric descriptive methods were used to describe differences in preoperative characteristics between groups in primary and secondary outcome measures. Binary logistic regression was then performed to determine the likelihood of a poor outcome based on preoperative factors, with appropriate adjustment for important confounding variables.

Results

A total of 158 participants met the inclusion criteria. Regarding primary outcome measures, 133 participants had a good postoperative outcome following TKA (84.2%) and 21 had a poor outcome (13.3%). There were no significant differences in preoperative baseline characteristics between patients of good compared to poor outcome; none of the examined preoperative factors were associated with a significant increase in odds of a poor outcome. However, there was a tendency for female gender to be associated with an increased odds of poor outcome (OR=1.82 [0.66-4.98]).

Secondary outcome measures found older age at surgery was a predictor of postoperative gait aid use (OR=1.08 [1.02-1.14], p=0.01). Female gender increased the likelihood of postoperative pain on movement (OR=3.44 [1.48-8.00], p=0.004). Poorer fitness for surgery increased the odds of postoperative pain at rest (OR=3.42 [1.20-9.77], p=0.02) and postoperative pain on movement (OR=2.19 [1.01-4.75], p=0.047). And presence of preoperative pain at rest increased the likelihood of postoperative pain on movement (OR=5.09 [1.80-14.43], p=0.02).

Conclusions

No preoperative variables were predictive of overall poor TKA outcome on primary outcome measures. However, there was a tendency for female gender to be associated with an increased odds of poor outcome. The size of the study had limited power to identify any but the strongest associations thus a small to moderate effect on outcome cannot be excluded. Secondary outcome measures found female gender, poorer fitness for surgery and the presence of preoperative pain at rest to be associated with increased likelihood of poorer postoperative pain after knee replacement. The findings in this study suggested that patients undergoing knee replacement in public hospital settings have similar outcomes to the general population, including those in private health, despite having greater disease severity at time of surgery.

Angie Shiqi Xiang

Identifying lipidomic changes associated with cold exposure and brown adipose tissue activity

Prof Bronwyn A. Kingwell, Baker Heart and Diabetes Institute, Metabolic and Vascular Physiology Laboratory
Dr Andrew L. Carey, Baker Heart and Diabetes Institute, Metabolic and Vascular Physiology Laboratory
Prof Peter J. Meikle, Baker Heart and Diabetes Institute, Metabolomics Laboratory

I decided to undertake an honours project after fourth year primarily because I found a great team of supervisors that I wanted to work with. This year turned out to be immensely fruitful, and I have acquired lifelong skills particularly in writing, critical analysis and scientific communication. My advice for future students would be to find supervisors who are truly invested in you and your project. Their support and guidance is imperative for developing your confidence and independence especially given the time constraints of the honours year.

ABSTRACT

Background

Brown adipose tissue (BAT) has been of particular interest as a potential therapeutic target for obesity and associated metabolic disorders. BAT normally functions to undergo compensatory non-shivering thermogenesis in response to cold exposure, which is mediated via sympathetic activation of -adrenoceptors. It is theorised that maximal pharmacological BAT activation can increase whole-body energy expenditure by 25%, and has been shown to greatly improve markers of glucose and lipid homeostasis. Recent studies have revealed novel interactions between BAT and circulating lipid species, and highlight the potential to develop clinically relevant BAT activators and biomarkers. The aim of the present study was to measure the plasma lipidome before and after mild cold exposure in healthy individuals to identify lipid biomarkers of cold-stimulated sympathetic activity and BAT thermogenesis.

Method

Fourteen healthy male volunteers (age 22 ± 2 years; mean ± SD) were recruited and subjected to 90 minutes of mild cold exposure, after which their BAT activity was measured via 18F-fluorodeoxyglucose ([18F]FDG) positron emission tomography/computed tomography (PET/CT). Blood samples taken before and after cold exposure underwent mass-spectrometry-based lipidomic analysis which assessed the plasma concentrations of 729 individual lipid species. Additionally, blood samples were taken at 30-minute intervals throughout the trial to quantify plasma noradrenaline (NA) concentration as a surrogate marker of sympathetic activity.

Results

In summary, cold exposure did not alter total lipid concentration, but led to a significant change in non-esterified fatty acid (NEFA) lipid class concentration, as well as the concentrations of 40 individual lipid species from other classes. No changes in lipid species concentrations, either individually or combined in class/subclass groups, were significantly associated with BAT activity after Benjamini-Hochberg correction. However, the total lipid concentration change, along with the cold-induced concentration changes of 28 lipid classes and 434 lipid species, were significantly correlated with sympathetic activity post-Benjamini-Hochberg correction. Furthermore, the study identified 84 lipid species that underwent greater cold-induced changes than the established BAT-associated lipid, 12,13dihydroxy-9Z-octadecenoic acid (12,13diHOME), and 58 lipid species which had stronger correlations between cold-induced concentration change and BAT activity.

Conclusions

This study revealed novel lipid associations with BAT activity, NA concentration change and cold exposure for further exploration. The lipids which performed better than 12,13diHOME, in particular, represent promising targets for future BAT-directed interventions. Interestingly, many more significant correlations were identified between lipids and NA concentration change than between lipids and BAT activity. Taken together with the existing literature, this suggests that the effects of sympathetic BAT activity may be masked by other sympathetically stimulated tissues, and that future BAT studies should employ methods that allow assessment of BAT in greater isolation.

Faishal Farras Yanfaunnas

The Use of Low Dose IL- 2 as a Possible Treatment for Retinopathy of Prematurity

Professor Jennifer L. Wilkinson-Berka
Professor Mark E. Cooper
Department of Diabetes,
Central Clinical School

For my honours project I decided to do this project because I wanted to do a lab based project and I was very interested in the field of diabetes. It was a blast of a year with many experiences gained not just from lab work but also writing English work and also being more independent. For future students choose a project that you should probably be passionate about because you will be doing a lot of reading and learning then intricacies about your topic.

ABSTRACT

Background

Retinopathy of prematurity (ROP) is currently one of the leading causes of childhood blindness in well-developed countries. This disease happens in low birth weight pre-term infants with the administration of supplemental oxygen in the neonatal intensive care unit (NICU) one of the main causes of ROP. This causes a decrease of oxygen mediated angiogenic factors in the developing retinal vasculature which leads to the destruction of the developing retinal vasculature, this is known as phase 1 of ROP. In phase 2 as the supplemental oxygen is removed, an influx of angiogenic factors causes an excessive growth of the retinal vasculature and leads to neovascularization. These vessels are inadequate to support the retina and may lead to retinal detachment which can cause blindness. Inflammation has emerged as one of the key factors in ROP with recent studies showing that it may contribute to development of ROP. It was previously thought that the retina is immuno-privileged but recent studies have demonstrated that immune cells indeed migrate to the retina due to the leakage of the blood retinal barrier (BRB). Studies now explore to ways in which to dampen the inflammation, one of which is though Foxp3+ Tregs which can enact suppressive capabilities on the immune cells on the retina such as microglia. The administration of low dose IL-2 may be a candidate to increase Tregs due to the high affinity of Tregs to bind with IL-2 and the ability of this cytokine to promote the survivability and functionality of Tregs.

Method

We sought to determine this by using a well-established model of ROP in mice named oxygen-induced retinopathy (OIR) where newborn mice at post-natal day (P) 7 are put into an oxygen chamber with 75% oxygen to mimic the events in the NICU. They are then taken out at P12 and are culled at P18. Low dose IL-2 is injected at P6, 7, 8 11, 13 and 16. The mice were then examined for vascular pathology using wholemounts stained with isolectin. Flow cytometry was used to examine if low dose IL-2 increased the number of Tregs without influencing the abundance of other immune cells that may be responsive to IL-2.

Results and Conclusions

Our results showed that low dose IL-2 indeed reduced the vascularpathology as well as increase the number of Tregs in the lymphoid organs and the blood of mice with OIR. Low dose IL-2 also minimally influenced the abundance of other immune cells such as CD8+ T cells, NK and NKT cells which may contribute to the vascular pathology and shows promise as a future treatment in ROP. Future studies measuring the effect of low dose IL-2 on the retinal immune cells as well as its effects on the angiogenic factors may help in understanding the factors causing vascular pathology improvements as well as future clinical trials may be in consideration in the future.

Sabrina Yeh

Patterns of antibiotic prescribing in the paediatric community

Professor Jim Buttery

Professor of Paediatric Epidemiology. Departments of Epidemiology and Preventative Medicine & Paediatrics, School of Public Health and Preventive Medicine & School of Clinical Sciences, Monash University; Infection and Immunity, Monash Children's Hospital; Monash Immunisation, Monash Health; Murdoch Children's Research Institute; Ritchie Centre, Hudson Institute; Clayton, Victoria, Australia.

Associate Professor Chris Pearce

President, Australasian College of Health Informatics, Director of Research, Outcome Health, Adjunct Associate Professor in Health Informatics, University of Melbourne, Adjunct Associate Professor in General Practice, Monash University; Chair, Digital Health Committee of the Australian College of Rural and Remote Medicine

I commenced my BMedSc (Hons) after completing Year 4C at Monash Children's Hospital/ Monash Centre for Health Research and Implementation. My project involved investigating antibiotic prescribing within our paediatric community. I was lucky with my project as it combined several of my interests. The breadth of the project meant it covered areas in public health, paediatrics, infectious diseases and health technology. An opportunity arose in the middle of the year to investigate antibiotic prescribing overseas at Shenzhen Children's Hospital, China. This was an eye-opening experience seeing healthcare in a different system.

Through my BMedSc year I have gained valuable research experience, developed skills in managing large data and dedicated time to hobbies outside of medicine. I vastly enjoyed working on my project this year with a hugely supportive supervisorial team. Overall, I've had a great year.

For students interested in a BMedSc, I am more than happy to be contacted at sqyeh1@student.monas.edu. I highly recommend spending time contacting past students about previous projects and supervisors.

ABSTRACT

Aim and Background

Antibiotics are the most commonly prescribed medication in paediatrics. We analysed antibacterial prescribing trends in n two distinct primary care settings; a retrospective analysis of paediatric community care in Victoria from 2013-2017 and prescribing patterns in a single outpatient clinic within a tertiary Chinese metropolitan paediatric hospital.

Method

Antibiotic prescribing data from de-identified, digital records on children (age<18 years) were retrieved from 231 anonymised general practices in south-eastern Melbourne, Victoria from 2013-2017. Sex, age, antibiotic characteristics and repeat prescriptions were analysed. Rates of broad-spectrum antibiotic usage and reasons for prescribing were also evaluated.

For the second study, antibiotic prescription data from paediatric (<18 years) computerised records were retrieved from the infectious diseases outpatient services at Shenzhen Children's Hospital in 2017; sex, age, diagnosis, and antibiotic characteristics were analysed.

Results

788,711 antibiotic prescriptions were captured, from a total of four million paediatric presentations to Victorian general practices. Antibiotic prescribing rates reduced by 31% over the 5-year period. The most commonly prescribed antibiotics were amoxycillin (43% of total) followed by cephalexin, amoxycillin-clavulanate, phenoxymethylpenicillin and cefaclor.

Prescription of broader spectrum antibiotics, such as cefaclor and amoxycillin-clavulanate, decreased over the five-year period, whilst cephalexin and phenoxymethylpenicillin usage increased. Diagnoses most associated with cefaclor and amoxycillin-clavulanate prescriptions included otitis media other upper respiratory tract infections. 28.8% of antibiotic prescriptions included a corresponding repeat script.

In China, a total of 1040 antibiotic prescriptions were captured with an overall antibiotic prescription rate per presentation of 20%. Cephalosporins were the most commonly used antibiotic class, in particular second and third-generation cephalosporins. Antibiotic prescribing rates remained stable throughout the 2017 period. Diagnoses classed under the respiratory, gastrointestinal and skin & soft tissue system accounted for the majority of diagnoses (93%).

Conclusions

From 2013-2017, there was a marked decline in antibiotic prescription rates in the paediatric population in Victorian general practices. Encouragingly, prescribing of broad spectrum antibiotics reduced at a swifter rate, consistent with prescribing guidelines. This study provides the largest targeted examination of antibiotic prescribing patterns for Australian children to date.

In China, antibiotic prescribing rates remained stable in the paediatric infectious diseases outpatient population throughout 2017. This study provides a targeted examination of antibiotic prescribing patterns for children within a major Chinese metropolitan tertiary paediatric hospital.

Renee Zeng

Prevalence and determinants of antibiotic use among women in early pregnancy living in rural Vietnam

Professor Jane Fisher, Dr Minh Le
Global Public Health, School of Public Health and Preventive Medicine

After fourth year, I really wanted something new and different from a typical 'medical' school year and that was the reason I did a BMedSc(Hons). I have learnt beyond just research skills but been able to spend an entire year on something I am passionate about which is truly rewarding. Doing a BMedSc(Hons) for me wasn't about the project by itself but the process and path I took to get to the end. It is super fulfilling!

Happy to be contacted: rgzen1@student.monash.edu

ABSTRACT

Background

Antibiotics are one the most commonly used medications in pregnancy. However, antibiotics in pregnancy have been found to be associated with foetal malformations, low birth weight and asthma in infancy. Antibiotic use in low-and-middle-income countries (LMIC) is affected by structural determinants and prescriber, dispenser and patient factors in a setting where the infectious disease burden is high. This has led to the use of antibiotics inappropriately, either incorrectly or at suboptimal therapies. In addition, non-prescription use, which is the use of prescription medications without obtaining a prescription, is common in LMICs. However, to date, no studies have examined the prevalence and determinants of antibiotic use in early pregnancy in LMICs.

Aim

The aim of the project was to describe the prevalence and determinants of antibiotic use among women in early pregnancy living in rural Vietnam.

Method

This study was nested within the competitively funded NHMRC study located in the Ha Nam province, Vietnam: Learning Clubs to improve women's health and infant's health and development in Vietnam: a cluster randomised control trial. Our study analysed a component of the baseline data, collected at 20 weeks gestation or less of the cluster randomised control trial. Through a structured individual interview schedule, 1245 women were asked about sociodemographic characteristics, health and pregnancy characteristics, health service usage and knowledge, attitudes and behaviours in pregnancy were described. The primary outcome was antibiotic use and its characteristics of use.

Results

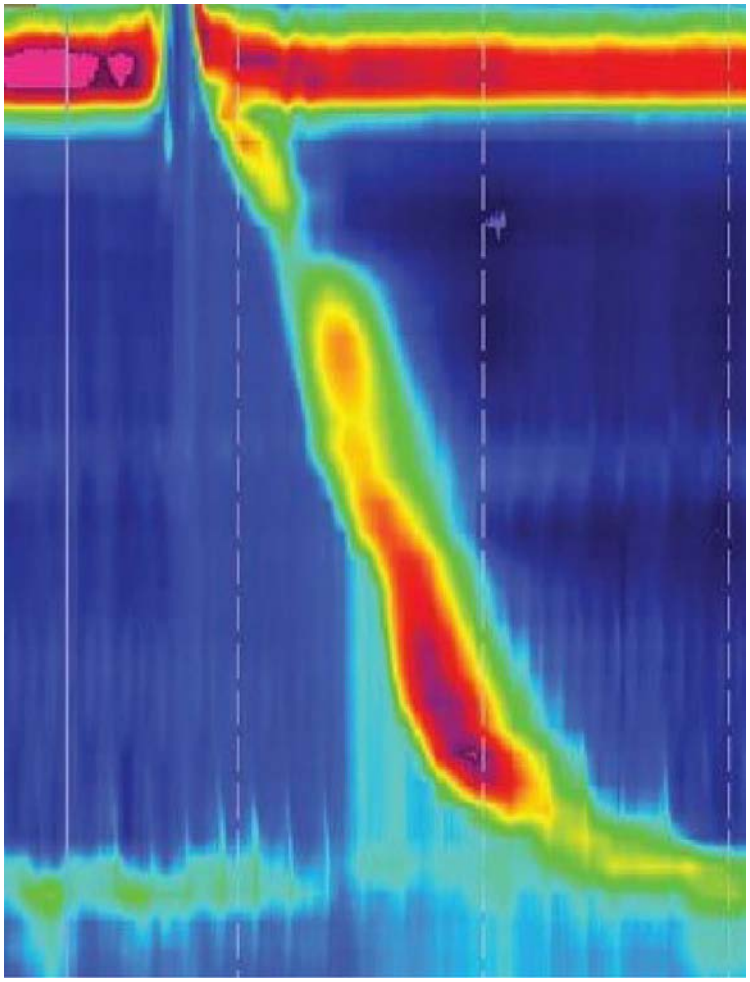
This study found that 162 women (13%) had taken antibiotics in their current pregnancy. The median duration of use was 3 days. The most common indication for antibiotic use was respiratory condition (n=95, 55.5%). Just under half of antibiotic users had used antibiotics without a medical prescription.

Women who were older (p=0.05), more advanced in gestational age (p=0.016) and used other medications in pregnancy (p=0.001), were more likely to use antibiotics. In logistic regression analysis, women with a chronic condition were more likely to use antibiotics (OR 1.8, P=0.03, 95% CI 1.1-3.0). Women with higher DASS21 scores were also more likely to use antibiotics (OR 1.01, P=0.006, 95% CI 1.00-1.03). In addition, having more ultrasounds also predicted antibiotic use (OR 1.1, P=0.007, 95% CI 1.0-1.2). Women who believed that they would seek professional advice around medication use in pregnancy were more likely to take antibiotics (OR 2.0, P=0.02, 95% CI 1.1-3.6)

Among those who used antibiotics, self-medication was associated with a shorter number of days of use (p<0.001). Younger women were twice as likely to self-medicate (OR=2.1, P=0.032, 95% CI 1.1-4.0) as well as those with a respiratory condition (OR 3.4, P<0.001, 85% CI 1.7-6.6).

Conclusions

Our study is the first to identify significant associations between poorer physical and emotional wellbeing and antibiotic use. In addition, it was noted that self-medication of antibiotic tended to be for respiratory conditions, including for viral infections, and non-serious symptoms. Our research points to the need for targeted health promotion activities educating women around the risks and benefits of antibiotic use, especially self-medication, in pregnancy.



Oesophageal HRIM

MONASH University

More information

Faculty of Medicine,
Nursing and Health Sciences
Monash University,
Victoria 3800
Australia

BMedSc(Hons)

Tel: +61 3 9902 0859
Email: med-bmedsc-hons@monash.edu
Web: med.monash.edu.au/bmedsc-hons/

facebook.com/Monash.University

twitter.com/MonashUni