RACP Foundation Research Awards

FINAL REPORT

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<th>Project / Program Title</th>
<th>Blood Pressure and Volume State in Kidney Disease</th>
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<td>Award Received</td>
<td>2014 RACP Jacquot Research Entry</td>
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<td>Report Date</td>
<td>5 February 2015</td>
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<td>Administering Institution</td>
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<td>Funding Period</td>
<td>Start Date: 6 February 2014</td>
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**PROJECT SUMMARY**

High blood pressure is an important heart and kidney risk factor, treatment of which is proven to reduce morbidity and mortality. The diagnosis and management of blood pressure is critical in those who suffer with milder forms of kidney dysfunction through to those with advanced end stage kidney disease treated with renal replacement therapy (haemodialysis, peritoneal dialysis and kidney transplantation). Beyond these groups, studies of the general population in Australia reveal that around 30% of people have high blood pressure, around 50% of which is untreated.

This project aims to define characteristics and long term outcomes of those in the general population – including associations of novel risk factors such as dietary salt intake on the development of kidney disease. In more advanced kidney disease, definition, optimal targets and key management of blood pressure remains controversial. We have undertaken a comprehensive review of this common clinical problem, looking at patterns within the first 120 days of haemodialysis as well as assessing the true prevalence of hypertension in both incident and prevalent dialysis patients. We aim to follow this with assessment of the impact of intensive early education on management of blood pressure and volume state in this group. Overall, we aim to improve disease burden as well as the high mortality rates seen in patients with kidney disease, in addition to identifying risk factors for development of kidney disease for those in the general population.

**PROJECT AIMS / OBJECTIVES**

1. Assess the burden and effect of hypertension and dietary salt intake on the development and progression of chronic kidney disease and cardiovascular disease using data from the Australian Diabetes and Obesity Lifestyle study
The Australian Diabetes, Obesity and Lifestyle study (AusDiab) is a national population based longitudinal survey of diabetes mellitus and associated risk factors in Australians that occurred in 1999. 11,247 subjects completed the baseline survey including physical examination, blood and urine testing. 6537 of the original cohort returned for follow up in 2004-2005, and then at 12 years allowing the assessment of disease incidence. The prevalence of CKD is well characterised using creatinine methodologies. The relationship between baseline BP, treated and untreated hypertension to incident CKD as well as the interaction with dietary salt intake will be assessed. This complex analysis is currently being undertaken using Stata Statistical software (version 12.1) using the knowledge gained from the clinical epidemiology degree that has been undertaken as part of my PhD studies. Publication submission will be in the second half of 2015.

2. Assess the prevalence and burden of hypertension in a representative Australian satellite haemodialysis cohort

This trial project received ethics approval from the Southern health Human Research Ethics Committee, commencing in late 2013. This aim has achieved final data collection, with recruitment of 40 prevalent haemodialysis patients from Moorabbin and Casey satellite dialysis centres. We assessed 3 measures of blood pressure - at home measures, taken 3 times daily for 7 days, with concurrent pre and postdialysis blood pressure (dialysis based measures) as well as an interdialytic 44 hour ambulatory blood pressure monitor to assess blood pressure burden. This data will allow us to assess true blood pressure burden in this population as well as the current accuracy of our current measurement techniques in the Australian haemodialysis population. Data is in the analysis phase and will be ready for publication in the first half of this year.

3. Assess patterns of haemodynamics and volume state in incident haemodialysis patients over 12 months using retrospective data from a single centre

This aim has been achieved through a comprehensive review of incident dialysis patients to Monash Health (all campuses) between Jan 2011 to Jan 2012. Records for 98 patients, specifically addressing the first 120 days of dialysis were reviewed. Major indicators such as blood pressure and volume patterns were the focus of the review, with additional clinical indicators such as medication burden, biochemical parameters and team review (clinic, dietitian, social work) also described. This is the most comprehensive review in this unit to date regarding clinical practices in the incident period of dialysis, and analysis of these patterns reveal poor volume control and blood pressure control during this period, with intradialytic weight gains and medication burden remaining high to 120 days, despite apparent regular clinical review, suggesting that more intensive and comprehensive education of patients may be the critical determinant in ameliorating these burdens.

4. Determine the impact of early intensive education and intervention in the first 90 days of haemodialysis as measured through effects on BP, volume state, medication (tablet) burden and health related quality of life

This pilot study will examine whether an educational program over the first 12 weeks of dialysis leads to establishment of positive early habits surrounding fluid intake and subsequent interdialytic weight gain. In turn, this is postulated to lead to improved blood pressure control and improved interdialytic haemodynamic stability and ultimately improved health related quality of life.

Previously published data demonstrates normal distribution of systolic blood pressure with a standard deviation of up to 22mmHg in this measure. We anticipate 30% patient dropout due to modality change, transplantation or death. Based on a clinically important difference in systolic blood pressure between groups of 10mmHg at 12 months we plan to enrol 45 patients in this trial (power 0.8, alpha 0.05). We have approximately 100 patients commencing dialysis in our centre over 12 months, therefore enrolment in this trial is feasible. Patients will be randomised to standard clinical care or to the education based program over 12 weeks. This is comprised of fortnightly education sessions with nurse practitioners and ongoing feedback regarding progress. Monthly physician based assessments will be undertaken. Dialysis measures will be collected.
fortnightly as part of routine dialysis care, monthly pathology will be undertaken as part of in unit care and repeat health related quality of life assessments will be undertaken at the completion of the 12 week program. The intervention group will undertake 3 monthly refreshed education sessions through to 12 months. Final follow up of both patient cohorts will be undertaken at 12 months post commencement to assess ongoing patterns of volume state, weight and blood pressure in addition to health related quality of life. Primary outcome will be a decrease in interdialytic weight gain expressed as a percentage of ideal body weight with secondary outcomes to include attainment of normal predialysis blood pressure, reduction in medication burden and improvement in health related quality of life scores and xerostomia scores at 3 and 12 months.

This interventional trial has received provisional ethics approval in 2014 and will be commenced with revisions completed at the completion of Aim 1.

SIGNIFICANCE AND OUTCOMES

Renal disease consumes more than 5% of the Australian health budget and the proportion of people with chronic kidney disease is increasing, particularly in the setting of an ageing population. The number of patients commencing renal replacement therapy in any year in Australia is concurrently climbing with 2257 patients commencing in 2010, a rate of 101 per million population per year. Mean age at commencement is 60.7 years with 14% of subjects demonstrating hypertension as a primary cause of end stage renal disease. Older patients are vastly more likely to have increased comorbid burden at baseline, have poorer health related quality of life and are potentially more vulnerable to the stressors involved in the commencement of renal replacement therapy. Improved mortality rates are persistent in haemodialysis populations with just under one quarter of patients dying (largely of cardiovascular causes) in the first 12 months after haemodialysis commencement. Across all causes of kidney failure, hypertension is highly prevalent yet despite high medication burden blood pressure remains uncontrolled in both a large proportion of the general population as well as the majority of haemodialysis patients. Increases in BP have shown associations with adverse cardiac structural change, long considered a marker for incipient cardiac morbidity and mortality.

This body of research will help to define the BP associations with chronic kidney disease development and progression, the clinical care paradigm at haemodialysis commencement and the true BP burden experienced by patients. Finally, through education of patients at a time when they are most at risk, we hope to positively modify not only physiological parameters on haemodialysis (BP, need for ultrafiltration, haemodynamic instability) but assess the translation of these improved parameters to change in cardiovascular parameters and the patient centred outcome of improved health related quality of life. Translation of this practice into a new policy of clinical care for early haemodialysis will assist in maintenance of cardiovascular health and health related quality of life for patients, not only ameliorating individual burden of disease but concurrently decreasing the public health care burden associated with renal disease through improved health maintenance.

PUBLICATIONS / PRESENTATIONS

Review article - hypertension and volume in haemodialysis


Cochrane Review - Protocol Publication

This review is under final editorial approval with the Cochrane Renal Group and is slated for publication in the first half of 2015

Review article - hypertension, volume and home dialysis

3. Michelle C Lewicki Kevan R Polkinghorne, Peter G Kerr: Should dialysis at home be mandatory for all suitable ESRD patients? Seminars in Dialysis Article first published online: 7 DEC 2014
DOI: 10.1111/sdi.12322

Abstract presentation ANZSN 2013


Abstract presentation ANZSN 2014

5. Lewicki MC Ng I Schneider AG: HMG CoA Reductase Inhibitors (statins) for Preventing Acute Kidney Injury after Surgical Procedures Requiring Cardiac Bypass: A Systematic Review and Meta-Analysis