

ISN Trial-List

November 2017



Once a month, the ISN-ACT (Advancing Clinical Trials) team collects and publishes a list of important nephrology trials from the latest medical literature.

Hypertension

ISN Academy: [Hypertension](#)

Community health worker-led case management improves hypertension control in urban poor

Effect of a Community Health Worker–Led Multicomponent Intervention on Blood Pressure Control in Low-Income Patients in Argentina: A Randomized Controlled Trial

[He, et al. JAMA. 2017;318\(11\):1016-25](#)

The prevalence of hypertension is rising around the world, contributing to a growing burden of cardiovascular and chronic kidney disease. Untreated or inadequately treated hypertension is common and especially affects low income individuals. He, et al. addressed this challenge in poor urban areas in Argentina by conducting a cluster randomized trial involving 1432 participants at 18 publicly funded healthcare centres. Intervention centres established a community health worker–led program for participants presenting with uncontrolled hypertension (>140/90mmHg). In addition to routine physician review, participants at the intervention centres received regular home visits, dietary advice and health education, supervised home blood pressure monitoring and text-message reminders. Control centres provided usual care according to national guidelines. Over the 18 month intervention period, the mean blood pressure of those at the intervention centres fell from 152/92mmHg to 132/80mmHg compared to a fall of 150/90mmHg to 138/84mmHg in those at the control centres (mean difference in reduction 6.6mmHg; $p<0.001$). The mean intervention cost per participant for the entire intervention period was \$US114.60. The effect of the intervention remained at all time points and loss to follow up was low. This study demonstrates the potential benefits of health worker-led programs in primary care. It is not clear which aspects of the multicomponent intervention contributed most to the effect and generalisability to other health-systems and countries cannot be assumed. These results suggest that a renewed focus on personalised community health care may help to meet the global challenge of hypertension.

Chronic Kidney Disease

ISN Academy: [Chronic Kidney Disease](#)

Nurse-led pre-dialysis care may reduce hospitalisations and maximise choice of RRT modality

Augmented Nurse Care Management in CKD Stages 4 to 5: A Randomized Trial

[Fishbane, et al. Am J Kidney Dis. 2017;70\(4\):498-505](#)

The time leading up to commencement of dialysis is challenging for patients, carers and clinicians. Multiple decisions must be made and sequential steps followed to avoid commencing dialysis in hospital or without a fistula – both of which are associated with increased mortality. Structured pre-dialysis care is important to educate patients regarding RRT options and assist them and clinicians in arranging the necessary procedures required to meet shared goals. Fishbane, et al. randomised 130 participants with stage 4-5 CKD to care co-ordinated by a nurse or to usual care at three nephrology clinics. The nurses assisted participants with home visits, structured pre-dialysis education and assistance with decision making. A care plan was also agreed with the patient and treating clinician. The intervention program was provided for up to 18 months and participants were followed for a further 6 months. Those in the intervention group had a significantly lower rate of hospitalisation (0.61 vs 0.92 admissions per year; $p=0.04$) over the study period. Moreover, there was a higher number of participants commencing RRT with peritoneal dialysis or pre-emptive transplant (37% vs 10%) and fewer commencing haemodialysis in hospital (42% vs 77%) or with a catheter (37% vs 69%). While this study is limited in size and statistical power, it emphasises the role of nurse-led pre-dialysis care as a means to support patients through this difficult transition and maximise their choices.

Chronic Kidney Disease, Fluid and Electrolytes

ISN Academy: [Chronic Kidney Disease, Fluid and Electrolytes](#)

Strict control of serum potassium may slow progression of uraemic neuropathy

Randomized, Controlled Trial of the Effect of Dietary Potassium Restriction on Nerve Function in CKD

[Arnold, et al. Clin J Am Soc Nephrol. 2017;12\(10\):1569-77](#)

Uraemic neuropathy is common in advanced CKD and no disease modifying therapies are available. Neurophysiology studies in patients on dialysis have shown that correction of hyperkalaemia may improve nerve function. Arnold, et al. sought to test the hypothesis that lowering serum potassium would slow the progression of neuropathy in CKD. Forty-seven participants with a mean eGFR of $35 \pm 8 \text{ mL/min/1.73m}^2$ were randomized and followed over a two-year period. The intervention group received individualised dietary advice aimed at maintaining serum potassium $\leq 4.5 \text{ mmol/L}$ (4.5 mEq/L). Sodium polystyrene sulfonate was provided if this target was not met. The control group received general dietary advice only. Mean serum potassium during the study period was lower in the intervention group (4.6 ± 0.5 vs 4.8 ± 0.4 ; $p=0.03$). The primary outcome, total neuropathy score (evaluated by a blinded observer), increased in both arms over the duration of the trial, however the increase was reduced in the treatment group compared to the control group (0.4 ± 2.2 vs 2.8 ± 3.3 ; $p < 0.001$). An improvement in gait speed and nerve excitability was also seen in the treatment group. No changes in other measures of nerve function were seen. This study suggests elevated potassium (within the normal range) may play in the pathophysiology of uraemic neuropathy – although the small study size and loss to follow up (only 70% completed the final two-year visit) limits the strength of the conclusions. Further studies to test this intriguing hypothesis are warranted.

Mineral and Bone Disorders, Hemodialysis

ISN Academy: [Mineral and Bone Disorders, Hemodialysis](#)

Etelcalcetide, an intravenous calcimimetic, effectively suppresses PTH

A phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of etelcalcetide (ONO-5163/AMG 416), a novel intravenous calcimimetic, for secondary hyperparathyroidism in Japanese haemodialysis patients

[Fukagawa, et al. Nephrol Dial Transplant. 2017;32\(10\):1723-30](#)

Cinacalcet, an oral calcimimetic, effectively suppresses PTH secretion in ESKD and reduces the incidence of parathyroidectomy, although its true impact on cardiovascular events and mortality is not clear. Fukagawa, et al. report the results of a phase III trial of a novel intravenous calcimimetic - etelcalcetide - in a double-blind trial of 155 participants with secondary hyperparathyroidism on dialysis ($\text{PTH} \geq 300 \text{ pg/mL}$ [31.5 pmol/L]). Participants received thrice weekly doses of etelcalcetide (titrated to target PTH and calcium) or placebo for 12 weeks. The primary outcome of achieving Japanese Society for Dialysis Therapy target PTH of $60\text{-}240 \text{ pg/mL}$ ($6.3\text{-}25.2 \text{ pmol/L}$) was achieved in 59.0% of the etelcalcetide group as compared to 1.3% of the placebo group. Drug-related adverse events were more common with etelcalcetide than with placebo (19.2% versus 3.9%) however there were no severe adverse events and treatment was discontinued in only 2 participants. In conclusion, this study shows etelcalcetide, a novel intravenous calcimimetic administered thrice weekly, to be efficacious and tolerable in Japanese dialysis patients.

Mineral and Bone Disorders, Chronic Kidney Disease

ISN Academy: [Mineral and Bone Disorders, Chronic Kidney Disease](#)

Cholecalciferol improves vascular function in vitamin D deficient CKD

A Randomized Trial of Vitamin D Supplementation on Vascular Function in CKD

[Kumar, et al. J Am Soc Nephrol. 2017;28\(10\):3100-08](#)

Cardiovascular disease is the prime cause of mortality in CKD. Observational studies suggest vitamin D may improve endothelial function (thought to be mediated via increased nitric oxide production), however this has not been confirmed in a clinical trial. Kumar, et al. sought to determine the impact of correcting vitamin D deficiency on vascular function. They randomised 120 participants with non-diabetic CKD stage 3-4 and 25-hydroxyvitamin D levels $\leq 20 \text{ ng/mL}$ in a double-blind fashion to receive two 300,000 IU doses of cholecalciferol or placebo at baseline and 8 weeks. At 16 weeks, endothelium-dependent brachial artery flow-mediated dilatation was significantly improved in

the cholecalciferol group compared to placebo (between-group difference in mean change $5.49 \pm 1.15\%$; $p < 0.001$). Significant improvements were also found in pulse wave velocity and levels of IL-6, although other markers of inflammation and vascular dysfunction (E-selectin, vWF and CRP) were not significantly different. These results provide support for a randomized trial examining the impact of correction of vitamin D deficiency on clinical endpoints in patients with CKD.

Transplant

ISN Academy: [Transplant](#)

Increased acute rejection with belatacept compared to tacrolimus

A Randomized Controlled Clinical Trial Comparing Belatacept With Tacrolimus After De Novo Kidney Transplantation

[De Graaf, et al. Transplantation. 2017;101\(10\):2571-81](#)

Belatacept (an inhibitor of CD28-CD80/86 mediated co-stimulation) has been associated with improved graft function compared to cyclosporin in a previous randomised controlled trial, however an increased risk of acute rejection was noted. De Graaf, et al. aimed to investigate the utility of monitoring T-cell subsets to predict acute rejection in belatacept-treated patients. They performed a randomised trial of 40 standard-risk renal transplant recipients randomised to belatacept (at the same dosage as the 'low-intensity' arm of the BENEFIT trial) or tacrolimus and followed for one year. Both groups received basiliximab, mycophenolate and prednisolone. The rate of acute rejection was higher in the belatacept group compared to the tacrolimus group (55% vs 10%; $p = 0.006$) and all of the 3 cases of graft loss occurred in the belatacept group. Monocyte CD86 was saturated at all timepoints in belatacept treated participants, suggesting sufficient co-stimulation blockade. None of the studied T-cell subsets were predictive of rejection. This study, while small in size, raises important questions about the risk of acute rejection with belatacept and may inform the design of future trials.
