Hemodialysis, Acute Kidney Injury

No short-term benefits of high-cutoff dialysis for myeloma cast nephropathy, although the possibility of long-term benefit remains

**Effect of High-Cutoff Hemodialysis vs Conventional Hemodialysis on Hemodialysis Independence Among Patients With Myeloma Cast Nephropathy: A Randomized Clinical Trial**


Cast nephropathy is the most common cause of acute kidney injury in patients with multiple myeloma and reduced renal function adversely affects prognosis. High-cutoff membranes are designed to reduce the burden of circulating light chains and to prevent or reverse kidney injury. The MYRE study recruited 98 patients from 48 centres in France with newly diagnosed myeloma, biopsy-proven cast nephropathy and an indication for hemodialysis. All patients received chemotherapy with bortezomib and dexamethasone. Both groups received eight 5-hour sessions of hemodialysis in the first 10 days with three additional weekly sessions until 3 cycles of chemotherapy had been completed. For these study sessions, the intervention group used a high-cutoff membrane (Theralite), whereas the conventional treatment group used a standard high-flux membrane. Any additional hemodialysis was delivered according to local practice. Ninety-four patient were included in the modified intention-to-treat analysis. There was no difference in the primary outcome of dialysis independence at 3 months (19/46 (41%) in the high-cutoff group and 16/48 (33%) in the standard group; p=0.42). However, by 6 and 12 months, the proportion of dialysis-independent patients appeared greater in the high-cutoff group (57% vs 35%, p=0.04 and 61% vs 38%, p=0.02, respectively). The proportion of patients alive and not on dialysis was comparable at 12 months in the high-cutoff group (24/37 vs 17/38, p=0.15). As expected, the reduction in serum-free light chain levels was significantly greater with high-cutoff dialysis, although this did not translate into shortened time to dialysis independence; median time to dialysis independence was 2 months in the high-cutoff group versus 1 month in the conventional dialysis group (p=0.26). Overall mortality at 12 months did not differ (9/46 (20%) vs 10/48 (21%)). This study failed to achieve its primary endpoint and prove the original hypothesis as designed by the trial leadership, but the potential improvement in dialysis independence at 6 and 12 months could be important and requires confirmation in a dedicated trial. The conclusions are limited by the small sample size and secondary nature of the endpoints at 6 and 12 months. Debate over the merits of high-cutoff dialysis for myeloma cast nephropathy is set to continue.

Focus on Mental Health: Chronic Kidney Disease

**Sertraline not effective for depression in CKD**

**Effect of Sertraline on Depressive Symptoms in Patients With Chronic Kidney Disease Without Dialysis Dependence: The CAST Randomized Clinical Trial**


Depression is a common co-morbidity in patients with chronic kidney disease (CKD) and the efficacy and side-effect profile of commonly used anti-depressants is not well understood. Hedayati, et al. randomised 201 participants with non-dialysis CKD stages 3-5 and major depressive disorder (diagnosed by neuropsychiatric interview) to receive sertraline or placebo. The dose of treatment was titrated up to a maximum of 200mg/day based on tolerability and effect. The primary outcome was change in depression score (Quick Inventory of Depressive Symptomatology – Clinician Rated, range 0-27) between baseline and 12 weeks. After excluding eight participants who exited the study within the first two weeks, the modified intention-to-treat analysis showed an improvement in depression score of 4.1 in the treatment group and 4.2 in the placebo group (95% CI for between group mean difference -1.1, 1.3; p=0.83). Regression analysis confirmed no differences in the number of patients responding to therapy (≥ 50% improvement in depression score) or achieving remission of depression (depression score ≤ 5). Although only
conducted at 3 centres, the results of this study are strengthened by its double-blind design, formal diagnosis of major depression and high treatment adherence. It adds to a growing body of evidence suggesting that selective serotonin reuptake inhibitors (SSRIs) may have minimal impact on depression in patients with chronic medical illness. A role for these agents in severe depression is not excluded, but their general use in patients with CKD is not supported by evidence. Future work will need to focus on alternative agents or non-pharmacological therapy.

Focus on Mental Health: Hemodialysis

Mindfulness in the dialysis unit: it can be done

**Brief Mindfulness Meditation for Depression and Anxiety Symptoms in Patients Undergoing Hemodialysis: A Pilot Feasibility Study**


Hemodialysis patients have high rates of anxiety and depression which may go undetected or unaddressed. Mindfulness meditation has gained popularity and shown benefits not only in psychiatric disorders, but also some chronic physical illnesses. The use of mindfulness for dialysis patients has not been tested in a rigorous trial. In a pilot study, Thomas, et al. recruited 41 hemodialysis patients with depression or anxiety (as determined by scores ≥6 on Patient Health Questionnaire-9 (PHQ-9) and/or General Anxiety Disorder-7 (GAD-7) instruments). Patients were randomised to receive guided individual mindfulness sessions three times per week. Each session lasted 10-15 minutes and was conducted while the patient was on dialysis. The intervention and control groups received psychoeducational literature regarding anxiety and depression. By 8 weeks, 71% of participants in the mindfulness group completed the intervention (receiving > 80% of scheduled sessions). Participants rated their enjoyment of the sessions 8 out of 10, suggesting that mindfulness was well received; however there were no significant changes in PHQ-9 or GAD-7 scores. The authors conclude that it is feasible to deliver a mindfulness program in an RCT context to patients while on dialysis. We look forward to larger, adequately powered studies to determine the effectiveness of this intervention. The use of pilot studies to demonstrate that interventions can be delivered before launching into larger, resource-intensive trials should also be more widely used.

Mineral & Bone Disorders

Sevelamer does not reduce FGF-23 levels in normophosphataemic patients with CKD

**Randomized Clinical Trial of Sevelamer Carbonate on Serum Klotho and Fibroblast Growth Factor 23 in CKD**


Fibroblast growth factor 23 (FGF-23) is a phosphaturic hormone produced in response to rising serum phosphate. It plays a key role in the pathology of bone disease and vascular calcification in CKD. Klotho is a coreceptor for FGF-23 and low levels are associated with adverse cardiovascular outcomes. Elevated FGF-23 and reduced Klotho are both apparent in CKD prior to hyperphosphataemia. The impact of phosphate binders on FGF-23 and klotho levels in different stages of CKD is unclear as previous studies have produced divergent results. Liabeuf, et al. conducted a multicentre double-blinded randomised controlled trial to determine if phosphate lowering therapy could reduce levels of FGF-23 and boost Klotho in normophosphataemic patients with CKD Stage 3b-4. Seventy-eight patients at 14 clinics, with an eGFR of 15-45ml/min/1.73m², a phosphate >3.1mg/dl (1.0mmol/l) and FGF-23 > 80 relative units/ml were randomised to receive sevelamer (4.8g three times per day with meals) or placebo. All patients received 100,000IU of cholecalciferol at baseline. Treatment continued for 12 weeks. Despite a reduction in urine phosphate:creatinine ratio, no significant changes were observed in FGF-23, alpha-klotho or serum phosphate. Per-protocol analyses did not change these conclusions. The results are in line with studies using lanthanum instead of sevelamer and raise questions about the efficiency of targeting phosphate levels in pre-dialysis CKD.
Mycophenolate may preserve residual renal function in peritoneal dialysis

Protective effect of mycophenolate mofetil on residual renal function in peritoneal dialysis patients: An open label feasibility study


Loss of residual renal function is a key determinant of prognosis in both hemodialysis and peritoneal dialysis (PD). Mycophenolate has been shown to reduce or slow the progression of renal fibrosis in a range of renal diseases. Wang, et al. set out to determine if this antifibrotic action could be used to preserve residual renal function by recruiting 60 participants starting PD with a measured GFR > 5ml/min/1.73m² (calculated by mean of urea and creatinine clearance). They were randomised (in open-label fashion) to 1.0-1.5g mycophenolate mofetil per day (in divided doses) for 6 months followed by 0.5-0.75g per day for another 6 months. Both groups were treated to a systolic blood pressure of <140mmHg, although use of ACE inhibitors and ARBs was not permitted. After 12 months, there were significant differences in favour of mycophenolate, with the treatment group having a higher measured GFR (5.44 vs 4.43, p<0.001) and urine output (955 vs 786ml/day, p=0.024). There were no significant differences in adverse effects between groups. While these results may encourage further research into this novel approach to the preservation of residual renal function, the open-label nature of the trial and the lack of description of allocation concealment mean they should be interpreted with some caution. In addition, close attention will need to be paid to the risks of immunosuppression and the clinical importance of an eGFR difference of 1 ml/min and a urine output difference of 169ml/day are uncertain.