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# Does incremental initiation of haemodialysis preserve native kidney function ? A multi-centre feasibility randomised controlled trial.

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Background:

Incremental Haemodialysis(IHD), a method of individualising haemodialysis(HD) dose according to level of residual renal function(RRF) such that as RRF reduces, HD dose is upwardly adjusted. Retrospective data suggests potential benefit of this approach in preserving RRF, a key predictor of survival for dialysis patients.

Method:

A randomised, intention-to-treat, multi-centre trial was designed to determine the feasibility of a future definitive trial of IHD to establish if this approach preserves RRF. The trial was designed to estimate effect size of potential benefit in terms of RRF.

55 patients with renal urea clearance(KrU)≥3ml/min/1.73m2BSA and within 3-months of starting HD were randomised across 4 centres to either conventional thrice-weekly HD(3XHD) for 3.5-4 hours or IHD. The IHD protocol involved initiation of HD twice-weekly after randomisation and upward adjustment of HD frequency and time as RRF was lost.

3XHD patients were dialysed to Standard Kt/VDialysis>2.0. IHD patients were dialysed to Standard Kt/VDialysis+Standard Kt/VRRF>2.0. Both groups were dialysed to same target, except that urea clearance incorporated RRF in IHD arm. Patients were withdrawn for transplant, dialysis modality change or patient's choice. Follow up was for 6-months (primary outcome data) but secondary outcome data will be for 12-months.

The primary outcome was rate of change of RRF in the first 6-months after randomisation (effect size of intervention). Recruitability, retainability, protocol adherence and rate of adverse events were also measured as a primary objective. As a secondary outcome, we determined proportion of patients with KrU≥2 and ≥3ml/min/1.73m2BSA at 6-months. Impact of dialysis treatment was measured using questionnaire-based assessments at baseline and 6-months.

Results:

26 patients were randomised to 3XHD and 29 to IHD. Baseline demographics including age, weight, haemoglobin, blood pressure, Charleson Comorbidity Index, were not significantly different between study arms. Baseline KrU was 5.1±SD 1.8 ml/min/1.73m2BSA in 3XHD arm and 5.72±SD 2.49 ml/min/1.73m2BSA in IHD arm. At 6-months, KrU reduced to 2.68±SD 1.73 in 3XHD arm and 3.80±SD 1.85 in incremental arm. In first 6-months, 3 patients recovered to dialysis independence (3XHD=1:IHD=2). Slope of RRF was not

significantly different between two arms(p=0.39). The proportion of patients with significant KrU>2ml/min/1.73m2BSA at 6-months was significantly higher in IHD arm(92%) compared to 3XHD arm(65%), p=0.032. Rate of major adverse cardiac events, fluid overload, hyperkalaemia, vascular access events, deaths and infections did not differ significantly between groups. There were 2 deaths in 3XHD arm(4025 patient days) versus 1 in IHD arm in the first 6-months(4666 patient days).
There was no significant difference in Clinical Frailty Score, Montreal Cognitive Assessment score, depression score(PHQ-9), Quality of Life(EQ-5D-5L) and Illness Intrusiveness Rating Scale between groups at baseline and 6-months.

Conclusion:

Rate of loss of RRF(slope) was not significantly different between 3XHD and IHD arms but IHD was associated with significantly higher probability of retaining KrU>2ml/min/1.73m2. There was no evidence of any clinical detrimental effect of IHD in terms of mortality, fluid overload or hyperkalaemic events. IHD does not appear to be harmful and may confer a small benefit to preservation of RRF. A definitive study is required to define clinical benefits further.