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Dialysis Dosing in Acute Renal Failure

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In the winter issue of **ICU Management** 2005, Drs Kellumand Venkataraman reviewed evidence on timing of initiation of renal replacement therapy in Acute Renal Failure (ARF). In this article, they review the limitations of research to date on the appropriate dose of renal replacement therapy of patients with ARF.

The appropriate dose of renal replacement therapy (RRT) of patients with acute renal failure (ARF) is a matter of considerable debate. The dose of intermittent dialysis is quantified using the unitless index, Kt/V, where K represents urea clearance, t is the time of dialysis and V is the volume of distribution of urea. Existing literature supports a singlepool Kt/V urea of at least 1.2 per treatment, at least 3 times weekly, as the minimum dose in patients with end-stage renal disease (ESRD) (National Kidney Foundation 1997). Arguably, most patients with ARF are more ill, malnourished and catabolic than ESRD patients and hence warrant “more” RRT. While supported by small, retrospective and non-randomized studies (Paganini 1996; Schiffle 1997), until recently this hypothesis had not been tested by randomized trials.

Although an optimal dialysis dose has not been established in patients with ARF, it is generally accepted that the delivered dose of dialysis should be at least as great as that recommended for ESRD. Despite this, a recent prospective study of 40 patients (136 dialysis treatments) with ARF treated with intermittent haemodialysis (IHD), reported that prescribed Kt/V was less than 1.2 in 49% of treatments, and more importantly delivered Kt/V was less than 1.2 in nearly 70% of treatments (Evanson et al. 1998). In a recent study, Schiffl et al. assigned 160 critically ill, but haemodynamically stable, patients with ARF to daily or every other day haemodialysis, in alternating order (Schiffl et al. 2002). The two study groups were similar at baseline. Mortality was 28% in patients assigned to daily IHD as compared to 46% with alternate-day dialysis (P=0.01). Daily haemodialysis also resulted in faster resolution of ARF (mean [± SD], 9 ± 2 days vs. 16 ± 6 days; P=0.001), better control of uraemia and fewer hypotensive episodes during haemodialysis than conventional haemodialysis. Although this study is supportive of a more intensive dialysis prescription in ARF, it has several important limitations. First, the exclusion of haemodynamically unstable patients eliminated the sickest patients (these patients were treated with continuous RRT instead) and diminished generalizability. Second, the non-random assignment of patients to groups may have introduced bias, although the reported baseline characteristics of the two groups appear similar. Finally, the delivered dose of therapy in the alternate-day group was substantially lower than accepted as “adequate” haemodialysis as described above.

In continuous haemofiltration, dose of therapy correlates with effluent flow rate (Clark et al. 1992; Clark et al. 2003). Using effluent flow as an index of dose of therapy, a recent single centre RCT demonstrated that higher haemofiltration doses improved patient survival in ARF compared to conventional doses, while further increases in dose were not helpful (see table 1: Ronco et al. 2000). Of note, more than 90% of patients in this study received the prescribed dialysis dose. However, a second recent smaller RCT did not show similar results. In this study, 106 patients with oliguric ARF (defined as refractory to furosemide) were randomized to three (almost equal) groups for early high- and low-volume and late low-volume haemofiltration (see table 1: Bouman et al. 2002). No differences in 28-day survival or duration of ARF were found between these groups. This study was however limited in that it was underpowered and probably enrolled less sick patients as suggested by very high survival rates.

Similar to IHD in ARF, CRRT delivery may not reach the levels prescribed. In a single centre retrospective review of CRRT dosing patterns, we found that the mean CRRT dose prescribed for patients with ARF was only 24.46 ± 6.73 ml/Kg/h, and that the mean dose delivered was merely 16.55 ± 5.41 ml/Kg/h (68% of the prescribed dose, p<0.000001) (Venkataraman et al. 2002). While there was high concordance between prescribed and delivered effluent flow rates in this study, treatment time was reduced (16.1 ± 3.53 hours/day) due to interruptions in therapy.

Although these clinical studies suggest that more intensive renal support may improve survival, they have significant limitations and hence are not widely accepted into clinical practice. An ongoing multicentre trial (Palevsky et al. 2005) is now comparing intensive renal support to

conventional management of renal replacement therapy in critically ill patients with acute renal failure to provide a more definitive answer to this question.

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