

Adequacy of haemodialysis and or haemofiltration treatments for patients with acute kidney injury

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Abstract

Traditionally, the dose of haemodialysis or haemofiltration delivered to patients with kidney failure is assessed by urea clearance. For patients with chronic kidney disease below a critical urea clearance threshold, patient wellbeing is compromised. It was suggested, therefore, that the dose of dialysis or haemofiltration delivered could also affect outcomes for patients with acute kidney injury. Two major prospective multicentre clinical trials have recently reported that a higher intensity of renal support, by either intermittent haemodialysis or continuous renal replacement therapy, did not improve patient survival or recovery from dialysis. It must be recognised, however, that urea clearance is only one component of renal supportive therapy, and other aspects, including volume control, electrolyte homeostasis and acid-base balance, may be equally important targets for patients with acute kidney injury.

Introduction and context

The National Cooperative Dialysis Study, the first randomised controlled study of dialysis dose, defined an 'adequacy' threshold for end-stage chronic kidney disease patients receiving chronic haemodialysis [1] based on the dialyser clearance of urea, a small solute marker of nitrogen turnover, which was defined in terms of a dimensionless parameter known as the normalised urea clearance, or Kt/V (K , dialyzer urea clearance; t , dialysis session duration; and V , urea volume distribution). Below a sessional threshold Kt/V of 0.9 for standard thrice-weekly schedules, complication-free survival was compromised within months [2]. Subsequent observational studies suggested that higher doses resulted in improved longer-term outcomes [3,4], and by consensus the minimum target Kt/V was raised to 1.2 [5]. A subsequent prospective randomised controlled study, the Hemodialysis (HEMO) study, reported that higher doses did not appear to further improve outcome [6]. However, subgroup analysis suggested that women may benefit from higher Kt/V doses, fuelling suggestions that using standard Kt/V targets to prescribe dialysis may lead to under-dosing in women

and small men [7]. These studies suggest that, for standard thrice-weekly therapy, medium-term survival (measured in months) is dependent on achieving a minimum level of small solute removal, as defined by the National Cooperative Dialysis Study.

Just as the amount of dialysis delivered to patients with end-stage chronic kidney disease is important in determining survival, it was reported that the dose of intermittent haemodialysis or continuous renal replacement therapy (CRRT) was also important in determining survival in patients with acute kidney injury (AKI) [8-10], although this was not a universal finding [11]. As patients with AKI continue to have high mortality, and evidence-based clinical management is somewhat limited [12], two prospective multicentre trials were designed to investigate the effect of dose of renal replacement therapy on outcome in patients with AKI [13,14].

Recent advances

The Veterans Affairs/National Institutes of Health (VA/NIH) study essentially randomised patients to

initially receive either an intensive or less intensive dose of intermittent haemodialysis, or an intensive or less intensive dose of CRRT [13], depending upon severity of illness at the time of randomisation. (During the course of the study patients were switched between treatment modalities according to haemodynamic stability.) During haemofiltration, it is assumed that urea is effectively cleared (to the extent that the concentration in the effluent ultrafiltrate is equal to that of plasma water) so that urea clearance can simply be assessed by the total ultrafiltration volume achieved. In this study, more intensive renal replacement therapy did not show any survival advantage for either the intermittent haemodialysis or CRRT groups. However, the minimum haemodialysis target Kt/V of 1.2 was somewhat higher than that typically prescribed for patients with AKI by the recruiting centres. In addition, there was no survival advantage for the haemofiltration cohort compared to those treated by dialysis. Haemofiltration clears solutes primarily by convection, thus removing a larger spectrum of solutes than haemodialysis, which predominantly clears small water soluble solutes by diffusion.

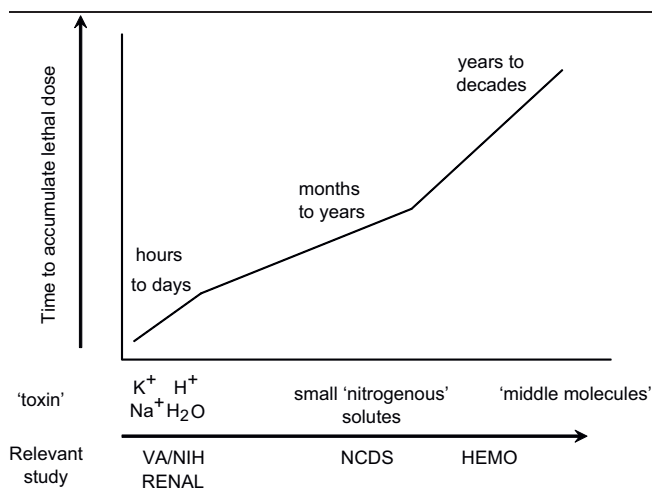
The second study, the RENAL (Randomised Evaluation of Normal versus Augmented Level of renal replacement therapy in ICU) study, assessed the effect of an augmented dose of CRRT (an ultrafiltration rate of 40 ml/kg/h versus 25 ml/kg/h) [14]. Once again, this study failed to show any significant effect of dose of convective renal replacement therapy on patient outcomes, although the delivered dosages were less than that prescribed and both small patients (<60 kg) and very heavy patients (>120 kg) were excluded.

Implications for clinical practice

What implications do these studies have for the clinical management of patients with AKI? Although urea can dissociate to cyanate in plasma water and then form carbamylated products in a reversible fashion, with some analogy to glycosylation [15], it would appear that toxicity from the accumulation of small nitrogenous solutes is not the major determinant of short-term outcome (days to weeks) in patients with AKI.

AKI frequently occurs in the setting of multiple organ failure, and mortality remains high, with patient outcome typically dependent upon the severity of the underlying condition and associated co-morbidities. The replacement of organ function may play a critical short-term role in maintaining life in patients already destined by other factors to have the potential to recover. However, urea clearance is only one component of renal replacement therapies. For example, failure to correct persistent volume overload is associated with not only

Figure 1. Schematic hypothetical representation of the time course for the accumulation of azotemic toxins in patients with both acute kidney injury and chronic kidney failure



The schematic illustrates that different 'toxins' play a role over time, and as such may require different clinical management strategies. HEMO, Hemodialysis; NCDS, National Cooperative Dialysis Study; RENAL, Randomised Evaluation of Normal versus Augmented Level of renal replacement therapy in ICU; VA/NIH, Veterans Affairs/National Institutes of Health.

increased post-surgical morbidity [16], but also increased risk of AKI [17] and mortality [18]. Thus, for patients with AKI, the adequate removal of even smaller moieties than urea is the principal determinant of the 'adequacy' of renal replacement. These moieties are the neglected 'uraemic' toxins, including potassium, sodium, hydrogen ions and water [19] (Figure 1). The consequences of the accumulation of these moieties, hyperkalaemia, pulmonary oedema, and acidosis, may be lethal in minutes [20].

Although the delivery of higher doses of haemofiltration or more frequent haemodialysis did not improve overall outcome, higher volume CRRT exchange cycles and more frequent haemodialysis treatments will help correct acidosis, and may be appropriate during the initial resuscitation phase of AKI. Correction of volume overload may help explain the positive findings and improved clinical outcomes reported from some of the earlier trials of increased dose of renal support [9], compared to the more recent VA/NIH and RENAL studies, which had similar fluid balance targets.

Abbreviations

AKI, acute kidney injury; CRRT, continuous renal replacement therapy; RENAL, Randomised Evaluation of Normal versus Augmented Level of renal replacement

therapy in ICU; VA/NIH, Veterans Affairs/National Institutes of Health.

Competing interests

The author declares that he has no competing interests.

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