Effect of Intermittent Hemodialysis Frequency on Metabolic Control in Acute Renal Failure

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Quantification of the prescribed and delivered doses of renal replacement therapy (RRT) in end-stage renal disease (ESRD) is now commonly performed, since recent data demonstrate a clear relationship between dialysis dose and outcome. In recent years, some of the quantification techniques developed for ESRD patients have been extended to the acute renal failure (ARF) setting. This extension has allowed the assessment of the specific effect of the frequency of intermittent hemodialysis (IHD) on delivered dialysis dose and metabolic control. In this review, after a discussion of the manner in which therapy prescription factors differ in the ARF and ESRD settings, the issue of the frequency of IHD in the ARF setting is explored.

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Key words

Intermittent dialysis, azotemia, acute renal failure, hypercatabolism

Introduction

Quantification of the prescribed and delivered doses of renal replacement therapy (RRT) in end-stage renal disease (ESRD) is now commonly performed, since recent data demonstrate a clear relationship between dialysis dose and outcome (1–4). In recent years, some of the quantification techniques developed for ESRD patients have been extended to the acute renal failure (ARF) setting (5–13). This extension has allowed the assessment of the specific effect of the frequency of intermittent hemodialysis (IHD) on delivered dialysis dose and metabolic control. In this review, after a discussion of the manner in which therapy prescription factors differ in the ARF and ESRD settings, the issue of the frequency of IHD in the ARF setting is explored.

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Therapy prescription factors in ARF

Prescribing RRT to a critically ill ARF patient involves consideration of a number of factors. As shown in Table I, the factors of specific importance in ARF may be both qualitatively and quantitatively different from those applying to the ESRD setting. For example, the clinical significance of both urea distribution volume (V) and the normalized protein catabolic rate (nPCR) in critically ill ARF patients differs greatly from that in relatively stable ESRD patients. In the latter group, V reflects total body water at dry weight, while nPCR provides an estimate of dietary protein intake. On the other hand, the frequent occurrence of severe volume overload in intensive care unit (ICU) ARF patients prevents attainment of dry weight, at least early in the ARF course. Previous kinetic analyses in ARF (6,14) have confirmed that V, expressed as a percentage of body weight, is substantially higher than typical values reported for stable ESRD patients (50% – 60% of body weight).

The nPCR is used as an estimate of dietary protein intake for stable ESRD patients in net nitrogen balance and is typically in the 0.75 – 1.2 g/kg/day range. On the other hand, nPCR and dietary protein intake are uncoupled in ARF due to the severe pro-

TABLE I RRT prescription factors in ARF

Extent of protein hypercatabolism
Body size/total body water (including effect of volume overload)
Access recirculation
Desired level of metabolic control
Ability of chosen RRT to achieve treatment goal

RRT = renal replacement therapy; ARF = acute renal failure.

tein hypercatabolism (nPCR 1.5 – 4.0 g/kg/day) and net negative nitrogen balance that frequently exist (5–7,15–19). Hypercatabolism is a hallmark of ARF and is essentially a marker of illness severity. Another difference in nPCR between ESRD and ARF is this parameter's daily variability frequently observed in the latter setting.

The primary goals of therapy represent another fundamental difference between ESRD and ARF, at least in terms of small solute removal. In ESRD patients, recent studies performed in patients receiving standard thrice-weekly hemodialysis suggest dialysis dose (i.e., Kt/V or urea reduction ratio) is an important determinant of outcome. Due to the interrelationship between dialysis dose, nPCR, and time-averaged azotemia control, the latter is not used as a therapy target in ESRD patients. On the other hand, a desired level of azotemia control is one of the primary considerations when a RRT is prescribed to a critically ill ARF patient. Therefore, the selection of a particular RRT and the attendant treatment intensity are really determined by the desired metabolic control level.

Effect of IHD intensity on ARF outcome

Retrospective studies (20–22) published in the 1970s and early 1980s suggested that a reasonable goal for IHD is initiation of therapy before the blood urea nitrogen (BUN) concentration reaches 100 mg/dL. In addition, these studies suggested that IHD intensity should allow the predialysis BUN to be maintained below the same value.

The effect of IHD intensity on ARF outcome was prospectively assessed by Gillum *et al*. (23) more recently. A total of 34 patients received either intensive or nonintensive IHD. Patients in the intensive group generally received daily dialysis for 5 – 6 hours/treatment, while a conventional dialysis frequency (approximately once every other day) was prescribed to the nonintensive group. These two different regimens resulted in mean predialysis BUN values of approximately 60 and 100 mg/dL in the intensive and nonintensive groups, respectively. Relatively intensive IHD did not favorably influence outcome in this study, since survival was not significantly different between the two groups.

Although this study remains the only prospective trial of ARF RRT intensity to date, its design requires comment. The study population was quite small and not a homogeneous group, since ARF etiologies were very diverse. Therefore, extrapolation of this study's results specifically to the ICU ARF population may be problematic. The use of nonultrafiltration control dialysis machines and bioincompatible membranes also is generally at odds with present IHD practice in the ICU. Finally, sufficient data to estimate dialysis dose and protein catabolic rate were not provided.

Effect of IHD schedule in ARF

Our group has recently assessed the effect of IHD frequency on efficiency in hypercatabolic ARF patients (7), particularly in relation to the efficiency of continuous RRT (CRRT). We developed a computer-based model designed to permit individualized RRT prescription to ARF patients. The critical input parameter is the desired level of metabolic control, which is the time-averaged BUN (BUN_a) or steady-state BUN (BUN_s) for IHD or CRRT, respectively. The basis for the model was a group of 20 patients who received uninterrupted CRRT for at least 5 days. In these patients, the nPCR increased linearly (r = 0.974) from 1.55 ± 0.14 g/kg/day (mean±SEM) on day 1 to 1.95 ± 0.15 g/kg/day on day 6. From this relationship, BUN versus time profiles were obtained for simulated patients treated with either a CRRT at varying levels of urea clearance (500 – 2000 mL/hr) or IHD regimens (K = 180 mL/minutes, T = 4 hours) of variable frequency (3 – 7 treatments/week).

One part of this study was the development of IHD frequency requirements to attain varying levels of desired time-averaged azotemia control for patients of varying dry weight (Figure 1). For a reasonable BUN_a target of 80 mg/dL, our analysis demonstrated that IHD frequency requirements ranged from 3.2 to 6.2 treatments/week for 50- and 100-kg dry weight patients, respectively. Our analysis also showed that the attainment of more intensive metabolic control (BUN_a = 60 mg/dL) was not achievable even with daily dialysis in relatively large patients (dry weight >80 kg).

We also assessed the effect of variable IHD intermittence by plotting both IHD BUN_a and CRRT BUN_s versus the ratio nPCR/$(Kt/V)_d$, where $(Kt/V)_d$ is the normalized daily therapy dose. A linear relationship was observed when these regression analy-

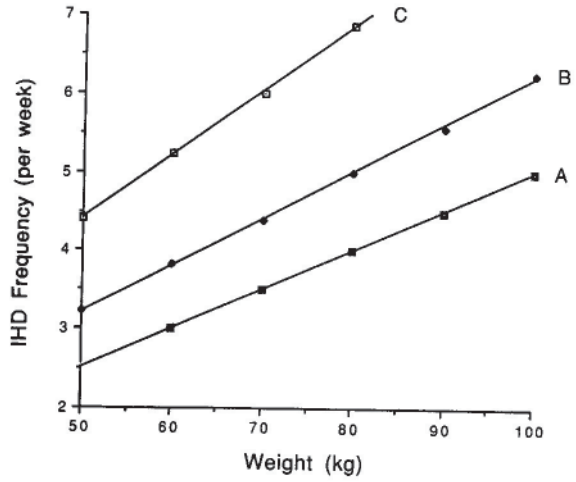

FIGURE 1 Predicted IHD frequencies required for the attainment of varying desired levels of time-averaged azotemia control (BUN_a). The frequencies are shown for patients ranging in size from 50 to 100 kg. The target BUN_a values for curves A, B, and C are 100, 80, and 60 mg/dL, respectively. Reprinted with permission from Reference 7. IHD = intermittent hemodialysis.

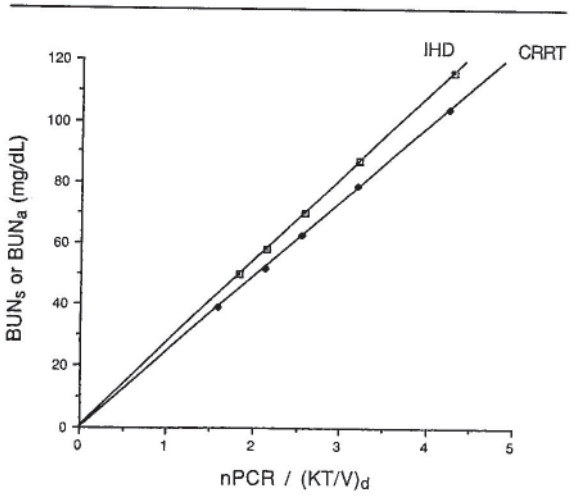

FIGURE 2 Steady-state RRT azotemia control versus the ratio $nPCR/(Kt/V)_d$. The curves are shown for a patient of dry weight 70 kg. The CRRT line represents BUN_s values, while the IHD line represents BUN_a values. Reprinted with permission from Reference 7. RRT = renal replacement therapy; nPCR = normalized protein catabolic rate; CRRT = continuous RRT; BUN_s = steady-state blood urea nitrogen; BUN_a = time-averaged BUN.

ses were performed (Figure 2). The two regression lines shown are for a simulated patient of dry weight 70 kg. Because nPCR was constant in these steady-state simulations (1.95 g/kg/day), variations in the abscissa were due entirely to changes in $(Kt/V)_d$. In turn, changes in therapy dose were related to changes in K for CRRT and in treatment frequency for IHD. Therefore, the points determining the CRRT line represent K values ranging from 750 mL/hour [highest $nPCR/(Kt/V)_d$ value] to 2000 mL/hour [lowest $nPCR/(Kt/V)_d$ value]. On the other hand, the points on the IHD line represent treatment frequencies ranging from 3/week [highest $nPCR/(Kt/V)_d$ value] to 7/week [lowest $nPCR/(Kt/V)_d$ value]. The figure demonstrates that the degree of divergence between the CRRT BUN_s and IHD BUN_a lines decreases with increasing IHD frequency, or decreasing $nPCR/(Kt/V)_d$. This convergence demonstrates that the inherent inefficiency associated with an intermittent therapy, relative to that of a continuous therapy, decreases with increasing treatment frequency.

Summary

Methods to quantify dialysis dose in ARF have been presented, with special attention paid to the effect of IHD frequency on metabolic control and efficiency. Future studies will need to confirm the applicability of these methods in ARF patients. These methods may be useful if another prospective assessment of the effect of IHD intensity on outcome is performed.

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