Normalization of Dialysis Dose for Daily Dialysis

The equilibrated Kt/V (eKtV) is widely used in hemodialysis (HD) as a measure of the intensity (magnitude) of an individual dialysis treatment. Adequate eKt/V for thrice-weekly hemodialysis (twHD) has been extensively studied, and a value in the range 1.0 – 1.1 per treatment (3.0 – 3.3 weekly) is generally considered to represent adequate therapy for this specific frequency of dialysis. However, for other schedules, summing eKt/V’s and time-averaging the clearance is not appropriate. This was first demonstrated several years ago by the observation that a weekly eKt/V of 2.0 in continuous ambulatory peritoneal dialysis (CAPD) is therapeutically equal to a weekly eKt/V of 3.0 in twHD. That paradox has been resolved by the standard Kt/V (stdKt/V), which accounts for the first order nature of solute removal by dialysis, and which correctly predicts a normalized weekly stdKt/V of 2.0 for both CAPD and twHD.

The equivalent renal clearance (EKR) has also been advanced as a method to normalize dose for varying treatment schedules. However, mathematical consideration shows that EKR is an exact time-averaged clearance. Analysis of data reported for daily dialysis by Piccoli et al. in the present issue of Hemodialysis International shows that the EKR calculated for daily dialysis is identical to the sum of eKt/V’s for the individual dialyses. We therefore conclude that EKR is not a suitable parameter for normalizing the dialysis dose, because it fails to reflect the effect of dialysis frequency in HD therapy.

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Key words

Daily hemodialysis, kinetics, urea, adequacy

Introduction

The report by Piccoli and colleagues in this issue [1] on monitoring dosage in daily dialysis addresses a very timely concern. They evaluated several different methods of dose calculation, with the primary purpose of determining the optimal way to minimize variability in the measurement of the total delivered dose with 6 treatments per week. Their report provides valuable guidelines for monitoring dose in daily dialysis. However, the interrelationships among the methods of dose calculation are also of considerable interest and are the subject of this commentary.

The spectrum of dialysis treatment has been greatly expanded over the past few years. Clinical therapy now encompasses (a) continuous ambulatory peritoneal dialysis (CAPD), (b) CAPD combined with 1 or 2 hemodialysis (HD) sessions per week, and (c) intermittent hemodialysis with a wide range of frequencies (3 – 6 times per week) and intensities (2 hours to 8 hours nocturnal). A normalized dose parameter suitable for quantitative comparison of dialysis dose across this wide spectrum of therapy is needed.

The concept of Kt/V was developed from thrice-weekly HD (twHD) therapy [2]. Adequate twHD was subsequently shown to require a minimum equilibrated Kt/V (eKt/V) of 1.05 (equivalent to a single-pool Kt/V of 1.2 – 1.5, depending on t) to be given during each of the three weekly dialyses [3]. Although this dose parameter has been validated only for twHD, the dose provided with more frequent dialysis is now often described as the sum of individual eKt/V values over a week (ΣeKt/V) and is compared to ΣeKt/V for twHD.

Solute removal by dialysis is first order—that is, the rate of solute removal (J) equals concentration (C) times clearance (K). Dialysis efficiency (J) therefore falls sharply as the dose of each dialysis (Kt/V, intensity) increases, owing to the fall in C. Doubling the frequency at the same Kt/V results in a much greater increase in total dose than does doubling the intensity, Kt/V, at the same frequency. Consequently, it is not appropriate to use the ΣKt/V to compare doses under varying treatment schedules. Implicit in the weekly ΣKt/V calculation is the assumption that the total clearance provided by any therapy schedule can be time averaged (TAK) regardless of the frequency of dialysis. That is,

\[ \text{TAK} = \frac{\Sigma \text{Kt/V} \cdot (V)}{T} \]  

where T is the total averaging time (typically 1 week). Neither TAK nor ΣKt/V are appropriate measures to compare the

[1] Piccoli et al.

[2] Adequate treatment was defined by an eKt/V of 1.05.

[3] Adequate treatment was defined by an eKt/V of 1.05 (equivalent to a single-pool Kt/V of 1.2 – 1.5, depending on t) to be given during each of the three weekly dialyses.
The steady-state relationship between $G$, $TAC$, and $TAK$ is defined as

$$EKR = \frac{G}{TAC} \quad (4)$$

and

$$EKR_{\tau/V} = \frac{[EKR (7) (1440) / N] / 40}{V} \quad (5)$$

where $G$ is the urea nitrogen generation rate, $TAC$ is the time-averaged urea nitrogen concentration over a full week of treatment, $N$ is number of dialyses per week, and 40 is the standard volume normalization parameter chosen by Casino.

The kinetic meaning of $EKR$ can best be seen from the steady-state relationship between $G$, $TAC$, and $TAK$:

$$G = TAK (TAC) \quad (6)$$

which can be rearranged to give

$$TAK = \frac{G}{TAC} \quad (7)$$

A comparison of equations (4) and (7) shows that $EKR = TAK$, and that $EKR$ defines total dose simply as the sum of the $Kt/V$ values regardless of treatment schedule. The $EKR$ does not account for the first order nature of solute removal.

The clinical data reported by Piccoli and colleagues [1] provide an opportunity to examine this assessment of $EKR$. That group calculated and reported the single-pool variable volume $Kt/V$ value for each session ($Kt/V$ per session) using the Daugirdas approximation formula [8]. They also calculated the $EKR_c$ from each session’s data using Casino’s plots [6,7].

Equation (5) was used to calculate mean $EKR_c(t)/V$ for each patient from the mean $EKR_c$ and $t$ values reported for each patient. The $EKRc(t)/V$ was computed both per session and per week.

The $Kt/V(Daugirdas)$ values for each session are 0.65 – 0.97 and are in a range where $V$ is systematically underestimated and $Kt/V$ is systematically overestimated. Therefore, the $Kt/V(Daugirdas)$ values were corrected for this effect ($corrKt/VDaug$ per session), using the Tattersall algorithm for correction of volume error [9].

$$corrKt/VDaug = \left[ \frac{Kt/VDaug}{[t / (t + tp)]} \right] / (t + tp) \quad (8)$$

where $tp$ is patient equilibration time (35 minutes).

Table I lists the $Kt/V(Daugirdas)$, $corrKt/VDaug$, and calculated $EKR_{\tau/V}$ values. It is apparent that all of these calculations of dose agree closely, and that the mean values for $corrKt/VDaug$ and $EKR_{\tau/V}$ are almost identical per session and per week. These clinical data demonstrate that the $EKR$ parameter is almost identical to $TAK$, and it can be concluded that $EKR$ does not account for the first order nature of dialysis therapy, and is therefore not suitable to normalize dose for varying treatment schedules.

Fig. 1 graphically illustrates this conclusion. The weekly values for $corrKt/VDaug$ and $EKR_{\tau/V}$ are both plotted as a function of $eKt/V$ per session. These two weekly dose parameters for daily dialysis can be seen to be identical summations of the individual $Kt/V$ values, as shown in Table I. Note that the weekly $Kt/V(Daugirdas)$ plotted for thrice-weekly dialysis indicates that a weekly $Kt/V$ of 3.2 would be required for CAPD therapy clinically equivalent to that in $twHD$ with an $eKt/V$ of 1.05.

In contrast, the curves for stdKt/V in Fig. 1, plotted for 3- and 6-times-weekly dialysis as a function of individual $eKt/V$ values, are highly curvilinear. They reflect decreasing efficiency with increasing $eKt/V$ per session. Notice that, on the curve for $N = 3$, identical stdKt/V values of 2.0 are predicted for adequate CAPD and $twHD$. As noted above, the $EKR_{\tau/V}$ line for $N = 3$ predicts that CAPD would require a weekly $Kt/V$ of 3.2 for therapy equivalent to an $eKt/V$ of 1.05 in $twHD$, and that a weekly $Kt/V$ of 2.0 in $CAPD$ would be grossly inadequate therapy corresponding to an $eKt/V$ of 0.68 in $twHD$. These relationships for $EKR_c$ are highly inconsistent with clinical experience and results, because the
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model fails to account for the first order nature of dialysis therapy.

References


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