Inherent Errors in the Quantitation of Dialysis Delivery: Implications For CAPD and Daily Hemodialysis

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When compared to intermittent dialysis, the theoretical advantages of continuous dialysis may be less important than its practical disadvantage: the inability to accurately quantify dialysis. With intermittent dialysis the change in blood urea nitrogen over the course of the treatment allows the ratio of K (urea clearance) to V (volume of distribution of urea or total body water) to be determined, hence an accurate Kt/V. In continuous dialysis this approach cannot be used due to the steady-state nature of blood urea levels. Instead, V is estimated, generally from the Watson equations. This estimate has sufficient inaccuracy to result in substantial unrecognized underdialysis in many patients.

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Key words

Dialysis delivery, Kt/V, body water, daily hemodialysis, CAPD

The quantitation of dialysis delivery

Even though continuous ambulatory peritoneal dialysis (CAPD) provides a lower level of solute clearance than hemodialysis, patient outcome with the two procedures is similar. One hypothesis accounting for the relative equivalence of CAPD and thrice-weekly hemodialysis despite different levels of dialysis delivery is based on the advantages of continuous therapy (1,2). If true, this hypothesis would suggest that while daily hemodialysis should be superior to thrice-weekly hemodialysis, its intermittency makes it less desirable than CAPD. However, there is a strong reason to take the opposite view and consider its intermittency an advantage.

For argument's sake, let us assume the following statements are true:

1. In hemodialysis patients, morbidity and mortality are minimized at a Kt/V of 1.4/treatment.
2. In CAPD patients, morbidity and mortality are minimized at a Kt/V of 2.1/week.
3. At these "target" levels of Kt/V, peritoneal dialysis and hemodialysis have equivalent outcomes.

The question to be considered is this: Assuming a measured Kt/V at the target level, should an anuric end-stage renal disease (ESRD) patient, whose sole goal is to obtain the best possible dialytic outcome, choose CAPD or hemodialysis? The answer is related to inherent problems in the quantitation of dialysis.

Dialysis is most commonly quantified by measuring Kt/Vurea. In both hemodialysis and CAPD, treatment times (t) can be accurately measured, but V (the volume of distribution of urea, equivalent to total body water) is estimated. In CAPD, K (urea clearance) can be accurately determined by measuring dialysate and plasma urea levels together with the dialysate drain volume; in hemodialysis, K is estimated. Superficially, then, it would appear that it should be possible to determine Kt/V more accurately in CAPD than in hemodialysis, since in CAPD only one of the three determinants of Kt/V is estimated, while in hemodialysis two of these determinants are estimated.

However, this is an incorrect analysis. Even though K and V are not known with accuracy in hemodialysis, their ratio can be accurately determined, and only this ratio is needed to accurately measure Kt/V. This becomes apparent when one recalls that Kt/V in hemodialysis is closely related to the percentage decrease in urea over the course of the treatment, a relationship that requires no assumptions about K or V (3–6). In hemodialysis, an incorrect, low V will result in a proportionate error in K and an accurate Kt/V. In CAPD, by contrast, an estimated V that is less than the actual V will result in a

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measured Kt/V that is greater than the actual Kt/V (Figure 1). While the issue of urea rebound postdialysis in hemodialysis is a significant one, it can be addressed using delayed blood sampling and/or modifications of the usual methods of calculating Kt/V (7,8). As a result, an accurate Kt/V can be determined in hemodialysis but is problematic in peritoneal dialysis, where the error in V translates into a proportional error in Kt/V.

This difference between the measured and actual Kt/V means that CAPD patients can theoretically be classified by the relationship of these two values and by whether the measured and actual dialysis deliveries are above or below target levels. Using an arbitrary target value for Kt/V of 2.1/week, patients can be subdivided into four groups (Figure 2): (1) those having unrecognized, inadequate dialysis (actual Kt/V < 2.1, measured Kt/V > 2.1); (2) those with recognized inadequate dialysis (both actual and measured Kt/V < 2.1); (3) those with misdiagnosed dialysis inadequacy (actual Kt/V > 2.1, measured Kt/V < 2.1); and (4) those with recognized adequacy of dialysis (both actual and measured Kt/V > 2.1). The extent to which measured and actual Kt/V diverge in CAPD patients is largely a function of the magnitude of the error in estimating V.

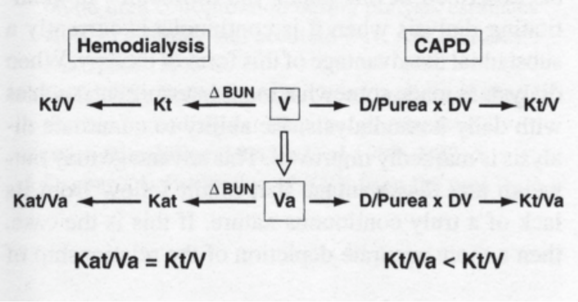

FIGURE 1 In CAPD, Kt/V is calculated by determining the product of the dialysate-to-plasma urea concentration (D/Purea) and the dialysate drain volume (DV) and dividing this product by the estimated V. The measured Kt/V will be greater than the actual Kt/V when the estimated V is less than the actual value (Va). Thus Kt/Va < Kt/V. In hemodialysis, the extent of the change in blood urea nitrogen (BUN) over the course of a treatment (reflecting the change in the concentration of urea in body water, V) is the predominant determinant of the estimated clearance (K). If Va is larger than the estimated V, then the actual urea clearance (Ka) will also be larger than the estimated K. This occurs because, with a larger V, any given change in BUN must represent a greater urea clearance. Thus inaccuracies in V result in proportional (and canceling) changes in K. As a result, Kat/Va = Kt/V.

How inaccurate is the estimate of V in ESRD patients receiving peritoneal dialysis? The extent of the inaccuracy depends in part on the specific method used to estimate V. One method of estimating V is to use a fixed percentage of body weight, typically 58%. When body water estimates using this approach were compared to those using the isotope dilution method in 20 peritoneal dialysis patients, the error was substantial and ranged from an underestimate by as much as 12.4 L to an overestimate by as much as 20.1 L (9).

Using an arbitrary percentage of body weight to estimate body water is widely recognized as having a low level of accuracy (10). The most common approach is to use the Watson equations to estimate body water. The Watson equations were generated from a reanalysis of 30 published studies (723 adult subjects) in whom body water was quantified by dilution methodology (11). All study subjects were considered to be healthy, with no disturbances in body water metabolism. Even given these restrictive inclusion criteria, the equations' prediction of body water differed substantially from the values obtained by dilution methods. The standard deviation in the correlation between the Watson prediction and actual body water exceeded 3.5 L in both the male and female subjects, indicating that about one-third of subjects had errors in body water estimates that were greater than this level.

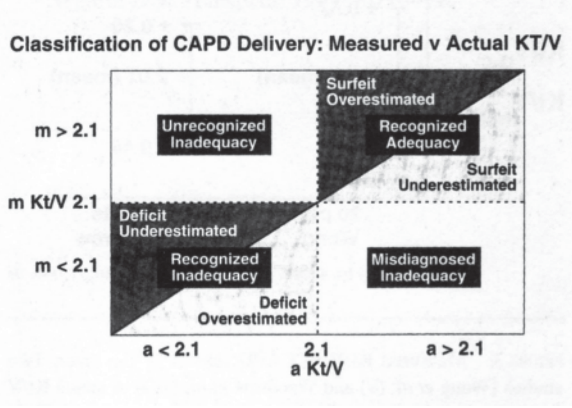

FIGURE 2 Adequate dialysis is assumed to be a Kt/Vurea of 2.1/week. Virtually all CAPD patients will fall into one of four groups depending upon the relationship of their measured and actual Kt/V.

Two studies have compared Kt/V values calculated using the Watson equations with values using actual body water determined by deuterium dilution methodology (9,12). In both studies, highly significant discordance was noted (Figure 3). In the study by Wong *et al*. (9), the "Watson Kt/V" overestimated actual (deuterium) weekly Kt/V by as much as 0.89. Woodrow *et al*. (12) reported a similar lack of agreement between deuterium Kt/V and "Watson Kt/V," consistent with the findings of Wong.

It should be noted that all of Wong *et al*.'s study patients were considered to be at their dry weight. It is well recognized that the error in estimating V using the Watson equations is even greater in patients who are fluid-overloaded. Examination of the Watson equations reveals that any increase in body weight is calculated as consisting of only 25% – 34% water. The increase in weight in edematous patients is, however, 100% water. Recommendations have been published to reduce this error, but the approach is largely guesswork (13).

But an additional problem is that the Watson equations tend to systematically underestimate V, particularly in patients with renal disease. In 27 patients with varying levels of renal function and states of hydration, Watson V underestimated V measured by tritium dilution in all but 4 patients with a mean underestimate in all patients of 3.6 L (Reference 14 and Kong CH, personal communication). When V is underestimated, the actual Kt/V is less than the Kt/V calculated using the Watson formula. In Wong *et al*.'s (9) study, the average Kt/V using the Watson V was 7.4% higher than when actual (deuterium) body water was used in the calculation. Using the Watson equations yields results biased in favor of an overestimate of delivered dialysis.

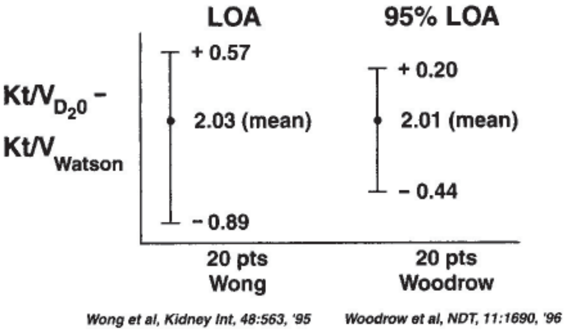

FIGURE 3 Measured Kt/V in CAPD: extent of the error. Two studies [Wong *et al*. (9) and Woodrow *et al*. (12)] of actual Kt/V (by deuterium dilution determination of V) compared with Kt/V using Watson estimates of V. The figure shows the population means for the deuterium-based Kt/V (Kt/VD_2O) and the limits of agreement (LOA) for the difference between Kt/VD_2O and the Watson Kt/V.

Let us now return to the original question raised at the start of this paper. With the stated assumptions, should the ESRD patient choose CAPD or hemodialysis? As a result of errors in estimating V in CAPD patients, more than half of patients with a measured Kt/V of 2.1 will, in fact, have a Kt/V less than this value. Their morbidity and mortality will, as a consequence, be increased. This increase will not be balanced by any decrease in morbidity and mortality for patients receiving an actual Kt/V greater than their measured value of 2.1, since the assumptions note that morbidity and mortality were "minimized" at an actual Kt/V of 2.1 (i.e., higher Kt/V values did not further reduce morbidity and mortality). Thus, statistically, the ESRD patient can expect an outcome that is worse with CAPD than with hemodialysis.

A current view of the relationship of the frequency of dialysis and its "quality" is shown in Figure 4A. As described in this paper, the difficulties in quantitating dialysis when it is continuous is currently a substantial disadvantage of this form of therapy. When dialysis is made somewhat more intermittent, such as with daily hemodialysis, the ability to quantitate dialysis is markedly improved. This advantage may outweigh any disadvantage that might follow from its lack of a truly continuous nature. If this is the case, then a more accurate depiction of the relationship of

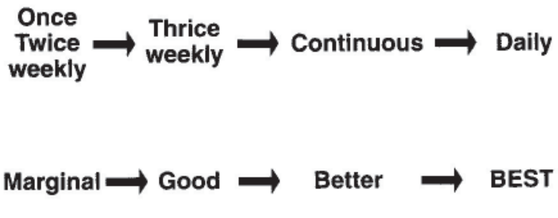

FIGURE 4A A current view of the relationship of dialysis frequency versus dialysis quality indicates that continuous dialysis provides the best therapy.

FIGURE 4B A revised view of the relationship of dialysis frequency and dialysis quality taking into account the practical problem of dialysis quantification.

dialysis quality versus frequency may be that shown in Figure 4B.

References

1 Keshaviah P. Urea kinetic and middle molecule approaches to assessing the adequacy of hemodialysis and CAPD. Kidney Int 1993; 43(Suppl 40):S28–38.
2 Keshaviah P, Nolph KD, Van Stone JC. The peak concentration hypothesis: A urea kinetic approach to comparing the adequacy of continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis. Perit Dial Int 1989; 9:257–60.
3 Basile C, Casino F, Lopez T. Percent reduction in blood urea concentration during dialysis estimates Kt/V in a simple and accurate way. Am J Kidney Dis 1990; 15:40–5.
4 Jindal KK, Goldstein MB. Urea kinetic modeling in chronic hemodialysis: Benefits, problems and practical solutions. Semin Dial 1988; 1:82–5.
5 Depner TA. Estimation of Kt/V from the urea reduction ratio for varying levels of dialytic weight loss: A bedside graphic aid. Semin Dial 1993; 6:242.
6 Daugirdas JT, Depner TA. A nomogram approach to hemodialysis urea modeling. Am J Kidney Dis 1994; 23:33–40.
7 Daugirdas JT, Schneditz D. Overestimation of hemodialysis dose (ΔKt/V) depends on dialysis efficiency (Kt/V) by regional blood flow but not by conventional 2-pool urea kinetic analyses. ASAIO J 1995; 41:M719–24.
8 Daugirdas JT. Estimation of the equilibrated Kt/V using the unequilibrated post dialysis BUN. Semin Dial 1995; 8:283–4.
9 Wong KC, Xiong DW, Kerr PG, *et al*. Kt/V in CAPD by different estimations of V. Kidney Int 1995; 48:563–9.
10 Tzamaloukas AH, Murata GH. Urea volume estimates in peritoneal dialysis: pitfalls and corrections. Int J Artif Organs 1996; 19:321–4.
11 Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr 1980; 33:27–39.
12 Woodrow G, Oldroyd B, Turney JH, Davies PSW, Day JME, Smith MA. The effect of measurement of total body water and validity of urea kinetic modelling in peritoneal dialysis (Abstract). Nephrol Dial Transplant 1996; 11:1690.
13 Tzamaloukas AH. Effect of edema on urea kinetic studies in peritoneal dialysis patients. Perit Dial Int 1994; 14:398–401.
14 Kong CH, Thompson CM, Lewis CA, Hill PD, Thompson FD. Determination of total body water in uraemic patients by bioelectrical impedance. Nephrol Dial Transplant 1993; 8:716–19.