Advances in Peritoneal Dialysis

Dialysis adequacy indices that may be used to evaluate the efficiency of small-solute removal include Kt/V, fractional solute removal (FSR), and equivalent urea clearance (EKR). To analyze possible relationships between those indices, we used the two-compartment variable-volume urea kinetic model to simulate several dialysis modalities: hemodialysis (HD) performed three times or six times weekly, automatic nightly peritoneal dialysis (PD), and continuous ambulatory PD. Instead of targeting a chosen Kt/V value, we selected a weekly FSR of 1.81 as the target adequacy index. We determined hemodialyzer clearances and diffusive mass transport parameters for the peritoneal membrane that yielded the desired value of FSR for a typical patient and dialysis schedule.

By theoretic analysis, EKR and FSR are proportional: EKR / FSR = \( \frac{V}{T_c} \), where \( V \) = urea distribution volume in the body and \( T_c = \) time of the dialysis cycle, usually 1 week. Thus, FSR and EKR have the same meaning and scaling in PD and HD, and may be equivalently applied for assessment of dialysis efficacy.

Key words
Urea kinetic model, Kt/V, fractional solute removal, equivalent renal clearance

Introduction
In clinical practice, the adequacy of dialysis is often assessed using a Kt/V index (\( K = \text{clearance}; t = \text{treatment time}; V = \text{body water volume} \)) that describes the removal of a small solute (usually urea) from the body (1,2). Clearance \( K \) in the Kt/V index has two different definitions: In hemodialysis (HD), \( K \) is an instantaneous clearance, that is, the clearance of the hemodialyzer or hemofilter; the \( K \) in peritoneal dialysis (PD) is a treatment clearance that describes the outcome of the treatment and that depends on the treatment time (3). For PD, the rate of instantaneous solute removal is described as a dialysance called the diffusive mass transport parameter of peritoneal membrane (\( K_{\text{BP}} \)) or the mass-transport area coefficient (MTAC). The Kt/V used for PD is in fact equivalent to the fractional solute removal (FSR); for HD, Kt/V and FSR are different concepts (3).

The application of FSR and equivalent urea clearance (EKR) respectively require a choice of the appropriate reference solute mass in the body and of the solute concentration in the blood. For example, reference values may be the maximal urea mass or concentration (4,5), or the average pre-dialysis (3,6) or time-averaged urea mass or concentration (3,6,7).

In the present study, we applied urea kinetic modeling to compare Kt/V, FSR, and EKR across various schedules and modalities of renal replacement therapy. This sort of analysis may be important when a patient’s dialysis regimen is changed, when a new treatment modality is introduced, or when a patient shifts from one modality to another (from PD to HD, for example). We addressed these questions:

- How must various treatment modalities be arranged to reach the same FSR?
- What values of Kt/V and EKR are obtained for the same patient if different treatment modalities with the same weekly FSR are applied?

We analyzed the questions using a variable-volume two-compartment urea kinetic model.

Materials and methods

Dialysis adequacy indices
We formulated three different definitions of the equivalent urea clearance (EKR). The pEKR is the urea generation rate, \( G \), divided by peak concentration, \( C_0 \). The paEKR uses the peak average concentration, \( \text{paC}_0 = \)
Hemodialysis performed as 1-hour, 35-minute sessions and modalities:

- Automated nightly peritoneal dialysis (ANPD)
- CAPD, defined as 4 exchanges daily, 7 days per week
- Hemodialysis performed as 3-hour, 10-minute sessions three times per week (HD3×)
- Hemodialysis performed as 1-hour, 35-minute sessions six times per week (HD6×)

The taEKR uses the reference clearance, $\Delta M_0$, normalized by the initial mass of the solute, $M_0$. The taEKR is defined as $\frac{G}{C_\text{ref}}$, where $C_\text{ref}$ is equal to $C_0$, or $\Delta C / \Delta M_0$ (4). The taEKR uses the time-averaged solute mass as the reference factor (3). Thus, $FSR = \frac{\Delta M_R}{\Delta M_0} / M_\text{ref}$, where $M_\text{ref}$ is equal to $M_0$, $\Delta C / \Delta M_0$, or $\Delta m / \Delta t aC$. From the definitions of taEKR and FSR, we derived their ratio by using the principle that the amount of solute removed during the treatment cycle must be equal to the amount of solute generated during that time period, $\Delta M_R = GTc$:

$$\frac{EKR}{FSR} = \frac{G / C_\text{ref}}{\Delta M_R / M_\text{ref}} = \frac{G / C_\text{ref}}{GTc / M_\text{ref}} = \frac{V_\text{ref}}{V_\text{t}}$$

where $V_\text{ref} = M_\text{ref} / C_\text{ref}$ respectively—that is, $V_\text{ref}$ is equal to $V_0 = M_0 / C_0$, $\Delta \Sigma C / \Delta M_0 = \Delta C_0 / \Delta M_0$, and $\Delta C / \Delta M_0 = \Delta m / \Delta t aC$. Equation [1] demonstrates that FSR and EKR are strictly correlated, and that the coefficients of proportionality for various definitions of these indices depend slightly on the variations of $M$ and $C$ during the treatment cycle.

Assumptions for computer simulations

Assuming the same fractional solute removal, $FSR = 1.81$ [a value that corresponds to a typical weekly $Kt/V$ treatment clearance in continuous ambulatory peritoneal dialysis (CAPD)], we simulated various dialysis schedules and modalities:

- CAPD, defined as 4 exchanges daily, 7 days per week
- Automated nightly peritoneal dialysis (ANPD) performed daily in a 10-hour session, with 5 exchanges of dialysis fluid, one exchange every 2 hours
- Hemodialysis performed as 3-hour, 10-minute sessions three times per week (HD3×)
- Hemodialysis performed as 1-hour, 35-minute sessions six times per week (HD6×)

To reach the same FSR, the PD clearance (mass transport parameter of the peritoneal membrane, $K_{BD}$) was 13 mL/min in CAPD and 32 mL/min in ANPD. Clearances were 216 mL/min for HD3× and 156 mL/min for HD6×.

The post-dialysis total body water was 35 L. Water was added at a rate of 0.7 mL/min (7 L of water weekly), and the same amount of water was removed by means of residual water clearance (0.1 mL/min) and as a result of ultrafiltration during the treatment sessions. The changes of water volume in the body during HD were linear; during PD, the changes were determined according to the Pyle model (9). Two types of dialysis fluid were used in CAPD, three infusions with 1.36% glucose and one infusion with 3.86% glucose daily, each infusion using 2 L of dialysis fluid. For ANPD, 2 L of 1.36% glucose dialysis fluid was applied in all exchanges.

For simulations, we used typical treatment schedules and parameters (1,2,8). The values of the patient parameters were urea generation rate, 7 mg/min; residual urea clearance, 0.7 mL/min; and intercompart-mental clearance, 600 mL/min. The volumes of the extracellular and intracellular compartments were related to total body volume, $V$: $V_{\text{extracellular}}(t) = 0.35 V(t)$ and $V_{\text{intracellular}}(t) = 0.65 V(t)$. The simulations were carried out to achieve the metabolic steady state of the patient during the treatment cycle time. For that steady state, adequacy parameters were calculated.

Results

Figure 1 shows the changes of urea concentration in the extracellular compartment of the body. The time-averaged concentration, $taC$, was about 0.7 mg/mL in HD and 1.1 mg/mL in PD. The amplitude of the urea concentration changes was highest for HD3×; it was negligible in CAPD.

Table I shows the weekly values of EKR and FSR according to the three variant definitions; the urea distribution volumes, $V_\text{ref}$; and the urea concentrations in the extracellular compartment of the body, $C_\text{ref}$. Fractional solute removal was the same for all simulated dialysis modalities (FSR = 1.81, including 0.2 contribution of residual urea clearance). In contrast, $Kt/V$ (with $K$ being the instantaneous clearance for HD and PD) was different; it varied from 2.5 for HD6× to 4.83 for CAPD. Using the other definition of $Kt/V$ (with $K$ being the treatment clearance), the $Kt/V$ values were equal to FSR—that is, 1.81—for all treatments.
The adequacy indices EKR and FSR had the highest values for the definitions based on the time-averaged quantities, ranging between $taEKR = 6.43 \text{ mL/min}$ and $taFSR = 1.84$ for CAPD, and $taEKR = 10.71 \text{ mL/min}$ and $taFSR = 2.94$ for HD3×. The $pFSR$ had the same value for CAPD and HD3× ($pFSR = 1.81$), but the difference between taFSRs was 60%. The difference between the values of the indices calculated according to the various definitions (time-averaged, peak average, and peak) for the same treatment method was about 60% for HD, but was negligible for CAPD (about 1%).

The EKR/FSR ratio differed only slightly between modalities and definitions (ranging from 3.5 mL/min to 3.75 mL/min, Table I), and correlated with the fluctuations of water volume in the body ($V_{ref}$), as expected from its definitions (see equation [1]).

**Discussion**

The concept of $Kt/V$ means different things in different therapies, and the relationship between $Kt/V$ and mortality appears to be much different for treatment modalities such as PD and HD (1,2). This discrepancy between HD and PD is caused by the different definitions of $Kt/V$ as applied to these two treatments (3). In particular, $K$ has different definitions in HD and CAPD: in HD, $K$ is an instantaneous clearance (that is, the clearance of the hemodialyzer); in CAPD, $K$ is a treatment clearance (3). Note that we standardized the efficiency of various treatments by using the instantaneous clearance for both HD and CAPD, but in CAPD literature, $Kt/V$ is in fact the same as FSR (3).

The difference between the index values calculated according to the various definitions (peak, peak...
average, time-averaged) was about 60% for HD3x, but much lower for ANPD and CAPD because of the highly intermittent course of HD.

The choice between the normalization coefficients in definitions of EKR and FSR is not obvious. Given current knowledge, it is not possible to state that one or the other definition is better; however, some authors have declared their preferences (6). On the other hand, the EKR/FSR ratio is similar for the various definitions (Table I), indicating that, when using the same definition variant, EKR and FSR change in a parallel manner for the various treatments. That finding shows that those indices are interchangeable measures of adequacy.

We conclude that, in practice, EKR and FSR provide the same comparative evaluation of various dialysis modalities and schedules. They may therefore be considered equivalent measures for comparative studies of dialysis adequacy.

References

Corresponding author:
Bengt Lindholm, MD, Divisions of Baxter Novum and Renal Medicine, K55, Karolinska University Hospital Huddinge, Stockholm S-14186 Sweden.
E-mail:
bengt.lindholm@klinvet.ki.se