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EFFECT OF SLOWING BLOOD FLOW TECHNIQUE ON POST-DIALYSIS UREA REBOUND AND EQUILIBRATED DIALYSIS DOSE

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ABSTRACT

The Smye method has been proposed to estimate the equilibrated post-dialysis blood urea nitrogen “BUN” based on an intradialytic sample obtained approximately one hour from the beginning of dialysis [1]. However, the effects of access recirculation “AR” and cardiopulmonary recirculation “CPR” on the Smye computation and the corresponding details of how blood is sampled have not been studied. The accuracy of the Smye technique was examined. In one method, the intradialytic and post-dialysis blood samples are obtained at constant blood flow. In the other, the intradialytic and post-dialysis blood samples are obtained after two minutes of slow flow, to determine the effects of both AR and CPR. Seventeen patients undergoing high efficiency dialysis and three- to four-hour treatment times were studied, in whom substantial AR was excluded based on slow flow urea rebound measurements during and just after dialysis. In this group equilibrated Kt/V $_{eq}$"Kt/V" values computed using the Smye-derived equilibrated post-BUN estimates (constant flow samples, 1.22±0.058, slow flow samples, 1.23±0.064) were similar to $_{eq}$"Kt/V" calculated from the 30-minute post-dialysis BUN specimen "1.23±0.049, P = NS". In eight other patients with severe AR "mean 35% ± 4.5", the accuracy of the constant flow Smye estimates was poor when the degree of AR was not constant throughout the dialysis session.

KEYWORDS Equilibrated urea concentration, post dialysis urea rebound, urea kinetic modeling, equilibrated dialysis adequacy $_{eq}$"Kt/V".

1. INTRODUCTION

Since Gotch and Sargent's mechanistic analysis of the National Cooperative Dialysis Study data in 1985 [2], it has become widespread practice to assess dialysis adequacy based on the fractional index of urea removal "Kt/V". Although a variable

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volume single pool "VVSP" model of urea kinetics was used for this purpose, it has long been recognized that the kinetics of urea removal is best described by multicompartment models [3-6]. The need for a multicompartment analysis is best illustrated by the extent of postdialysis urea rebound which occurs 30 to 60 minutes after dialysis has been completed. Post-dialysis urea rebound "PDUR" is due to the intercompartmental equilibration of urea during hemodialysis and supports the concept of an intradialytic two-pool model to calculate the dialysis dose [7-9]. A two-pool fixed volume urea kinetic model was used in which urea generation is assumed to be zero, have attempted to predict the extent of postdialysis urea rebound by using one intradialysis blood urea concentration measurement and an equation which yields an estimate of the true equilibrium urea concentration [1,10].

The premise underlying the Smye technique is that the factors associated with postdialysis urea rebound also conspire to lower the intradialytic serum urea concentration during dialysis below that predicted from first-order kinetics. In its original description, the Smye method required a predialysis blood sample, a second intradialytic sample drawn 60 or 70 minutes from the beginning of dialysis, and a postdialysis sample [1, 10]. If these samples are both drawn at constant blood flow rate, or after stopping the blood pump and not clearing the dead space in the arterial line, then the urea concentration in the samples will reflect the urea levels actually processed by the dialyzer. In the presence of access recirculation, the urea concentration of both the intradialytic and postdialysis blood urea samples drawn in this manner may be markedly lower than the urea level present in the arterial blood. Another method of performing the Smye technique is to obtain the intradialytic and postdialysis samples 20 seconds after slowing the blood flow rate to 50 ml/min [10]. When the pump is slowed to 50 ml/min, access recirculation ceases, and the dialyzer inlet blood reflects the arterial BUN concentration "when the arteriovenous "AV" access is used" during dialysis. A third method is to obtain the intradialytic and postdialysis samples 2-minute after slowing the blood flow rate to 50 ml/min [11]. After the pump is slowed or stopped, the dialyzer no longer returns cleared blood to the heart and the arteriovenous gradient largely dissipates within two minutes; in

patients with an arteriovenous access, the mixed venous postdialysis urea concentration can be estimated from a sample obtained from the dialyzer inlet line two minutes after having slowed the blood flow rate to 50 ml/min [12, 13].

To assess the utility of the Smye technique we assayed intradialytic and postdialysis samples for urea taken both at constant blood flow and two minutes after slowing the blood flow rate to 50 ml/min. This information was used to estimate the postdialysis equilibrium urea concentrations with each set of samples. We then used the predicted equilibrated urea concentrations to compute equilibrated Kt/V values "one using the consatnt flow sample, and one using the 2-minute slow flow sample". The method was validated by obtaining a 30-minute postdialysis urea measurement in each patient, and using this measurement to compute the equilibrated Kt/V.

2. METHODOLOGY

2.1 Proposed Mathematical Model Design

The Variable-Volume, Double Pool "VVDP" model is illustrated in Fig. 1. In contrast to the single-pool model, total body water consists of distinct intracellular and extracellular compartments, with K_{ei} = intercompartmental urea mass transfer area coefficient "the caption in Fig. 1 defines the variables" [14].

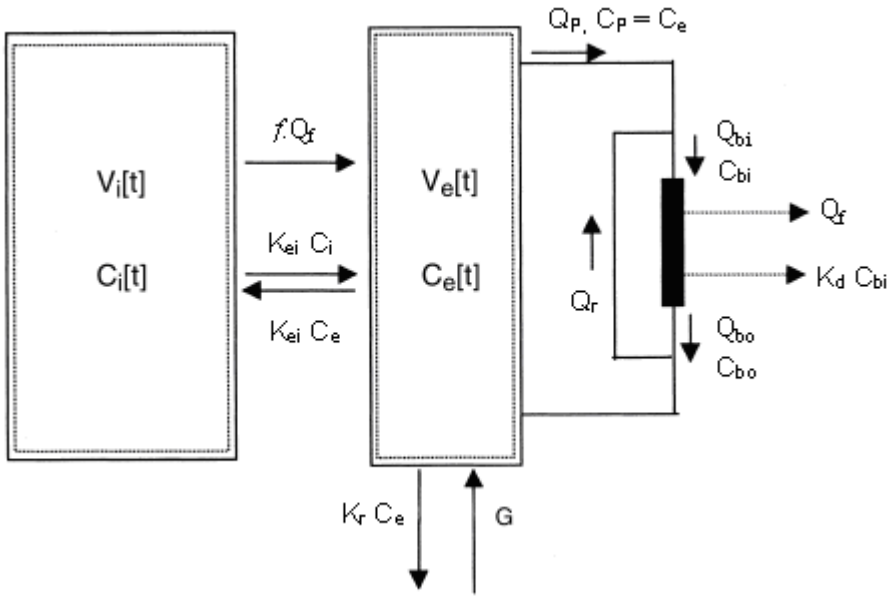

Fig.1. Variable-Volume, Double Pool urea kinetic model "VVDP".

Intercompartmental urea mass transfer K_{ei} was assumed to be ~10 ml/min/kg for children and ~800ml/min for adults [3-6]. The ratio of extracellular to intracellular volume "Ve/Vi" at dry weight was assumed to be ~1/3 [15].

V_i, intracellular fluid "ICF" volume C_i, ICF urea concentration; V_e, extracellular fluid "ECF" volume; C_e, ECF urea concentration; K_{ei}, intercompartmental urea mass transfer area coefficient; f, fraction of ultrafiltrate from ICF; Kr, residual renal urea clearance; G, urea generation rate; Q_f, ultrafiltration rate ">0" or interdialytic weight gain "<0"; K_d, dialyzer urea clearance. In the dialyzer-access circuit, flows "Q" and concentrations "C" refer to peripheral blood "p", dialyzer inlet "bi", dialyzer outlet "b_o", and access recirculation "r". For notational convenience, $K = K_d + K_r$, $C_e[0] = C_0$, $C_e[\infty] = C_{ss} = G / (K_d + Kr - Q_f)$, and $V_t = V_e + V_i$. Concentrations, flows, and K_d here refer to blood water "whole blood C/0.93, 0.9 whole blood Q or K_d".

Postdialysis urea rebound "PDUR" was expressed both as a function of the postdialysis BUN concentration "$PDUR_p$" and as a function of the intradialytic fall in BUN during dialysis "$PDUR_f$". $PDUR_p$ and $PDUR_f$ were defined as:

$$PDUR_p = 100 \times C_{eq30} / C_{post} \quad (1)$$

$$PDUR_f = 100 \times (C_{eq30} - C_{post}) / (C_{pre} - C_{post}) \quad (2)$$

Where C_{eq30} is equilibrated BUN of 30-minute post-HD (mg/dL) and C_{post} is the post-dialysis BUN "in mg/dL". Both measures of PDUR have been reported by others in the literature [7-9], and both measures are presented to allow a comparison with the used data. The Smye equation predicts that the equilibrated BUN "C_{eq}" will be:

$$C_{eq} = C_{pre}\, e^{-at} \quad (3)$$

$$Where\ a = 1/(t — t_{intra})\ ln\ (C_{intra}/C_{post})$$

Where, C_{pre} and C_{post} are the pre- and post-BUN, C_{intra} is the BUN of the intradialytic sample, t is the dialysis session length, and t-intra is the time during

dialysis at which the intradialytic sample is taken. Because t_{intra}/t was always 1/3, the general Smye equation is simplified to:

$$C_{eq0} = C_{pre}/exp(1.5\ ln(C_{intra0}/C_{post0})) \quad (4)$$

$$C_{eq2} = C_{pre}/exp(1.5\ ln(C_{intra2}/C_{post2})) \quad (5)$$

Where C_{eq0} and C_{eq2} are the estimated equilibrated postdialysis BUN values based on the constant flow and slow flow samples, respectively, C_{intra0} and C_{post0} are the BUN concentrations of the intradialytic and postdialysis samples drawn at constant blood flow, and C_{intra2} and C_{post2} are the BUN concentrations of the samples drawn after two minutes of reduced blood flow. When there is access recirculation, the blood urea concentration at the dialyzer inlet will be reduced by a constant multiplier "f_{AR}" [16].

This multiplier, which is the ratio of inlet "A_1" to upstream "A_2" BUN, can be derived from the standard formula for access recirculation "A" [11]:

$$A = ((A_2 - A_1)/(A_2 - V)) \times 100 \quad (6)$$

Where A_2 is the arterial urea concentration with low flow or stop flow, A_1 is the dialyzer inlet "arterial" urea concentration with blood pump running and V is the dialyzer outlet "venous" urea concentration.

$$f_{AR} = A_1/A_2 = (100 - R)/(100 — AV/A_1) \quad (7)$$

As long as A and V/A_1 "the dialyzer urea reduction ratio" stay constant throughout dialysis, f_{AR}, or A_1/A_2 will remain unchanged. Thus, with access recirculation, C_{pre} will remain unchanged, C_{intra} will become $f_{AR} \times C_{intra}$, and C_{post} will become $f_{AR} \times C_{post}$. However, ln "C_{intra}/C_{post}" will then become ln ""$f_{AR} \times C_{intra}$"/"$f_{AR} \times C_{post}$"", which is unchanged. Thus, as long as AR is constant, and as long as the C_{intra} and C_{post} samples are drawn using the same technique, the Smye analysis should compensate for AR. With cardiopulmonary recirculation "CPR" the mathematics are

similar. As defined in [12], f_{CPR}, the ratio of BUN in the arterial to mixed venous blood due to return of cleared blood to the heart, can be expressed as:

$$f_{CPR} = 1/[(1+ K_{ac}/(CO - Q_{ac})] \quad (8)$$

Where K_d is the dialyzer clearance (K_d), CO the cardiac output, and Q_{ac} the access blood flow. If K_d and CO-Q_{ac} are constant throughout dialysis, f_{CPR} will be constant also. Because the Smye estimate for equilibrated BUN depends on the ratio of the postdialysis to intradialysis BUN, multiplying both values by f_{CPR} should leave the ratio and the predicted equilibrated BUN, unchanged. Single-pool Kt/V was computed using the Daugirdas second generation equation [17]:

$$Kt/V = - ln(R - 0.008t) + (4 -3.5R) UF/W \quad (9)$$

Two forms of this equation are computed, one representing an arterial Kt/V, based on samples taken at constant blood flow (Kt/V_{sp0}), in which $R = C_{post0}/C_{pre}$, t = dialysis session length in hours, UF = weight loss in kg, and W = post-dialysis weight in kg, and the other representing a mixed venous Kt/V, based on samples taken after two minutes of slow flow "Kt/V_{post2}", in which $R = C_{post2}/C_{pre}$. Equilibrated Kt/V "$_{eq}$Kt/V" was computed from three separate "equilibrated post" BUN values. In each case, $_{eq}$"Kt/V" is computed using the Daugirdas second generation formula, substituting the "equilibrated" postdialysis BUN for the immediate post-BUN when computing R, the post/pre-BUN ratio. $_{eq}$"Kt/V"$_{Sm0}$ and $_{eq}$"Kt/V"$_{Sm2}$ are computed using the predicted equilibrium BUN concentrations "C_{eq0} and C_{eq2}" from the constant flow "Sm_0" and 2-minute slow flow "Sm_2" Smye methods, respectively [1, 10, 18]. $_{eq}$"Kt/V"$_{30}$ was computed from the actual 30-minute postdialysis BUN sample. For simplicity, and to compensate for lack of complete rebound, the effects of urea generation were not subtracted from the 30-minute postdialysis BUN sample. For purposes of analyzing the data, several Kt/V values were defined, representing the single-pool arterial Kt/V value drawn at constant blood flow "Kt/V_{sp0}" subtracted from the $_{eq}$"Kt/V" value in question. To model the single pool urea distribution volume V, some estimate of K was required. Nominal blood flow rate was first corrected for pre-pump pressure effects. The corrected blood flow rate was then used with the dialysate

flow rate and the dialyzer K_0A to compute the dialyzer clearance K_d using equations previously cited [19]. The dialyzer clearance K_d was corrected to blood water clearance "K_{dW}" by multiplying K_d by 0.88 [19]. Single-pool urea volume was then obtained by algebraically solving for V from t, the $_{sp}$"Kt/V" value computed by the Daugirdas equation, and the value for K_{dW} obtained as outlined above.

2.2 Material and Method

Initially 20 chronic hemodialysis patients "9 males, 11 females" being treated at a large dialysis center were selected. All patients gave their full and informed consent and were evaluated during routine hemodialysis sessions as prescribed by their nephrologists. All patients were treated with Fresenius F-60, F-6, or F-7 polysulfone dialyzers. Dialysis session lengths ranged from 3.0 to 4.0 hours "mean 3.6±0.11". Three of these patients were suffering from severe access recirculation. In the remaining 17 patients, urea studies suggested that access recirculation was either absent or mild. To study the effects of AR on the Smye method completely, five additional patients were identified with severe access recirculation, and these patients were added under the same protocol. The data on the 25 patients were analyzed according to two subgroups: 17 patients with minimal AR and 8 patients with severe AR.

2.3 Experimental Protocol

Two intradialytic samples were taken from the arterial line sampling port after 1/3 of the dialysis session had elapsed. One sample was taken at constant blood flow and the other two minutes after slowing blood flow to 50 ml/min. Three postdialysis samples were taken, all from the arterial line sampling port. The first sample was taken immediately at the end of dialysis, at constant blood and dialysate flow. A second sample was obtained two minutes after slowing blood flow to 50 ml/min. At this point

the blood pump was stopped and the blood was returned. One of the lines was left in place. Thirty minutes after stopping dialysis, a third sample was taken from the needle tubing, after first removing and setting aside 10 ml to clear the needle tubing of infused saline. When studying the five additional patients with severe access recirculation, two additional samples were added: one was taken at 80 min from the beginning of dialysis, and 20 seconds after slow flow of 50 ml/min, and the other at the end of dialysis, and 20 seconds after slow flow of 50 ml/min. The purpose of these additional samples was to isolate the effects of AR from those of CPR "at this early time period, all rebound should be due to AR, whereas after 2 min, the rebound represents the combined effects of AR, CPR, and 10 to 20% of the compartment rebound". A further study was done in the three original patients in whom the ratios of the urea concentrations of the constant flow samples to those in the 2-minute slow flow samples indicated severe access recirculation. During the initial study in these patients, the A/V gradient "A:V BUN ratio of 0.70-0.75" far exceeded that which could be explained on the basis of cardiopulmonary recirculation "normally 0.94 for high efficiency dialysis [12]. When repeating the study, 20-second slow flow samples also were obtained, again, to isolate the effects of access recirculation from those of CPR, and to allow computation of AR according to the standard equation "AR = 100 × "20 seconds slow flow inlet - constant flow inlet"/"20 seconds slow flow inlet - constant flow outlet). These three patients did not, however, consent to a second 30-minute postdialysis sample.

3. RESULTS

The expected A/V "or 0/2 min" BUN ratio in patients undergoing high efficiency dialysis is about 0.93 to 0.94 [12]. In 17 patients the expected ratio for urea taken at 80 min from the beginning of dialysis is 0.93±0.008 and postdialysis is 0.93±0.12. In three patients the 0/2-minute BUN ratios were markedly reduced both intradialysis "0.73±0.039" and postdialysis "0.66±0.035". The results indicated that the three patients in question had severe AR, because, with the dialyzer clearances used, it

would have been impossible to achieve such high A/V gradients due to cardiopulmonary recirculation alone with physiologically compatible levels of cardiac output "cardiac output minus access flow would need to be in the range of < 1.0 liter/min".

Indeed, when studied a second time using additional 20-second slow flow samples, marked AR "32%, 35%, and 37%, respectively" was again demonstrated in these three patients. In the five additional patients with AR, AR averaged 35.2±6.6%, and the 0/2-minute BUN ratios were 0.72±0.06 intradialysis, and 0.64±0.06 postdialysis. The pooled results for the eight patients with severe AR are presented in Table 1. In the 17 patients with minimal AR the single-pool arterial Kt/V averaged 1.46 units “Table 1”, whereas Kt/V based on the 2-minute slow flow samples, which can be considered to be a "mixed venous" Kt/V despite the fact that it contains a small component of the "compartment effect" rebound, was 1.38 units. For the patients with severe AR the difference between arterial and mixed venous single pool Kt/V was greater, in that Kt/V decreased from 1.60 to 1.12. This was due to overestimation of single-pool arterial Kt/V due to access recirculation. For the first group "17 patients" with minimal access recirculation, the Kt/V computed using the 30-minute postdialysis samples was 1.23 units versus a single-pool arterial value of 1.46 units. The difference was -0.22 ± 0.028 Kt/V units. For the second group "8 patients" with severe access recirculation, the drop in Kt/V was much greater, from 1.60 to 0.94 Kt/V units “Table 1”, or -0.66±0.060 "P < 0.001 vs. patients with minimal access recirculation". For the group of patients with minimal AR, both constant flow and 2-minute slow flow Smye estimates of equilibrated Kt/V accurately predicted the $_{eq}$"Kt/V" based on the 30-minute postdialysis specimens. The Kt/V values of -0.23 and -0.22 predicted by the constant flow "Sm_0" and 2-minute slow flow "Sm_2" Smye techniques, respectively, were not significantly different from the measured Kt/V of -0.23±0.028 based on the 30-minute rebound sample. For the group of patients with severe AR, both Smye methods approximated the observed Kt/V of -0.66 on average, but the correlation “Table 2” between predicted and observed ΔKt/V with the constant flow Smye method "R = 0.34" was much lower than with the 2-minute slow flow Smye method "R=0.66".

Table 1. Modeling results.

	Minimal AR (n=17)	Severe AR (n=8)	P-value
C_{intra}: constant/ slow flow	0.93 ± 0.008	0.73 ±0.039	< 0.001
C_{post}: constant/slow flow	0.93 ± 0.12	0.66 ± 0.035	<0.001
Weight, kg	68.5 ± 4.8	81.2 ± 16.3	–
Sex (M:F)	7:10	3:5	–
Session length hours	3.6 ± 0.12	3.5 ± 0.16	–
Dialyzer K_0A ml/min	793 ± 3.8	748 ± 40	–
Q_b, ml/min	398 ± 1.5	393 ± 14	0.019
K/V hr^{-1}	0.41 ± 0.02	0.44 ± 0.020	–
C_{pre}, mg/dl	57.8 ± 4.3	64.2 ± 6.4	–
$PDUR_p$	22.4 ± 3.3	81.5 ± 9.8	< 0.001
$PDUR_f$	8.6 ± 0.75	28.2 ± 4.2	< 0.001
Kt/V_{sp0} constant flow	1.46 ± 0.059	1.60 ± 0.06	0.08
Kt/V_{sp2} slow flow	1.38 ± 0.046	1.12 ± 0.10	0.024
$_{eq}(Kt/V)_{30}$	1.21± 0.049	0.94 ± 0.1	< 0.001
$\Delta(Kt/V)_{30}$	-0.23 ± 0.02	-0.66 ± 0.06	< 0.001
$_{eq}(Kt/V)_{Smo}$	1.22 0.058	1.04 ± 0.16	0.14
$\Delta(Kt/V)_{Smo}$	-0.23 ± 0.02	-0.56 ± 0.10	< 0.001
$_{eq}(Kt/V)_{Sm2}$	1.22 ± 0.064	0.88 0.08	< 0.004
$\Delta(Kt/V)_{Sm2}$	-0.22 ± 0.036	-0.72 ± 0.075	< 0.001
Modeled single-pool V (V_{sp0})	36.6 ± 1.9	32.1 ± 2.3	–
Anthropometric V (V_a)	35.4 ± 1.9	38.5 ± 3.1	–

Table 2. Correlation results.

	Minimal AR	Severe AR
$V_{Anthropometric}$ with V_{sp0}	0.81	0.74
$\Delta(Kt/V)_{30}$ with K/V	0.78	0.48

$\Delta(Kt/V)_{30}$ with session length	-0.53	-0.55
Kt/V_{sp0} with $_{eq}(Kt/V)_{30}$	0.88	0.86
$_{eq}(Kt/V)_{Smo}$ with $_{eq}(Kt/V)_{30}$	0.94	0.65
$_{eq}(Kt/V)_{Sm2}$ with $_{eq}(Kt/V)_{30}$	0.89	0.84
$\Delta(Kt/V)_{Smo}$ with $\Delta(Kt/V)_{30}$	0.69	0.34
$\Delta(Kt/V)_{Sm2}$ with $\Delta(Kt/V)_{30}$	0.61	0.66

The comparisons between the equilibrated Kt/V predicted by the constant flow and 2-minute slow flow Smye techniques and the measured equilibrated Kt/V based on a 30-minute rebound sample are shown in Figs. 2 and 3. The Kt/V based on the 30-minute postdialysis sample (eKt/V_{30}) is plotted against single-pool Kt/V as shown in Fig. 2. It is evident from the Figure that the most marked overestimation of Kt/V was present in the patients with access recirculation. The magnitude of postdialysis urea rebound from 0 to 30 minutes, or the magnitude of ΔKt/V, failed to correlate with the patients' gender. In four patients who experienced marked hypotension during dialysis, the Kt/V (-0.19±0.052) was similar to that in patients without hypotension (-0.23±0.034, P =NS). Hypotension was not observed in any of the three patients with marked access recirculation. Correlations that were found to be predictive of ΔKt/V were with K/V and t (session length). The K/V term was calculated as the single-pool arterial Kt/V divided by the number of hours of dialysis. The magnitude of this correlation (R = 0.78) was substantial (P < 0.005) and these data suggest that the efficiency of dialysis is a major factor in determining ΔKt/V.

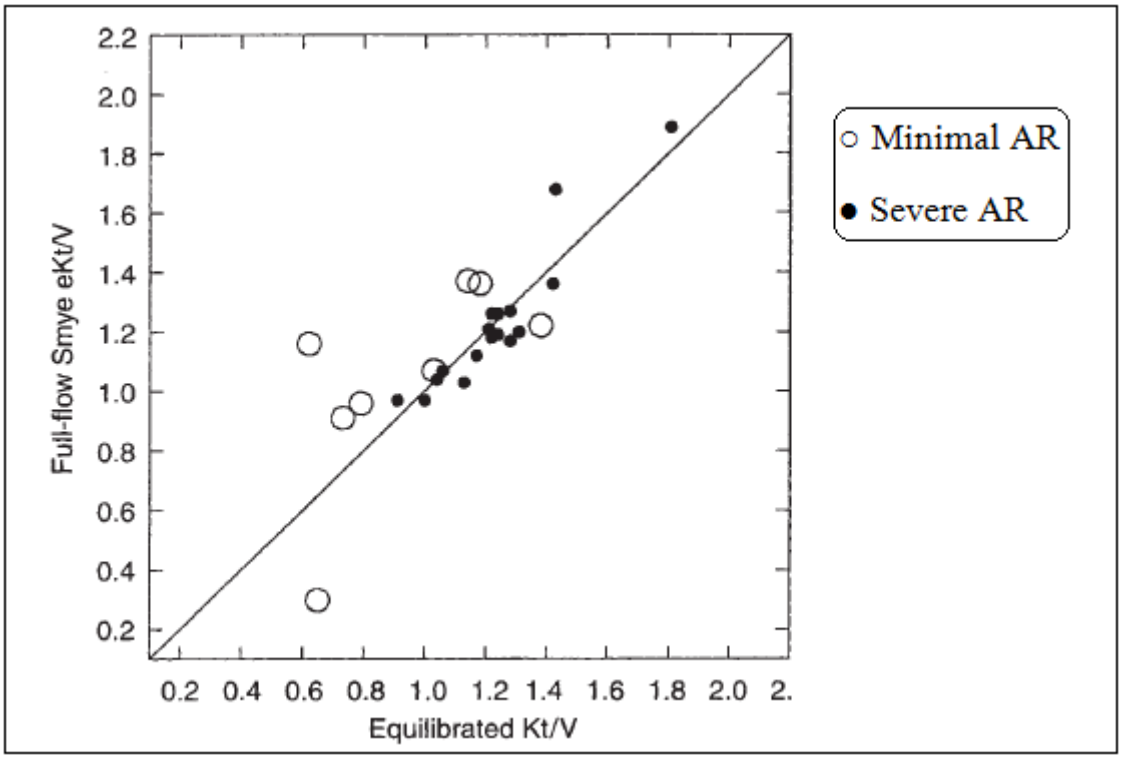

Fig. 2. Comparison of equilibrated Kt/V calculated based on the constant flow Smye technique compared with that computed from the 30-minute postdialysis specimens.

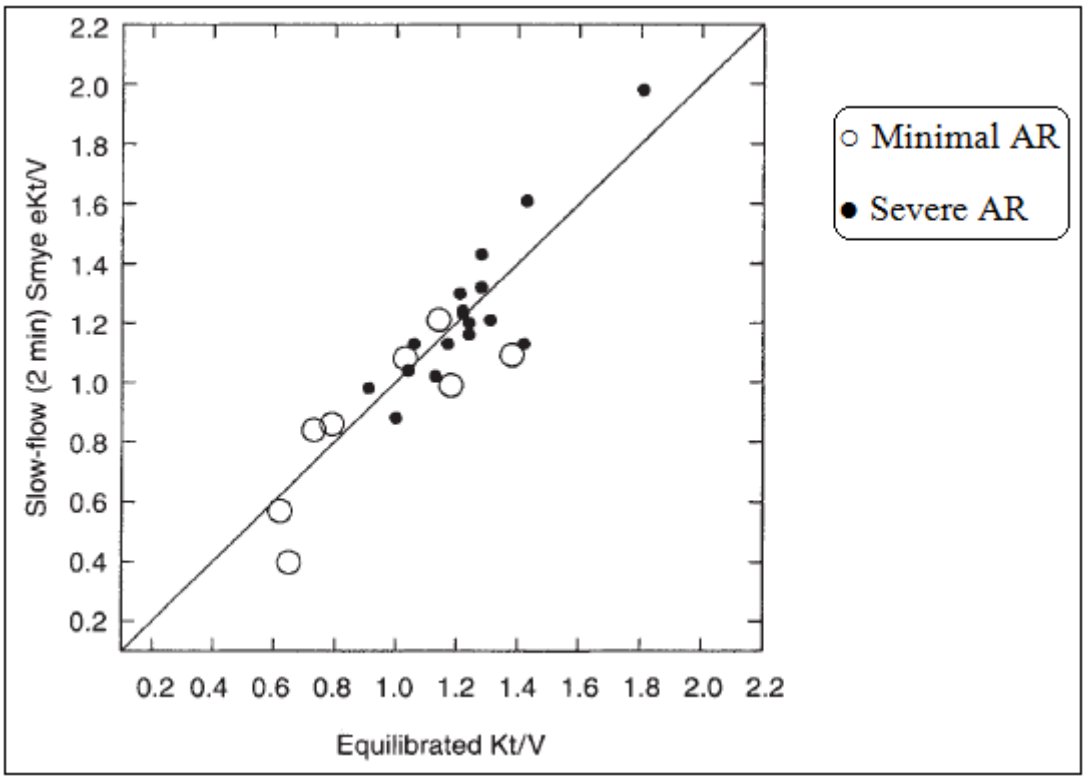

Fig. 3. Comparison of equilibrated Kt/V calculated based on the 2-minute

slow flow Smye technique compared with that computed
from the 30-minute postdialysis specimens.

4. DISCUSSION

The collected data suggest that substantial postdialysis urea rebound may occur when dialysis efficiency is high, even in patients undergoing relatively long dialysis session lengths of approximately 3.5 hours. In patients with minimal access recirculation (AR), for example, equilibrated Kt/V was 0.22 units lower than Kt/V derived from single-pool kinetics. The Smye-derived estimates of equilibrated Kt/V were very similar to the equilibrated Kt/V values based on the measured 30-minute postdialysis BUN specimens. Our data suggest that, in the absence of severe AR, either one of the two variations of the Smye technique tested (constant flow samples or 2-min slow flow samples) is accurate. The constant flow Smye technique considers the aggregate effect of access recirculation, cardiopulmonary recirculation, and compartment-regional blood flow effects. In the 2-minute slow flow variation of the Smye method, the effects of access recirculation and cardiopulmonary recirculation have been dissipated by the time that the intradialytic and postdialysis samples are drawn. The theoretical advantage of using the 2-minute slow flow method is, in patients with non-constant degrees of AR and/or CPR, the 2-minute slow flow method should still give an accurate result. However, in patients with severe AR, when the degree of AR is not constant throughout dialysis, the constant flow Smye technique will have a high degree of variability. The degree of AR may increase substantially during dialysis, due to reduced cardiac output and access flow as fluid is removed. In such patients, the constant flow Smye technique may underestimate the equilibrated postdialysis BUN markedly. In contrast, the 2-minute slow flow Smye method should not be subject to error, even in patients with non-constant access recirculation during dialysis, as all samples are obtained after the effects of access "and cardiopulmonary" recirculation have dissipated. Our own data suggest that much of the variance in postdialysis urea rebound among patients can be explained on the basis of the efficiency of dialysis, or the single-pool K/V ratio. In summary, two variations of the

Smye technique "sampling at constant flow and after 2-min slow flow" were accurate in patients with minimal AR. In patients with severe AR, the Smye method using constant flow samples had an unacceptable degree of variability, and markedly underestimated rebound in those patients in whom AR increased in the course of the dialysis session. The constant flow Smye method should not be used routinely. Rather, the blood flow should be slowed for either 20 seconds or two minutes prior to obtaining both the intradialytic and postdialysis samples. It is important to obtain both samples using exactly the same sampling technique.

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تأثير تقنية تقليل سريان الدم على معدل ارتجاع اليوريا بعد جلسة الغسيل الكلوى وجرعة الغسيل الحقيقية

لوحظ أن بعض النماذج الرياضية الحالية لا تأخذ فى إعتبارها معدل ارتجاع اليوريا بعد جلسة الغسيل الكلوي مما يسبب عدم دقة توقع حساب نسبة اليوريا فى الدم وأن البعض الأخر يأخذ فى إلاعتبار معدل إرتجاع اليوريا على أساس إستخدام تقنية ثبات سريان الدم فى حساباتها مما يؤدى الى عدم دقة النتائج خصوصا للمرضى الذين يعانون من إعادة غسيل الدم بعد إجراء الغسيل بمدة نصف ساعة والذى يطلق عليه خاصية الإرتجاع، وقد تم فى البحث التوصل الى نموذج رياضى جديد يقوم على

أساس إستخدام تقنية تقليل سريان الدم أثناء حساب معدل إرتجاع اليوريا مما نتج عنه تحسين كفاءة الغسيل الكلوى الحقيقية مقارنة بتقنية ثبات سريان الدم.