

ORIGINAL ARTICLE

Ionic dialysance and determination of Kt/V in on-line hemodiafiltration with simultaneous pre- and post-dilution

Caroline Créput¹, Daniel Toledano¹, Thierry Petitclerc¹

¹ Hemodialysis Center Henri Kuntziger, AURA, Paris - France

ABSTRACT

Purpose: A direct determination of Kt/V using ionic dialysance for estimating K and bio-impedancemetry for estimating V is compared with the usual indirect estimation based on the second generation Daugirdas equation during a new technique of hemodiafiltration with simultaneous pre- and post-dilution (mixed-HDF).

Methods: In 31 informed consented patients, the urea distribution volume (V) is estimated by total body water (V_{BCM}) measured by the Body Composition Monitor (BCM; Fresenius Medical Care, Bad Homburg, Germany) based on bio-impedance spectroscopy. The value $(K_{OCM} t)/V_{BCM}$ is calculated during 114 mixed-HDF sessions (duration 4 hours) from the measurement of ionic dialysance K_{OCM} by the OCM module, standard on the 5008 dialysis monitor (Fresenius Medical Care, Germany). The single pool $(Kt/V)_{sp}$ is determined from blood urea concentration measurements using the Daugirdas equation.

Results: Mixed-HDF is a very high-efficiency hemodialysis with a delivered dialysis dose Kt/V near from 2 per 4-hour session. $(K_{OCM} t)/V_{BCM}$ (1.97 ± 0.28) is consistent with $(Kt/V)_{sp}$ (2.01 ± 0.34) with a correlation coefficient at 0.72.

Conclusions: Direct calculation of Kt/V from estimating K by OCM and V by BCM is consistent with the usual indirect estimation by the second generation Daugirdas equation. Therefore, the regular determination of V by BCM allows the estimation of single-pool Kt/V at each session without the need of blood sampling.

KEY WORDS: Hemodiafiltration, Mixed-dilution, Bio-impedancemetry, Ionic dialysance, Kt/V index, Urea distribution volume

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INTRODUCTION

Adequacy of hemodialysis efficiency is currently based on the determination of the index (Kt/V) where (K) is the urea clearance, (t) the treatment time, and (V) the urea distribution volume at equilibrium assumed equal to total body water. There are two varieties of methods for determining Kt/V: 1) indirect methods provide an estimation of Kt/V from observing the change during the session

of blood urea concentration by using equations derived from urea kinetic modeling; 2) direct methods are based on an independent measurement of the three parameters K, t, and V.

Indirect determinations of Kt/V have been generalized during the last decades because they do not require measurements for estimating (K) which was very cumbersome and not suitable for clinical routine before the availability of ionic dialysance measurement. More recently, when pro-

viding a correct estimation of V, some dialysis monitors automatically give a direct estimation of Kt/V calculated from ionic dialysance without requiring blood urea concentration measurements (1).

The aim of our study using a new technique of on-line hemodiafiltration with pre- and post-dilution is to compare the value of Kt/V obtained by the usual indirect method based on the Daugirdas second generation equation with the value obtained by a direct method using ionic dialysance for estimating K and bio-impedancemetry for estimating V.

MATERIALS AND METHODS

Mixed-HDF

In on-line hemodiafiltration (ol-HDF), the volume of dialysate infused in post-dilution is limited by the hemoconcentration in the dialyzer. However pre-dilution treatment limits the efficiency of the dialysis session. Mixed-HDF is a pre/post ol-HDF technique with an automatic control of the pre/post dilution ratio for optimizing the efficiency of the treatment. This technique implemented on 5008 dialysis monitor (Fresenius Medical Care, Bad Homburg, Germany) uses a feedback system for controlling transmembrane pressure (TMP) in order to maintain mean TMP in the safe range of 250 mmHg to 300 mmHg without affecting the total volume of infused dialysate or the net ultrafiltration (2). The mean value of TMP is calculated from measurements by four pressure sensors located at the dialyzer input and output of the blood and the dialysate. If TMP rises beyond its maximum tolerated value, a fraction of infused dialysate is diverted from post- to pre-dilution, decreasing the fraction of plasma water through the dialyzer membrane (and thus the mean TMP), and vice versa if the mean TMP falls below the lowest value of the range.

Patients and Methods

Thirty-one chronic hemodialysis patients (22 males, 9 females; median age: 66.5 years, range: 34-88), hemodialyzed 4 hours, three times a week, on an arterio-venous access with a Fresenius 5008 dialysis machine, gave their informed consent for participating to the study. The patients' baseline characteristics are shown in Table I.

TABLE I - BASELINE CHARACTERISTICS OF THE PATIENTS (N = 31)

Age (years)	66.5 (34-88)
Sex (M/F) (% men)	22/9 (72%)
Dialysis vintage (years)	7.57 (0.75-17.41)
Causal nephropathy (n):	
Diabetic nephropathy	11
Polycystic kidney disease	4
Nephroangiosclerosis	6
IgA nephropathy	2
Malformative uropathy	1
Obstructive nephropathy	2
Other	5
Body weight (kg)	73.5 (51-95.5)
Arterio Venous Fistula	31 (100%)
Hematocrit (%)	36.6 ± 3.3
Hémoglobin (g/dl)	12.1 ± 1.1
Protidemia (g/l)	65 ± 1
Serum Albumin (g/l)	35.5 ± 1.5

Values are expressed as number (percentage) or median (range).

Four treatments by mixed-HDF were performed for each patient in two consecutive weeks after a long and a short consecutive interdialytic interval. All treatments were performed using a Fresenius FX1000 high-flux hemodialyzer (Fresenius Medical Care, Bad Homburg, Germany).

Determination of Kt/V

The indirect determination $(Kt/V)_{sp}$ of Kt/V is calculated using the second generation Daugirdas equation (3): $(Kt/V)_{sp} = -\ln((c_{end}/c_0) - 0.008 t) + (4 - 3,5 (c_{end}/c_0)) \Delta BW/BW$ where (t) is the session time (hours), (BW) the body weight, (ΔBW) the intradialytic weight loss, (c_0) and (c_{end}) the urea plasma concentration measured at the start and at the end of the session respectively. The post-dialytic blood sample was drawn from the arterial blood line 2 minutes after reducing the blood flow rate to 50 ml/min and turning off the dialysate flow. Plasma concentrations of urea are changed in plasma-water concentrations by

taking into account the total protein plasma concentration (Prot):

$$C_{(\text{mmol/kg})} = C_{(\text{mmol/L})} / (1 - 0.01 \cdot \text{Prot}_{(\text{g/dL})}).$$

The direct determination ($K_{\text{OCM}} t / V_{\text{BCM}}$) of (Kt/V) is calculated using an independent measurement K_{OCM} and V_{BCM} of K and V respectively. The value K_{OCM} is calculated from repeated measurements of ionic dialysance during the dialysis session by the Online Clearance Monitor (OCM) standard on the monitor 5008. The value V_{BCM} is the post-dialytic value of total body water determined by bio-impedance analysis using the Body Composition Monitor (BCM; Fresenius Medical Care, Bad Homburg, Germany) from two measurements performed on a mid-week session (once for each type of interval). This BCM is based on multi-frequential analysis (bio-impedance spectroscopy). Total body water is calculated from estimation of body impedance at infinite frequency by extrapolating values of impedance measured for 50 frequencies within the range 5 kHz to 1000 kHz. Determination of total body water immediately after the end of the dialysis session is not valid, because the water equilibrium in body fluid compartments is not reached. Thus, the measure should be performed at least 30 minutes after the session, which requires that the patient be retained. Therefore, the bio-impedance analysis is performed just before the session. The value (V_{BCM}) is the mean of total body water at the end of the session calculated by subtracting the intradialytic weight loss (ΔBW). In addition, these direct and indirect determinations of Kt/V are compared to:

- the value of Kt/V displayed on the screen of the 5008 dialysis monitor. This value is a direct determination ($K_{\text{OCM}} t / V_{\text{Wat}}$) calculated using K_{OCM} and the value V_{Wat} of total body water provided by Watson's formulas (4);
- the value $(\text{Kt/V})_{\text{eq}}$ of equilibrated Kt/V calculated from the indirect determination $(\text{Kt/V})_{\text{sp}}$ using the Daugirdas-Schneditz equation rate for an arterio-venous access (5):

$$(\text{Kt/V})_{\text{eq}} = (\text{Kt/V})_{\text{sp}} - (0.6 / t) (\text{Kt/V})_{\text{sp}} + 0.03.$$

Statistical analysis

Results are expressed as mean $\pm$ standard deviation (SD) or median and min-max for continuous variable. Continuous data were evaluated using paired Student *t* test. The probability $p < 0.05$ was considered statistically significant.

The agreement between two variables is represented by a Bland-Altman plot.

RESULTS

Both measurements of $(\text{Kt/V})_{\text{sp}}$ and K_{OCM} were obtained for 114 sessions in 31 patients. These 114 sessions were analyzed.

Duration of hemodialysis session was 231 ± 3 min. Mean effective blood flow rate was 390 ± 19 ml/min (range: 340-400 ml/min). The total volume of infused dialysate was 36.0 ± 5.4 L per treatment. The mean volume of dialysate infused in post-dilution was 22.4 ± 3.5 L per treatment corresponding to 60% of the total infusion volume. Values of c_0 , c_{end} , $(\text{Kt/V})_{\text{sp}}$, $(\text{Kt/V})_{\text{eq}}$, K_{OCM} , V_{BCM} , $(K_{\text{OCM}} t / V_{\text{BCM}})$, V_{Wat} and $(K_{\text{OCM}} t / V_{\text{Wat}})$ are reported in Table II.

The direct estimation $(K_{\text{OCM}} t) / V_{\text{BCM}}$ of Kt/V is slightly but not significantly lower than the indirect estimation $(\text{Kt/V})_{\text{sp}}$ with a mean difference at 0.036. The correlation coefficient between $(K_{\text{OCM}} t / V_{\text{Wat}})$ and $(\text{Kt/V})_{\text{sp}}$ is equal to 0.72 (Fig. 1). This coefficient does not change ($r = 0.72$) if the plasma-water concentrations of urea (mmol/kg) are substituted by plasma concentrations (mmol/l) as usually measured.

TABLE II - EXPERIMENTAL DATA OF THE PATIENTS (N = 31)

	Mean $\pm$ SD	Median	Range
c_0 (mmol/l)	20.1 $\pm$ 6.1	20	8-39
c_0 (mmol/kg)	21.6 $\pm$ 6.6	21.4	8-42
c_{end} (mmol/l)	3.9 $\pm$ 1.6	3.5	1-9
c_{end} (mmol/kg)	4.2 $\pm$ 1.7	3.9	1-10
$(\text{Kt/V})_{\text{sp}}$	2.01 $\pm$ 0.34	2.01	1.30-2.76
$(\text{Kt/V})_{\text{eq}}$	1.70 $\pm$ 0.24	1.70	1.20-2.27
K_{OCM} (ml/min)	258 $\pm$ 30	266	159-303
V_{BCM} (L)	30.5 $\pm$ 5.8	28.8	22-43
(% of body weight in males)	(46 $\pm$ 6)	(46)	(36-58)
(% of body weight in females)	(38 $\pm$ 6)	(38)	(26-49)
$(K_{\text{OCM}} t / V_{\text{BCM}})$	1.97 $\pm$ 0.28	1.97	1.38-2.65
V_{Wat} (L)	36.2 $\pm$ 5.4	35.4	27-47
(% of body weight in males)	(54 $\pm$ 3)	(53)	(50-60)
(% of body weight in females)	(47 $\pm$ 4)	(47)	(38-55)
$(K_{\text{OCM}} t / V_{\text{Wat}})$	1.67 $\pm$ 0.26	1.68	0.99-2.28

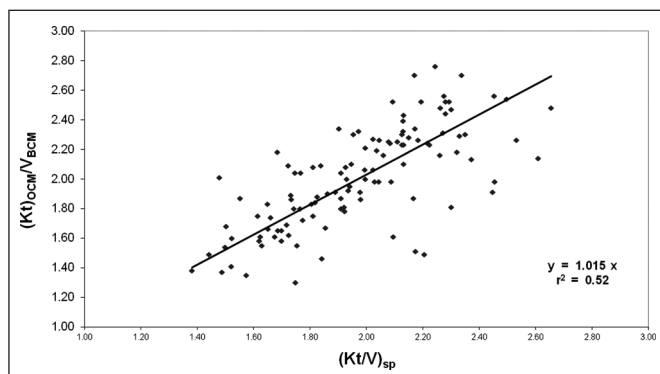


Fig. 1 - Correlation between $(Kt/V)_{sp}$ calculated from blood urea concentrations and $(K_{OCM} t)/V_{BCM}$ calculated from ionic dialysance and bio-impedance spectroscopy.

V_{Wat} overestimates V_{BCM} by about 20%. The direct estimation $(K_{OCM} t)/V_{Wat}$ is significantly ($p < 0.001$) lower than $(Kt/V)_{sp}$ by more than 15% and approaches the value of $(Kt/V)_{eq}$. The correlation coefficient between $(K_{OCM} t)/V_{Wat}$ and $(Kt/V)_{eq}$ is 0.58.

Bland-Altman diagrams (Fig. 2) show that the agreement with $(Kt/V)_{sp}$ is better for $(K_{OCM} t)/V_{BCM}$ than for $(K_{OCM} t)/V_{Wat}$. The difference between $(K_{OCM} t)/V_{BCM}$ and $(Kt/V)_{sp}$ increases slightly with the level of Kt/V (Fig. 2).

DISCUSSION

Because the measurement of urea clearance was difficult to implement in routine clinical practice before the availability of ionic dialysance, adequacy of dialysis is usually determined using equations derived from kinetic modeling for indirectly estimating the Kt/V index which represents the dialysis dose (Kt) normalized to total body water (V). Due to the need for blood sampling, Kt/V is estimated only intermittently. American and European guidelines suggest a monthly determination of Kt/V from arterial values of blood urea concentration measured before and after the dialysis session by using the second generation Daugirdas equation (6, 7).

In clinical practice, intra-patient variability of the dialysis dose is inevitable (8-9). Therefore, monitoring of dialysis adequacy can require more frequent assessment of Kt/V than is currently performed. On-line monitoring of ionic dialysance – a surrogate of urea clearance (10, 11) – allows the dialysis dose (Kt) to be measured automatically, non-invasively, and economically. The Kt/V index can thus be

directly calculated at each session, providing an estimation of total body water (V).

Anthropometric formulas allow total body water to be estimated very easily. Watson's formula is the most widespread anthropometry-based equation implemented in dialysis monitors for displaying on the dialysis monitor screen a direct estimation of (Kt/V) obtained from measurement of ionic dialysance. However Watson's formula overestimates V by 20% to 30% in comparison with the value V_{DDQ} of urea distribution volume determined from direct dialysis quantification (DDQ), which is generally considered as the gold standard in hemodialysis patients but is unsuitable for clinical routine (12-17).

The availability of devices based on bio-impedancemetric measurement allows a non-invasive determination of total body water, but the results largely depend on the technique (mono or multi-frequency analysis, spectroscopic analysis) and the model used for deducing the value of V from the measurement of impedance (18-21). We have chosen the BCM because we have previously shown that the value (V_{BCM}) of total body water (V) provided by this device is in good agreement with V_{DDQ} (22). In addition, V_{BCM} is also in good agreement with urea distribution volume at equilibrium measured by urea kinetic modeling (UKM) (23). The main result of our study is that $(K_{OCM} t)/V_{BCM}$ directly measured by ionic dialysance and bio-impedancemetry is consistent with $(Kt/V)_{sp}$ indirectly measured from urea plasma concentration measurements. The correlation coefficient (0.72) can be accepted as good when considering two fully independent methods. Moreover, this value is in agreement with the value reported by Ahrenholz et al ($r = 0.74$) (24).

Additional results are provided by our study:

- mixed-HDF allows a high reinfusion volume (36 L per session) and a high level of $(Kt/V)_{sp}$ (about 2 for a 4-hour session) greatly above international recommendations;
- our study confirms the overestimation of V by Watson's formula implemented in the dialysis monitor 5008, explaining the underestimation by more than 15% of single-pool Kt/V provided by this monitor. Due to this underestimation, $(K_{OCM} t)/V_{Wat}$ becomes in better agreement with $(Kt/V)_{eq}$ than with $(Kt/V)_{sp}$ as previously reported by McIntyre et al (8) and Wuepper et al (21). However, this value does not correspond to an actual equilibrated Kt/V, because the value of K calculated from ionic dialysance measurements does not take into account the compartmentalization of urea responsible for urea rebound (25). Moreover, the correlation coefficient between $(K_{OCM} t)/V_{Wat}$ and $(Kt/V)_{eq}$ is lower than the correlation coefficient between $(K_{OCM} t)/V_{BCM}$ and

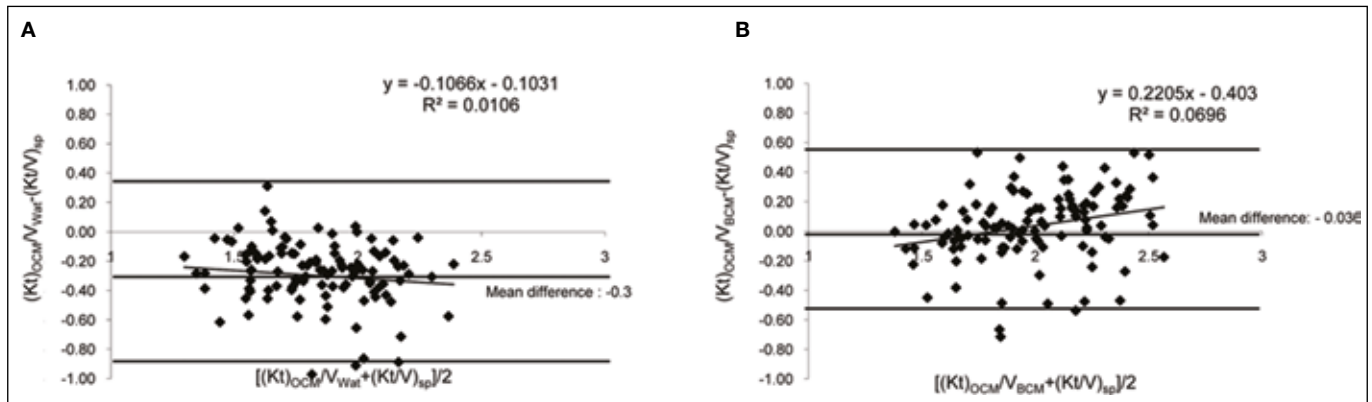


Fig. 2 - Bland-Altman diagrams: A) comparing $(Kt/V)_{sp}$ and $(K_{OCM} t)/V_{Wat}$ B) comparing $(Kt/V)_{sp}$ and $(K_{OCM} t)/V_{BCM}$

$(Kt/V)_{sp}$ (0.58 vs. 0.72) and in agreement with that reported by Granger-Vallée et al ($r = 0.52$) (26).

It should be pointed out that ionic dialysance has been validated in conventional hemodialysis as a good estimation of effective urea clearance of the patient, which is the dialyzer urea clearance taking into account the deleterious effect of access and cardiopulmonary recirculation (27-29). The calculation of ionic dialysance from dialysate conductivity measurements at the dialyzer inlet and outlet assumes no infusion in blood lines during the measure. Moreover, one might expect that, in hemodiafiltration with pre-dilution, ionic dialysance estimates dialyzer urea clearance and not the urea clearance of the system, which is lower because the blood at the dialyzer inlet is diluted by the reinfusion. Actually, ionic dialysance measured in ol-HDF is a valuable estimation of effective urea clearance of the system (and not of the dialyzer), as shown in the appendix and previously validated by Gross et al (30).

In conclusion, during mixed-HDF procedure, our study shows that the direct calculation of Kt/V from estimating K by OCM and V by BCM is consistent with the usual indirect estimation by the second generation Daugirdas equation. Therefore, the regular determination of V by BCM allows the estimation of single-pool Kt/V at each session without the need of blood sampling.

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APPENDIX

In hemodiafiltration with pre-dilution, the urea clearance provided by the dialysis system ($k = J_{urea}/c_{B-urea}$ where J_{urea} is the urea mass-transfer per time unit through the dialyzer membrane and c_{B-urea} the patient's blood urea concentration) is lower than the urea clearance of the dialyzer ($k_d = J_{urea}/c_{Bin-urea}$ where $c_{Bin-urea}$ is the blood urea concentration at the dialyzer inlet), because the blood at the dialyzer inlet is diluted by the reinfusion:

$$c_{Bin-urea} = \frac{Q_B}{Q_B + Q_{pre}} c_{B-urea} \quad (1)$$

where Q_B is the blood flow rate before the dilution and Q_{pre} the pre-dilution reinfusion flow rate. Consequently:

$$k = \frac{Q_B}{Q_B + Q_{pre}} k_d \quad (2)$$

The dialyzer urea clearance k_d is inevitably lower than the blood flow rate Q_{Bin} entering into the dialyzer ($Q_{Bin} = Q_B + Q_{pre}$), but it can be higher than Q_B , while k is inevitably lower than Q_B . Equations described below show that the measurement of ionic dialysance during ol-HDF with pre-dilution allows to calculate urea clearance provided by the ol-HDF system (and not by the dialyzer).

We use the following notations (see Fig. 3):

Q_D : flow rate of total dialysis fluid delivered by the monitor

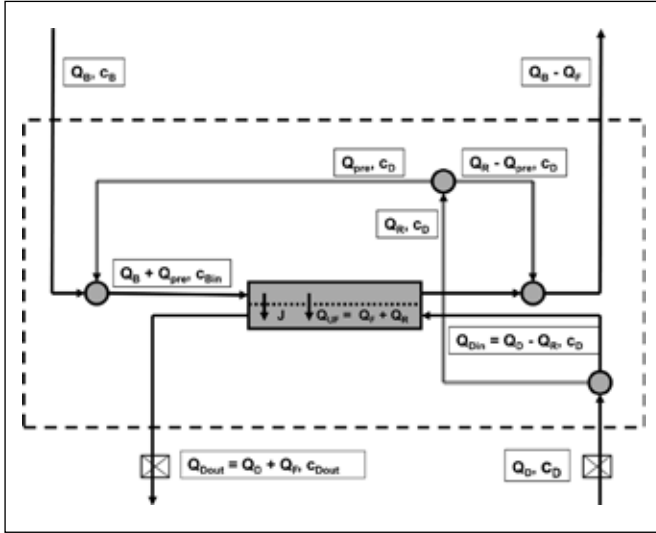


Fig. 3 - Schematic representation of mixed-HDF system with pre- and post- reinfusion.

Q_R : part of Q_D used for the reinfusion:
in conventional HD:

$$Q_R = 0 \quad (3)$$

Q_{pre} : part of Q_R used for pre-dilution:
in conventional HD:

$$Q_{pre} = 0 \quad (4)$$

Q_{Din} : part of Q_D delivered to the dialyzer inlet:

$$Q_{Din} = Q_D - Q_R \quad (5)$$

Q_F : net ultrafiltration rate (weight loss rate)

Q_{UF} : ultrafiltration rate through the dialysis membrane:

$$Q_{UF} = Q_F + Q_R \quad (6)$$

Q_B : blood flow rate before the pre-dilution

c_D : solute concentration in the dialysis fluid delivered by the monitor

c_B : solute blood concentration of the patient (before pre-dilution)

c_{Bin} : solute blood concentration at the dialyzer inlet (after pre-dilution)

Because of pre-dilution, c_{Bin} is not equal to c_B . Equation for solute conservation yields:

$$c_{Bin} = \frac{Q_B c_B + Q_{pre} c_D}{Q_B + Q_{pre}} \quad (7)$$

because $Q_B + Q_{pre}$ is the blood flow rate (Q_{Bin}) at the dialyzer inlet.

Mass-transfer through the dialysis membrane

The mass transfer (J) per time unit of a given solute (for example: sodium) through the dialyzer membrane is equal to:

$$J = Q_{UF} c_D + D (c_{Bin} - c_D) \quad (8)$$

where the solute dialysance (D) of the dialyzer represents the volume of blood at the dialyzer inlet totally equilibrated with the dialysate per time unit and is independent of c_{Bin} and c_D ²⁵.

Equation for solute conservation in dialysate is:

$$J = (Q_{Din} + Q_{UF}) c_{Dout} - Q_{Din} c_D \quad (9)$$

because $Q_{Din} + Q_{UF}$ is the dialysate flow rate (Q_{Dout}) at the dialyzer outlet.

Combining equations (8) and (9) yields:

$$c_{Dout} = \left(1 - \frac{D}{Q_{Din} + Q_{UF}} \right) c_D + \frac{D}{Q_{Din} + Q_{UF}} c_{Bin} \quad (10)$$

Conventional hemodialysis

In conventional hemodialysis (HD):

$Q_{Din} = Q_D$ (see equations 5 and 3)

$Q_{UF} = Q_F$ (see equations 6 and 3)

$c_{Bin} = c_B$ (see equations 7 and 4)

Consequently, equations (8) and (10) can be written:

$$J = Q_F c_D + D (c_B - c_D) \quad (11)$$

and:

$$c_{Dout} = \left(1 - \frac{D}{Q_D + Q_F} \right) c_D + \frac{D}{Q_D + Q_F} c_B \quad (12)$$

On-line hemodiafiltration

Reporting the values of Q_{Din} , Q_{UF} and c_{Bin} for ol-HDF (eqs. 5 to 7) in equations (8) and (10), these equations become:

$$J = (Q_F + Q_R) c_D + D_S (c_B - c_D) \quad (13)$$

and:

$$c_{Dout} = \left(1 - \frac{D_s}{Q_D + Q_F}\right) c_D + \frac{D_s}{Q_D + Q_F} c_B \quad (14)$$

where the solute dialysance (D_s) of the ol-HDF system is defined as:

$$D_s = \frac{Q_B}{Q_B + Q_{pre}} D \quad (15)$$

Measurement of ionic dialysance

Equations (13) and (14) are a generalization of equations (11) and (12) for ol-HDF. These equations are not valuable for HDF with dialysis fluid bags because the composition of dialysis fluid can be different of that of dialysate delivered by the monitor. Equation (15) shows that the solute dialysance (D_s) of the dialysis system is equal to the solute dialysance (D) of the dialyzer for conventional HD and for ol-HDF without pre-dilution and is lower than D for ol-HDF with pre-dilution.

Because the conductivity of a solution is related to its concentration of electrolytes, it is possible to substitute conductivity measurements for concentration measurements and to calculate during conventional HD the value

of D by a transitory change of dialysate conductivity. This value is called "ionic dialysance" of the dialyzer and takes into account the deleterious effect of vascular access and cardiopulmonary recirculation. Because equation (14) is formally identical to equation (12) by substituting D_s for D , the same method allows during ol-HDF sessions to calculate ionic dialysance of the ol-HDF system (and not of the dialyzer), provided that Q_D represents the total dialysis fluid flow rate delivered by the monitor (and not only the dialysate flow rate delivered to the dialyzer). The comparison of equations (2) and (15) shows that ionic dialysance measured in ol-HDF is a valuable estimation of effective urea clearance of the system (and not of the dialyzer).

Conflict of Interest Statement: None.

Address for correspondence:
Caroline Créput MD
Centre Henri Kuntziger
AURA
5 rue du Bessin
75015 Paris
France
e-mail: caroline.creput@auraparis.org

REFERENCES

1. Mercadal L, Ridet C, Petitclerc T. Ionic dialysance: principle and review of its clinical relevance for quantification of hemodialysis efficiency. *Hemodial Int*. 2005;9(2):111-119.
2. Pedrini LA, De Cristofaro V. On-line mixed hemodiafiltration with a feedback for ultrafiltration control: effect on middle-molecule removal. *Kidney Int*. 2003;64(4):1505-1513.
3. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. *J Am Soc Nephrol*. 1993;4(5):1205-1213.
4. 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(1):27-39.
5. Daugirdas JT, Schneditz D. Overestimation of hemodialysis dose depends on dialysis efficiency by regional blood flow but not by conventional two pool urea kinetic analysis. *ASAIO J*. 1995;41(3):M719-M724.
6. Hemodialysis Adequacy Workgroup Membership National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy, 2000. *Am J Kidney Dis* 37:S7-S64, 2001 (suppl 1).
7. European best practice guidelines for haemodialysis. 2. Hemodialysis adequacy. *Nephrol Dial Transplant*. 2002;17(suppl 2):16-31.
8. McIntyre CW, Lambie SH, Taal MW, Fluck RJ. Assessment of haemodialysis adequacy by ionic dialysance: intra-patient variability of delivered treatment. *Nephrol Dial Transplant*. 2003;18(3):559-563.
9. Lambie SH, Taal MW, Fluck RJ, McIntyre CW. Analysis of factors associated with variability in haemodialysis adequacy. *Nephrol Dial Transplant*. 2004;19(2):406-412.
10. Polaschegg HD. Automatic, noninvasive intradialytic clearance measurement. *Int J Artif Organs*. 1993;16(4):185-191.
11. Petitclerc T, Goux N, Reynier AL, Béné B. A model for non-invasive estimation of *in vivo* dialyzer performances and patient's conductivity during hemodialysis. *Int J Artif Organs*. 1993;16(8):585-591.
12. Pastan S, Gassensmith C. Total body water measured by bioelectrical impedance in patients after hemodialysis.

- Comparison with urea kinetics. *ASAIO J.* 1992;38(3): M186-M189.
13. Manzoni C, Di Filippo S, Corti M, Locatelli F. Ionic dialysance as a method for the on-line monitoring of delivered dialysis without blood sampling. *Nephrol Dial Transplant.* 1996;11(10):2023-2030.
 14. Daugirdas JT, Greene T, Depner TA, Chumlea C, Rocco MJ, Chertow GM; Hemodialysis (HEMO) Study Group. Anthropometrically estimated total body water volumes are larger than modeled urea volume in chronic hemodialysis patients: effects of age, race, and gender. *Kidney Int.* 2003;64(3):1108-1119.
 15. Kloppenburg WD, Stegeman CA, de Jong PE, Huisman RM. Anthropometry-based equations overestimate the urea distribution volume in hemodialysis patients. *Kidney Int.* 2001;59(3):1165-1174.
 16. Di Filippo S, Manzoni C, Andrulli S, et al. Ionic dialysance allows an adequate estimate of urea distribution volume in hemodialysis patients. *Kidney Int.* 2004;66(2):786-791.
 17. Teruel JL, Merino JL, Fernández-Lucas M, et al. Cálculo del volumen de distribución de la urea mediante dialisancia iónica. (in Spanish). [Urea distribution volume calculated by ionic dialysance]. *Nefrología.* 2006;26(1):121-127.
 18. Pastan S, Gassensmith C. Total body water measured by bioelectrical impedance in patients after hemodialysis. Comparison with urea kinetics. *ASAIO J.* 1992;38(3):M186-M189.
 19. Dumlér F. Best method for estimating urea volume of distribution: comparison of single pool variable volume kinetic modeling measurements with bioimpedance and anthropometric methods. *ASAIO J.* 2004;50(3):237-241.
 20. Kushner RF, Røxe DM. Bipodal bioelectrical impedance analysis reproducibly estimates total body water in hemodialysis patients. *Am J Kidney Dis.* 2002;39(1):154-158.
 21. Wuepper A, Tattersall J, Kraemer M, Wilkie M, Edwards L. Determination of urea distribution volume for Kt/V assessed by conductivity monitoring. *Kidney Int.* 2003;64(6): 2262-2271.
 22. Koubaa A, Potier J, de Préneuf H, Queffellou G, Garcia F, Petittclerc T. [Estimation of urea distribution volume in hemodialysis patients]. *Nephrol Ther.* 2010;6(6):532-536. French.
 23. Lindley EJ, Chamney PW, Wuepper A, Ingles H, Tattersall JE, Will EJ. A comparison of methods for determining urea distribution volume for routine use in on-line monitoring of haemodialysis adequacy. *Nephrol Dial Transplant.* 2009; 24(1):211-216.
 24. Ahrenholz P, Taborsky P, Bohling M et al. Determination of dialysis dose: a clinical comparison of methods. *NDT plus.* 2010; 3 (suppl 3): iii456.
 25. Petittclerc T. Do dialysate conductivity measurements provide conductivity clearance or ionic dialysance? *Kidney Int.* 2006;70(10):1682-1686.
 26. Granger Vallée A, Chenine L, Leray-Moragues H, et al. Ionic, single pool and equilibrated Kt/V: analysis of a seven year experience. *NDT Plus* (2011) 4 (suppl 2).
 27. Lindsay RM, Béné B, Goux N, Heidenheim AP, Landgren C, Sternby J. Relationship between effective ionic dialysance and *in vivo* urea clearance during hemodialysis. *Am J Kidney Dis.* 2001;38(3):565-574.
 28. Kuhlmann U, Goldau R, Samadi N, et al. Accuracy and safety of online clearance monitoring based on conductivity variation. *Nephrol Dial Transplant.* 2001;16(5): 1053-1058.
 29. Mercadal L, Du Montcel ST, Jaudon MC, et al. Ionic dialysance vs urea clearance in the absence of cardiopulmonary recirculation. *Nephrol Dial Transplant.* 2002;17(1): 106-111.
 30. Gross M, Maierhofer A, Tetta C, Senechal L, Canaud B. Online clearance measurement in high-efficiency hemodiafiltration. *Kidney Int.* 2007;72(12):1550-1553.