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Control of the dialysis dose by ionic dialysance and bioimpedance

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SUMMARY

Introduction: *The ionic dialysance monitor allows an automated measure of Kt in each dialysis session. Bioelectrical impedance analysis (BIA) determines the total body water which it is equivalent to the urea volume of distribution (V). If the Kt, determined by ionic dialysance, is divided by the V, estimated by bioelectrical impedance, a Kt/V at the end of dialysis session (Kt/VDiBi) is obtained.*

Aim of the Study: *To evaluate the agreement between the Kt/VDiBi and the Kt/V obtained by two simplified formulas: the monocompartimental (Kt/Vm) and the equilibrated (Kt/Ve) Daugirdas equations.*

Methods: *The Kt/VDiBi, the Kt/Vm and the Kt/Ve were determined in 38 hemodialysis patients (27 males and 11 females) in the same hemodialysis session. The patients were on dialysis three times a week for 3.5 to 4 hours. The V was determined by monofrequency bioelectrical impedance (50 kHz) at the end of the dialysis session.*

Results: *The Kt/VDiBi, Kt/Vm and Kt/Ve were 1.29 ± 0.26, 1.54 ± 0.29 and 1.36 ± 0.25, respectively ($p < 0.001$ between the Kt/VDiBi and the KtVm, and $p < 0.001$ between the KtV/DiBi and the Kt/Ve). The intraclass correlation coefficient showed better concordance between the KtV/DiBi and the Kt/Ve (coefficient 0.88) than between the Kt/VDiBi and the KtVm (coefficient 0.65). The relative difference of the Kt/VDiBi was 8.3 ± 6.4% with respect to the Kt/Ve and 18.4 ± 7.8% with respect to the Kt/Vm ($p < 0.001$). The relative difference between the Kt/VDiBi and the Kt/Ve was lower than 15% in the 84% of the patients and lower than 10% in the 64% of the patients.*

Conclusions: *If the V obtained by bioelectrical impedance analysis is included in the ionic dialysance monitor, we can obtain a Kt/V for each patient in real time, which is similar to the equilibrated Kt/V obtained from the Daugirdas equation.*

Key words: ***Ionic dialysance. Bioelectrical impedance. Dose of dialysis. Kt/V.***

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CONTROL DE LA DOSIS DE DIÁLISIS MEDIANTE DIALISANCIA IÓNICA Y BIOIMPEDANCIA

RESUMEN

Introducción: *El monitor de dialisancia iónica permite obtener el Kt de cada sesión de diálisis de forma automática. La técnica de bioimpedancia proporciona el parámetro correspondiente al contenido corporal total de agua que es similar al volumen de distribución de la urea (V). Si dividimos el Kt de la dialisancia iónica entre el V calculado por la bioimpedancia conseguimos un Kt/V (Kt/VDiBi).*

Objetivo: *El objetivo del presente trabajo es estudiar la concordancia existente entre el Kt/VDiBi y el Kt/V simplificado obtenido por las ecuaciones de Daugirdas correspondientes a los modelos monocompartimental (Kt/Vm) y equilibrado (Kt/Ve).*

Material y métodos: *El estudio se realizó en 38 enfermos en los que se calculó en la misma sesión de hemodiálisis el Kt/VDiBi, el Kt/Vm y el Kt/Ve. Se trata de 27 varones y 11 mujeres que se dializaban 3 veces a la semana, en sesiones de 3,5 – 4 horas de duración. El V se calculó al finalizar la sesión de hemodiálisis con técnica de bioimpedancia vectorial de monofrecuencia.*

Resultados: *Los resultados de Kt/VDiBi, Kt/Vm y Kt/Ve fueron: 1,29 ± 0,26, 1,54 ± 0,29 y 1,36 ± 0,25 respectivamente ($p < 0,001$ entre Kt/VDiBi y KtVm, y $p < 0,001$ entre KtV/DiBi y Kt/Ve). El coeficiente de correlación intraclase mostró una mejor concordancia entre Kt/VDiBi y Kt/Ve (coeficiente 0,88, concordancia excelente), que entre Kt/VDiBi y Kt/Vm (coeficiente 0,65, concordancia buena). La diferencia relativa del Kt/VDiBi fue 8,3 ± 6,4% con respecto al Kt/Ve, y 18,4 ± 7,8% con respecto al Kt/Vm ($p < 0,001$). La diferencia relativa entre Kt/VDiBi y Kt/Ve fue inferior a 15% en el 84% de los enfermos, e inferior a 10% en el 64% de los enfermos.*

Conclusiones: *Si introducimos en el monitor de dialisancia iónica el V obtenido por bioimpedancia, podemos obtener en cada sesión de hemodiálisis un Kt/V para cada enfermo que es equiparable al Kt/V equilibrado de la ecuación de Daugirdas.*

Palabras clave: ***Dialisancia iónica. Bioimpedancia. Dosis de hemodiálisis. Kt/V.***

INTRODUCTION

There are currently hemodialysis monitoring devices that automatically calculate the dialyzer ionic dialysance during the hemodialysis session.[1] Ionic dialysance is equivalent to urea clearance,[2,3] independently of the type of dialyzer used.[4] Assuming that ionic dialysance and urea clearance (K) are similar, the monitor yields the Kt throughout the dialysis session. By dividing that value by urea distribution volume (V) the Kt/V is obtained by real time ionic dialysance (KtVDi).[5-7]

The V value usually input in the dialysance monitor is derived from Watson's anthropometrical formula. The Kt/VDi thus obtained differs from that given by simplified usual formulas.[8] Other authors that calculated the V value by a percentage of the dry weight had similar difficulties.[6, 9]

One way of solving this problem consists in calculating the V value of each patient by dividing the Kt value obtained by ionic dialysance in a hemodialysis session by the Kt/V obtained within the same session by means of a simplified formula.[10] In this way, a V value is obtained for each patient that once it has

been input in the software it should allow obtaining a Kt/VDi similar to the simplified Kt/V used. The V value thus calculated does not correspond to the real urea distribution volume; it is a virtual value, which will be different depending on the simplified Kt/V value used for the calculations. A preliminary study showed that this procedure is useful, since agreement between both methods was excellent[11] and allowed controlling the dose of dialysis administered at each session, with both the conventional hemodialysis technique[12] and hemodiafiltration.[13]

Bioimpedance analyses yield several data on body composition, among which is total body water,[14] which is equivalent to the urea distribution volume. Bioimpedance constitutes another way to calculate the V value.

The aim of this study was to compare the Kt/obtained by ionic dialysance Kt and the V value V obtained by bioimpedance (Kt/VDiBi), with the simplified Kt/V obtained by means of Daurgidas equations for the mono-compartimental and steady state models, which are the ones most frequently used in clinical practice.

MATERIAL AND METHODS

All patients from the hemodialysis unit using a monitoring device with ionic dialysance reader (Integra® with Diascan® module, Hospal), stable clinical situation, time on dialysis for longer than 3 months, and with no apparent edemas were selected. Three out of 43 patients meeting these conditions were excluded from the beginning for having an amputated lower limb.

For the remaining 40 patients, at the same hemodialysis we calculated session the mono-compartimental Kt/V (Kt/Vm) and the steady state Kt/V (KtVe) by the simplified Daurgidas formulas,[15] the Kt value of the dialysis session given by the Diascan (KtDi) and the volume of body water by bioimpedance (VBi). The ratio between KtDi and VBi yielded the Kt/VDiBi. All bioimpedance analyses were done by the same observer (L.E.A.R.) immediately after the end of the hemodialysis session, after having disconnected the patient from the extracorporeal circuit.

All studies were done during the first hemodialysis session of the week. Post-dialysis urea concentration was determined from a blood sample obtained from the arterial line after having reduced the pump flow to 50 mL/min for 2 minutes, immediately after re-infusing the blood contained in the extracorporeal circuit. The predicted dry weight and post-dialysis weight was registered for each patient. The body mass index (BMI) was calculated using the predicted dry weight.

In two patients, there was an error with Diascan readings so that they were excluded from further analysis. The study was done on 38 patients (27 males and 11 females), with ages ranging 30-82 years (64 ± 15, mean and SD) and time on dialysis comprised between 4 months and 15 years (median 27 months). All patients received dialysis 3 times a week, in sessions of 3.5 or 4 hours duration, with an arterial flow of 300 mL/min. All patients used hollow fiber dialyzers with high-permeability biocompatible membranes: AN69 of 1.65 m^2 (7 patients), polyamide of 2.1 m^2 (8 patients), polysulfone of 1.8 m^2 (9 patients), and polyaril-ethersulfone of 2.1 m^2 (14 patients). In 29 patients the vascular access was an arterial-venous fistula and in nine a permanent central venous catheter.

The bioimpedance vectorial analysis was done by the distal tetrapolar classical technique, with sinusoidal current of 50 kHz frequency (model Quantum/S®, Akern, Florence, Italy). The electrodes were placed on the hemi-body contralateral to the vascular access (arterial-venous fistula or permanent jugular catheter). The calculation of the total body water was done with the Bodygram 1.3 software®. The impedance vector for each patient was graphically confronted (Grafo RXc) with the distribution of vectors from the reference healthy population. The hydration level for each patient was scored by means of a 7-points ordinal scale (from 0 to ± 3), depending on the plotting of the impedance vector at the percentiles 50%, 75%, 95% or > 95% of the main axis of the reference tolerability curve.[14]

Statistical analysis: the difference between the Kt/VDiBi and Kt/Vm and Kt/Ve (bias) and the absolute difference were analyzed in each patient. The ratio between the absolute difference and the arithmetic mean of the Kt/VDiBi and the corresponding simplified Kt/ expressed as a percentage (relative difference), is a dispersion value that indicates the inter-mode variability. Agreement studies were completed by means of the Pearson's correlation coefficient, the inter-class correlation coefficient,[16] and the Bland-Altman construct.[17] The results are expressed as mean and standard deviation. For mean comparisons the Student's t test was used. A p value < 0.05 was considered to be statistically significant.

RESULTS

The predicted dry weight for all 38 patients was 65.8 ± 12.6 kg, and the post-dialysis weight the day of the study was 66.1 ± 13 kg. The BMI was 25 ± 4.5 with no differences by gender (24.5 ± 3.6 in males and 26.4 ± 6 in women, p = n.s.). According to the hydration scale, 23 patients were within the 50th per-

centile (hydration level 0; normo-hydrated), 1 patient was at the 95th percentile (hydration level +2), and 14 patients were over the 50th percentile (hydration level -1 in 4; level -2 in 5, and level -3 in the remaining 5 patients).

For the whole group, VBi was 33.3. ± 7.5 liters (males 35.9 ± 7.1; females 27 ± 3.7 liters, $p < 0.01$). Expressed in percentage of the post-dialysis weight, it represents 50.6 ± 5.7 % for the whole group (males 52.6 ± 4.9%; females 45.4 ± 4.3%, $p < 0.001$).

The results for Kt/VDiBi, Kt/Vm and Kt/Ve were: 1.29 ± 0.26, 1.54 ± 0.29, and 1.36 ± 0.25, respectively ($p < 0.001$ between Kt/VDiBi and KtVm, and $p < 0.001$ between KtV/DiBi and Kt/Ve). There was a good correlation between Kt/VDiBi and Kt/Vm ($r = 0.9268$, $p < 0.001$) and between Kt/VDiBi and Kt/Ve, $r = 0.9274$. $p < 0.001$). The interclass correlation coefficient between Kt/VDiBi and Kt/Vm was 0.65 (good agreement) and between Kt/VDiBi and Kt/Ve was 0.88 (excellent agreement). Table I shows the differences between the different Kt/V models. The least inter-method variability was achieved with Kt/Ve.

Figure 1 shows the Bland-Altman construct that shows the agreement between Kt/VDiBi and Kt/Ve.

From the above data, it may be deduced that there is a good agreement between Kt/VDiBi and Kt/Ve. The level of agreement between both procedures is not influenced by gender (relative difference 8.8 ± 7 % in males and 7 ± 4.7 % in females, p = n.s.), or the hydration level (relative difference 8.7 ± 7.1 % in 23 normo-hydrated patients, 8.1 ± 5.2% in the 14 patients included in the lower part of the scale, which corresponds to a dehydration state, p = n.s.), or the body mass (Pearson's correlation between relative difference and BMI: $r = 0.0271$, p = n.s). There was a negative between the relative difference and Kt/Ve ($r = -0.3745$; $p < 0.05$) indicating that the higher the dialysis dose the lower the inter-method variability.

Table I. Level of agreement between Kt/VDiBi, Kt/Vm and Kt/Ve

	Kt/VDiBi-Kt/Vm	Kt/VDiBi-Kt/Ve	
Difference	-0.25 ± 0.11	-0.08 ± 0.10	$p < 0.001$
Relative difference (%)	18.4 ± 7.8	8.3 ± 6.4	$p < 0.001$
Confidence interval	15.8-21	6.2-10.4	
With relative difference < 10%	4/38 (11%)	26/38 (68%)	
With relative difference < 15%	13/38 (34%)	32/38 (84%)	

Kt/VDiBi: Kt/V obtained from the Kt obtained by ionic dialysance and the V values obtained by bioimpedance.
Kt/Vm y Kt/Ve: Daurgidas equations for the mono-compartimental and steady state Kt/V, respectively.

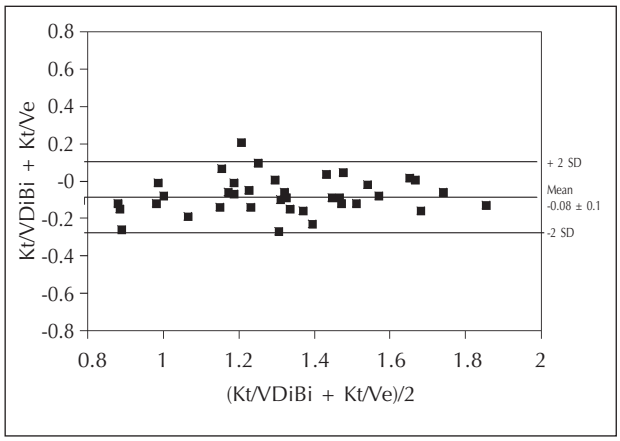

Fig. 1.—Bland-Altman construct to show the level of agreement between the Kt/V obtained by ionic dialysance and bioimpedance (KtVDiBi) and the steady state Kt/V by the Daurgidas equation (Kt/Ve).

The inter-method variability was higher in patients with a central venous catheter as a vascular access (relative difference 11.8 ± 8%) than in patients with arterial-venous fistula (7.2 ± 5.5%, $p < 0.05$); this difference may be explained because the dialysis dose received was lower in patients with a central venous catheter (Kt/Ve 1.22 ± 0.25 vs. 1.4 ± 0.24; $p < 0.05$).

DISCUSSION

The ionic dialysance-monitoring device automatically gives the Kt at each dialysis session. To obtain the Kt/V by ionic dialysance (Kt/VDi) a value for V must be introduced into the software. Here lies the difficulty of this procedure. It is assumed that the urea distribution volume is similar to the total body water content and usually V is calculated as a percentage of the corporal weight[6,9] or by the Watson's anthropometrical equation.[8, 13] The Kt/VDi thus obtained is different from the simplified Kt/V obtained with usual formulas, although in all cases there is a good correlation between them.[8]

The best procedure to calculate the V is by the relationship between the amount of cleared urea in one dialysis session and the decrease in its plasmatic concentration.[18] When he have used this method to obtain the Kt/VDi we have achieved a good correlation with the Daurgidas mono-compartimental simplified Kt/V.[19] This procedure cannot be done in routine clinical practice since it requires the collection of the dialyzate.

In the present work, the V value used has been the total body water content calculated by the electrical

bioimpedance. The bioimpedance is an easily applicable technique, with a low variability coefficient, especially when the standard technique is used in mono-frequency.[14] If we know the total body water content for each patient by bioimpedance and we introduce this value into the software of the ionic dialysance monitoring device, we automatically obtain the Kt/V by ionic dialysance (Kt/VDiBi), which value is very similar to the steady state Kt/V value yielded by the Daurgidas formula (Kt/Ve).

The Kt/VDiBi is slightly lower than Kt/Ve (1.29 ± 0.26 vs. 1.36 ± 0.25). Although the difference between both methods is statistically significant ($p < 0.001$), bias (-0.08 ± 0.10) and inter-method variability are (8.3 ± 6.4 %) small. In 84% of the patients, la inter-method variability was lower than 15%, and in 68% of them, lower than 10%. These data indicate that the level of agreement between the KtV/DiBi and the Kt/Ve is very high and the difference between both is completely assumable in the clinical practice. The inter-method variability between KtVDiBi and Kt/Ve is not influenced by gender, the body mass, or the normo- or dehydration state. We should highlight that by the bioimpedance analysis only one patient was within the overhydration side of the scale.

The data analyzing the correlation between total body water content calculate by bioimpedance and that calculated by dilution methods yield controversial results. Although in some works the results are similar,[20, 21] in others a significant variability has been observed.[22, 23] It is similar for anthropometrical methods. The total body water content by bioimpedance is similar to the urea distribution volume obtained by the formal model of the urea kinetics.[24,25] We should take into account that the V value considered is a virtual concept which only usefulness is achieving that the Kt/V obtained by ionic dialysance be similar to the Kt/V obtained by the simplified formulas. If we divide the Kt obtained by ionic dialysance by the simplified Kt/V used at each hemodialysis unit we will obtain a V value for each patient that once input into the ionic dialysance monitoring device will yield a Kt/Vdi, which is useful for patients' follow-up.[12] If we use the V value obtained by bioimpedance, the ionic dialysance device will yield a Kt/V (Kt/VDiBi) similar to the Daurgidas balanced Kt/V.

In order to eliminate the problem with V, some authors have suggested the convenience of calculating the dialysis dose by the Kt.[26] By using the Kt, a good correlation between the dialysis dose and survival is obtained, being possible to obviate the J curve due to the false Kt/V increase in hyponutrition cases.[27] This procedure presents the drawback of preventing the comparison of the dialysis dose in patients with different body size, and for the time being it has not been widely applied in clinical practice.

Bioimpedance is a technique that is progressively showing its usefulness for assessing the nutritional and hydration status of dialyzed patients.[28] It is very sensitive to changes in body water content, being able to detect changes of 0.87 kg.[29] Similarly to other studies,[25] we have performed the bioimpedance study immediately after ending the hemodialysis session, when patients were at their predicted dry wet. In fact, in only one patient the bioimpedance vector was within the overhydration area. It has recently been shown that the different parameters implicated in bioimpedance, among which is total body water, do not vary in repeated determinations for the first two hours of the post-dialysis period, provided that the patient is fasting.[30] These results indicate that bioimpedance is a technique with a good reproducibility that is not modified by rebound phenomena in solute plasma levels.

We may conclude that by means of the ionic dialysance Kt and the V value for each patient obtained by bioimpedance a Kt/V may be automatically achieved at each hemodialysis session, which is very similar to the balanced Kt/V obtained by the Daurgidas equation. This is a procedure for controlling the dialysis dose that is limited to those hemodialysis units equipped with both technologies.

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