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Monitoring hemodialysis dose with ionic dialysance in on-line hemodiafiltration

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SUMMARY

Until now, with the ionic dialysance measurement, it has been possible to determine hemodialysis dose in each session of hemodialysis (HD) and in the conventional hemofiltration (HDF) but not in the modality of on-line HDF. Recently it is possible with a new biosensor that allows to measure the dose in on-line HDF. The aim of this study was to evaluate the value of this biosensor in different dialysis situations comparing the dialysis dose measured in blood in comparison with the values obtained from the sensor.

We have analysed 192 hemodialysis sessions performed in 24 patients, 15 male and 9 female, mean age of 70.2 ± 12 years, included in on-line HDF. All treatments were done using 4008H (Fresenius) monitor equipped with on-line clearance monitoring (OCM), that measure, with non invasive monitoring, the effective ionic dialysance equivalent to urea clearance. Every patient received eight dialysis sessions: one with dialysate flow (Qd) 500 ml/min, two with HD and Qd 800 ml/min and five with on-line HDF. Other habitual haemodialysis parameters were no changed, dialysis time 200 ± 63 min (135-300) and blood flow 421 ± 29 ml/min (350-450). Initial and final ionic dialysance values (K), final Kt, Kt/V measured with OCM using V of Watson, and Kt/V determined in blood pre and postdialysis concentrations of urea (Daugirdas second generation), were measured.

The mean of initial K was 251 ± 21 ml/min and the final K was 234 ± 24 ml/min. The Kt measured with OCM was 50.6 ± 17 L, 51.2 ± 17 in men and 49.7 ± 16 in women. The V (Watson) was 34.5 ± 6 L. The Kt/V measured with the Kt of OCM and V was 1,499 ± 0.54 and Kt/V measured in blood samples was 1,742 ± 0.58. The correlation between both values was 0.956. The Kt was different according to dialysis modality used: in HD and Qd 500 was 44.7 ± 15 L, in HD and Qd 800 was 50.7 ± 17 and in on-line HDF (22.1 ± 7 L of reposition volume), was 51.8 ± 17 L. The Kt/V from blood samples also shows variation: in HD and QD 500 was 1.60 ± 0.55, in HD and Qd 800 was 1,726 ± 0.56 and in on-line HDF was 1,776 ± 0.59.

In this study has been observed a close correlation between the new biosensor OCM with the measures obtained from the blood samples. For this reason this sensor it is useful in all modalities of dialysis treatment, included on-line HDF. The sensor was able to discriminate the efficacy of different dialysis modalities used in this study.

Key words: ***Dialysis dose. Ionic dialisance. Non invasive monitoring. On-line hemodiafiltration.***

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VALORACIÓN DE LA MEDICIÓN DE LA DOSIS DE DIÁLISIS CON DIALISANCIA IÓNICA EN HEMODIAFILTRACIÓN ON-LINE

RESUMEN

Hasta la actualidad se podía determinar la dosis de diálisis en tiempo real y en cada sesión en hemodiálisis (HD) o hemodiafiltración (HDF) convencional, pero no en HDF on-line, con medición de dialisancia iónica. Recientemente se dispone de un nuevo sensor, on-line clearance monitoring (OCM), que permite la medición de la dosis en HDF on-line. El objetivo del estudio fue valorado en diferentes situaciones analizando la concordancia entre los resultados medidos en sangre y los obtenidos con el monitor.

Se estudiaron 192 sesiones en veinticuatro pacientes, 15 varones y 9 mujeres, de 70,2 ± 12 años, en programa de HDF on-line, con monitor 4008H Fresenius equipado con nuevo OCM que mide, de forma no invasiva, la dialisancia iónica efectiva equivalente al aclaramiento urea. Cada paciente recibió 8 sesiones, una con HD con flujo baño (Qd) 500 ml/min, dos con HD y Qd 800 ml/min y cinco con HDF on-line. Se mantuvo el tiempo, 200 ± 63 (135-300 min), y el Qb, 421 ± 29 (350-450 ml/min). Se determinó la dialisancia iónica inicial y final, el Kt final, el Kt/V el OCM con V de Watson y el Kt/V Daugirdas segunda generación en sangre.

La media de K inicial fue de 251 ± 21 ml/min y final de 234 ± 24 ml/min. El Kt medido por el OCM fue de 50,6 ± 17 L, 51,2 ± 17 L en varones y 49,7 ± 16 L en mujeres. El V Watson fue de 34.5 ± 6 L. El Kt/V medido con el Kt del OCM y V Watson fue de 1.499 ± 0,54 y el Kt/V determinado analíticamente fue de 1.742 ± 0,58. La correlación entre ambos Kt/V fue de 0,952. El coeficiente de correlación intraclase fue de 0,907 (fiabilidad excelente). El Kt varió según modalidad: HD y Qd 500 fue de 44,7 ± 15, HD y Qd 800 fue de 50,7 ± 17 y en HDF on-line, con 22,1 ± 7 L de reposición, fue de 51,8 ± 17 L. El Kt/V en sangre también varió según modalidad: HD y Qd 500 fue de 1,60 ± 0,55, HD y Qd 800 fue de 1.726 ± 0,56 y en HDF on-line fue de 1.776 ± 0,59.

Conclusiones: *La nueva versión de medida de la dialisancia iónica para HDF on-line ha sido valorada en este estudio comprobando la estrecha correlación con las determinaciones realizadas en sangre, validando su uso en esta modalidad de tratamiento. Este dispositivo discriminó bien las diferentes situaciones de eficacia de diálisis empleadas en el estudio.*

Palabras clave: ***Dializancia iónica. Dosis de diálisis. HDF on-line. Monitorización no invasiva.***

INTRODUCCIÓN

Currently, knowing the dialysis dose that patients receive is paramount. There are several observational studies that highlight the relationship between dialysis dose and mortality.[1-6] Other studies have related dialysis dose with anemia correction[7] and nutritional improvement.[8] Therefore, it seems reasonable to find interesting to know this parameter in an easy and accessible way at each hemodialysis session.

Petitclerc *et al.* found a good correlation between urea clearance and effective ionic dialysance, including the variations in ultrafiltration and vascular access recirculation. Until now, several studies have been published on determining the dialysis dose in real time and at each session, in hemodialysis (HD).[11-14] However, this determination was not possible with on-line hemodiafiltration (HDF), a dialysis modality that uses high reposition volumes. Recently, a new version of the biosensor is available that allows measuring the dialysis dose with this modality.

The aim of the present study was to assess and validate this new biosensor in different efficacy conditions, analyzing the agreement between results me-

asured in the blood and those obtained with ionic dialysance.

PATIENTS AND METHODS

A total of 192 hemodialysis sessions performed in 24 patients were studied; patients were 15 men and 9 women, mean age 70.2 ± 12 years (range 36-83), included in a regular program of on-line HDF. Three patients were on a 3 sessions/week schedule for 268 ± 22 minutes (210-300) per session, and the remaining 11 on a daily regimen (6 sessions/week) for 142 ± 8 minutes (135-150) per session. The etiologies of chronic renal failure were ischemic nephropathy (7 cases), chronic glomerulopathy (6 cases), adult polycystic renal disease (4 cases), unknown origin (3 cases), tubulointerstitial nephropathy (2 cases), diabetic nephropathy and systemic lupus erythematous, one case each. Remnant renal function was negligible.

All patients were dialyzed with a 4008H Fresenius monitor, equipped with the new OCM (*On-line Clearance Monitoring)* biosensor, which measures ionic dialysance though conductivity probes in a non-invasive way, also in on-line HDF modality.

Each patient received eight different dialysis sessions. One session was carried out with conventional hemodialysis (HD) and with a dialysis fluid flow (Qd) at 500 mL/min. Two sessions were also carried out with HD and Qd was increased to 800 mL/min. The remaining five sessions were carried out with on-line HDF with Qd set at 800 mL/min. The remaining dialysis parameters were kept constant in each of the 8 studied sessions: dialyzer, 1.8 m^2 of polysulfone (HF80) in 16 patients and 1.8 m^2 of poly-ethersulfone in (Arylane H9) in the remaining 8 patients; dialysis duration, 210 ± 65 min (135-300 min); blood flow, 418 ± 29 mL/min (350-450 mL/min); and frequency, 13 patients in 3 sessions per week, and 11 patients in daily sessions (Table I). All patients were dialyzed through an arterial-venous (AV) fistula as the vascular access. Mean hematocrit was 37.9 ± 4% (range: 30-49).

The procedure for measuring ionic dialysance was as usual through conductivity determination at the in-let and at the out-let of dialysis fluid, performing a second determination after a fluid conductivity change ± 1 mSm for 1 minute. The software uses the mathematical model of two equations for two unknown data, which will allow knowing the ionic dialisance.[9]

Besides determination of initial and final ionic dialysance, the final Kt volume and Kt/V of the OCM with Watson's V were followed-up, and the second generation Kt/V Daurgidas was calculated with pre- and postdialysis urea determinations in the blood. Since V is an inexact value, V was calculated according to Watson's formula (the most used), and similarly to previous studies[14-15], we calculated V through the Kt ratio of the Diascan from the Kt/V obtained in blood at several sessions.

Table I. Characteristics of gender, age, lean weight, dialysis duration and reinfusion volume

3 sessions/week	Age (years)	Lean weight (kg)	Dialysis duration (min)	Blood flow (mL/min)	Re-infusion volume (liters)
1. Male	64	62.5	270	450	32.1
2. Male	83	67.5	270	450	28.0
3. Female	79	52.0	270	450	32.6
4. Male	75	92.5	270	400	27.8
5. Male	66	68.5	270	400	24.2
6. Male	62	63.0	300	400	30.5
7. Male	79	72.0	240	400	23.5
8. Female	83	52.5	270	450	31.5
9. Female	80	44.5	210	400	23.1
10. Male	67	50.0	270	400	27.0
11. Female	76	84.0	300	400	30.0
12. Male	36	66.0	270	375	24.7
13. Female	58	83.0	270	400	27.4
6 sessions/week					
14. Male	72	85.5	135	450	13.5
15. Female	81	60.5	135	400	13.5
16. Male	69	75.0	150	400	16.2
17. Female	72	62.5	135	350	13.5
18. Male	79	61.5	135	450	16.8
19. Female	57	51.0	150	400	14.5
20. Female	58	72.5	150	450	18.0
21. Male	53	79.0	150	450	15.4
22. Male	83	70.0	135	450	17.2
23. Male	69	78.0	150	400	18.0
24. Male	83	56.0	135	450	16.2

STATISTICAL ANALYSIS

Results are expressed as mean ± standard deviation. Pearson's method was used to establish the correlation between the obtained Kt/V results, a linear regression curves between the OCM Kt/V and the second generation Daurgidas Kt/V were calculated. Besides, the interclass correlation coefficient was calculated as the most reliable measure to assess the agreement between both observations.[16]

RESULTS

Re-infused volume was 22.1 ± 7 liters in patients that received treatment with on-line HDF.

Table II. Individualized values of Kt, urea distribution volume, and Kt/V by different methods

3 sessions/week	Kt (liters)	Watson's V (liters)	V by (Kt)/(Kt/V) (liters)	Kt/V Daugirdas	Kt/V (OCM and Watson's V)
1. Male	77.3 ± 5	29.5	30.6	2.54 ± 0.14	2.22 ± 0.13
2. Male	65.5 ± 4	35.2	28.7	2.31 ± 0.15	1.86 ± 0.11
3. Female	65.6 ± 4	27.0	24.0	2.73 ± 0.20	2.43 ± 0.13
4. Male	62.8 ± 3	43.6	36.1	1.44 ± 0.07	1.72 ± 0.15
5. Male	70.7 ± 5	37.5	36.8	1.93 ± 0.16	1.89 ± 0.12
6. Male	73.6 ± 5	35.2	30.2	2.42 ± 0.19	2.09 ± 0.14
7. Male	54.3 ± 3	37.2	28.5	1.92 ± 0.16	1.46 ± 0.09
8. Female	66.9 ± 4	27.0	24.8	2.71 ± 0.27	2.49 ± 0.14
9. Female	47.7 ± 5	25.4	21.3	2.24 ± 0.14	1.87 ± 0.22
10. Male	63.0 ± 3	30.1	28.7	2.22 ± 0.21	2.09 ± 0.12
11. Female	69.1 ± 3	30.8	33.4	2.08 ± 0.20	1.92 ± 0.09
12. Male	57.8 ± 3	31.7	32.5	1.78 ± 0.12	1.43 ± 0.07
13. Female	65.2 ± 3	32.1	33.1	1.97 ± 0.11	1.83 ± 0.09
6 sessions/week					
14. Male	32.7 ± 2	43.1	30.4	1.09 ± 0.04	0.76 ± 0.06
15. Female	31.2 ± 1	29.4	22.4	1.41 ± 0.09	1.06 ± 0.04
16. Male	34.1 ± 2	39.6	37.4	0.93 ± 0.07	0.86 ± 0.06
17. Female	30.5 ± 1	29.4	24.9	1.21 ± 0.12	1.04 ± 0.04
18. Male	36.6 ± 2	32.7	32.4	1.12 ± 0.10	1.12 ± 0.07
19. Female	33.1 ± 2	27.4	22.1	1.50 ± 0.11	1.21 ± 0.08
20. Female	37.9 ± 2	33.4	28.0	1.38 ± 0.17	1.14 ± 0.07
21. Male	35.1 ± 3	42.5	34.2	1.06 ± 0.06	0.82 ± 0.07
22. Male	35.5 ± 2	35.6	32.2	1.12 ± 0.18	0.99 ± 0.05
23. Male	35.8 ± 3	40.2	33.2	1.07 ± 0.07	0.89 ± 0.07
24. Male	32.6 ± 6	31.1	24.1	1.34 ± 0.11	1.05 ± 0.09

The mean ionic dialysance for all the 192 sessions studied, measured by OCM, was 251 ± 21 mL/min (interval 202-314), with no statistical significant differences between patients in the 3 sessions/week regimen and those in a daily-session regimen. As for the mean of the final ionic dialysance, it decreased to 234 ± 24 mL/min (interval 172-301 mL/min), $p < 0.001$, confirming the efficacy loss during treatment.

Kt, measured by OCM, for all the 192 sessions, was 50.6 ± 17 L, 51.2 ± 17 in men and 49.7 ± 16in women. Watson' s V was 34.5 ± 5 L, and calculated with the ratio Kt OCM / Daurgidas Kt/V it was 29.6 ± L, $p < 0.001$. Individualized values are shown in Table II.

Kt/V measured by the OCM Kt and Watson's V for all the sessions was 1.499 ± 0.54. When the Kt/V was determined with the pre- and postdialysis blood samples, also for all the sessions, it was 1.742 ± 0.58. A good correlation was seen between both Kt/Vs (figç. 1), with r = 0.952. The interclass correlation coefficient was 0.907 (excellent reliability).

Kt measured with the OCM varied according to treatment modality. With HD and Qd at 500, Kt was 44.7 ± 15 L, with HD and Qd at 800, it was 50.7 ± 17 L, and with on-line HDF (with a replacement volume of 22.1 ± 7 L) it was 51.8 ± 17 L. Blood Kt/V also varied according to treatment modality. With HD and Qd at 500, Kt/V was 1.60 ± 0.55, with HD and Qd at 800, it was 1.726 ± 0.56, and with on-line HDF it was 1.776 ± 0.59.

DISCUSSION

In the present study, we have evaluated and validated the efficacy of a new biosensor to determine ionic dialysance (OCM), including the on-line HDF modality. We have verify its discriminating capability in different hemodialysis conditions: duration between 135-150 minutes, Qb between 350-450 mL/min, Qd 500 or 800 mL/min, high-efficacy urea clearance ranging from 200 and 315 mL/min, Kt/V ranging from 0.6-3.0, and lastly, conventional hemodialysis or on-line HDF. The good correlation (Figure 1) as well as the excellent reliability with the calculation of the observed interclass correlation coefficient, speaks for its use in clinical practice with complete guarantees, with the additional advantage that it can be determine at each session and no additional cost.

As we have already discussed, dialysis dose in one of the best indicators of appropriate dialysis and, therefore, it is very important to know the real dose that the patient is receiving with each dialysis treatment. According to DOQI guidelines,[17] the minimal current recommendations, for three sessions per week, are Kt/V higher than 1.2 and/or PUR higher than 65%. The HEMO study[18] was not conclusive to demonstrate that a higher dialysis dose (Kt/V > 1.65) could reduce mortality as compared to the usual dose (Kt/V > 1.25), although in the female group a 19% reduction in mortality was shown when they received a higher dose.[19] This same conclusion has been recently observed in another study[20] that has included 74,120 patients from the USA and 10,816 from seven countries of the DOPPS study.

The observed differences between the Kt/V determined by OCM, undervalued approximately 15%, and the Kt/V calculated from blood analysis (Daurgidas formula, second generation) is exclusively due to the mistake of introducing in the OCM an urea distribution volume. With the ionic dialysance biosensor, the most accurate method is to work with the Kt. This represents some advantages, both K and t are real values and measured by the monitoring device. If the Kt/V is set, we have to input the V, and so, a value that frequently

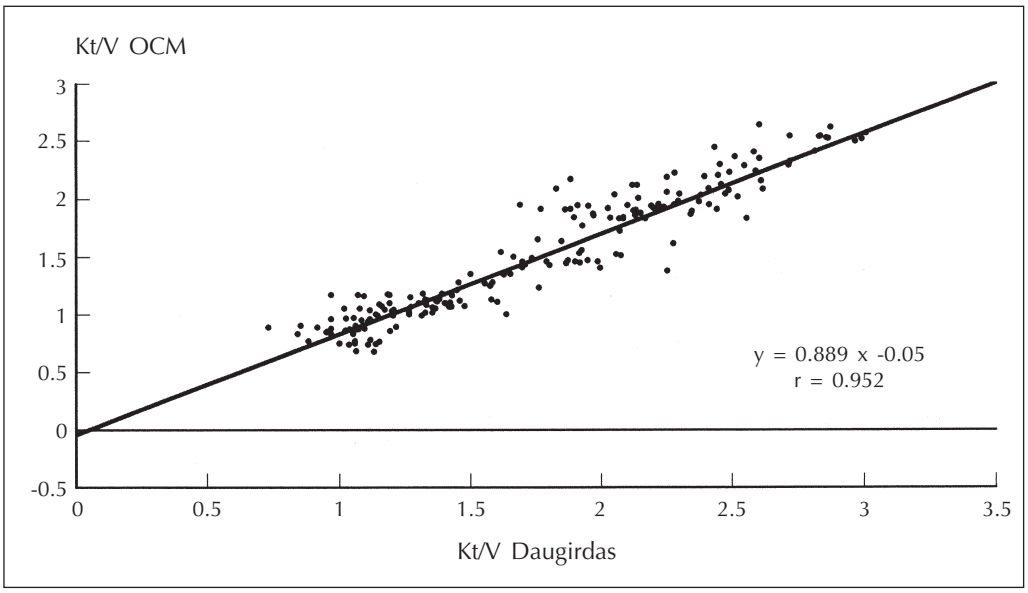

Fig. 1.—Correlation between Kt/V measured by ionic dialysance (OCM) and Kt/V determined by blood analysis (Daurgidas Second Generation).

is mistaken and can be manipulated in the device. Since 1999, Lowrie *et al.*[21] propose Kt as the marker for dialysis dose and mortality, recommending a minimum Kt of40-45 liters for women and 45-50 for men. According to these authors results in 3,009 patients, they observed a J-shaped survival curve when they distributed patients in quintiles by the PUR, whereas the curve was descendent when they used the Kt.[22] In the HEMO study,[19] the group of female patients with standard dose received a Kt of 38.2 L (lower than the minimum recommended) and in the group with elevated dose it was 51.7 L, whereas male patients received a Kt of 45.5 and 59.6 liters, respectively, in both groups higher than the recommended one. Therefore, according to these studies, it seems reasonable to work routinely with the Kt and assure a minimum dose higher than 40 L, particularly in women.

In conclusion, the new biosensor for measuring ionic dialysance for on-line HDF has been assessed in this study, verifying the close correlation with determinations from blood samples, and validating its use for this treatment modality. This device differentiated correctly the different conditions of dialysis efficacy used in the study. The systemic clinical use of ionic dialysance at each session guarantees the treatment efficacy. It is likely that prescribing a minimum Kt dose (40 L in women and 45 L in men) may the most simple and reliable way in daily clinical practice to improve global survival of the dialyzed population, particularly in women.

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