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Measure of dialysis dose by different integrated modules within the same monitoring device

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SUMMARY

The «gold standard» method to measure the mass balance achieved during dialysis for a given solute is based on the total dialysate collection. This procedure is unfeasible and too cumbersome. For this reason, alternative methods have been proposed including the urea kinetic modelling (Kt/V), the measurement of effective ionic dialysance (Diascan), and the continuous spent sampling of dialysate (Quantiscan).

The aim of this study was to compare the reliability and agreement of these two methods with the formulas proposed by the urea kinetic modelling for measuring the dialysis dose and others haemodialysis parameters.

We studied 20 stable patients (16 men/4 women) dialyzed with a monitor equipped with the modules Diascan (DC) and Quantiscan (QC) (Integra®. Hospal). The urea distribution volume (VD) was determined using anthropometric data (Watson equation) and QC data. Kt/V value was calculated according to Daurgidas 2nd generation formula corrected for the rebound (eKt/V), and using DC (Kt/VDC) and QC (Kt/VQC) data.

The total mass of urea removed was calculated as 37,93 ± 16 g/session. The VD calculated using Watson equation was 35.7 ± 6.6 and the VDQC was 35.06 ± 9.9. And they showed an significative correlation (r:0,82 p < 0.001). The (VDQC-VDWatson) difference was –0.64 ± 5.8L (ns). Kt/VDC was equivalent to those of eKt/V (1.64 ± 0.33 and 1.61 ± 0.26, mean difference –0.02 ± 0.29). However, Kt/VQC value was higher than eKt/V (1.67 ± 0.22 and 1.61 ± 0.26 mean difference 0.06 ± 0.07 p < 0.01). Both values correlated highly (R^2: 0.92 p < 0.001). Urea generation (G) calculated using UCM was 8.75 ± 3.4 g/24 h and those calculated using QC was 8.64 ± 3.21 g/24 h. Mean difference 0.10 ± 1.14 (ns). G calculated by UCM correlated highly with that derived from QC (R^2: 0.88 p < 0.001).

In conclusion, Kt/VDC and Kt/VQC should be considered as valid measures for dialysis efficiency. However, the limits of agreement between Kt/VQC and eKt/V were closer than Kt/VDC.

Key words: ***Dialysis dose. Urea distribution volume. Ionic dialysance. Continuous spent dialysate sampling. Urea generation.***

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MEDICIÓN DE LA DOSIS DE DIÁLISIS MEDIANTE DIFERENTES MÓDULOS INTEGRADOS EN UN MISMO MONITOR

RESUMEN

La recolección total del líquido de diálisis para cuantificar la cantidad total de urea eliminada durante la hemodiálisis (HD) se ha considerado la técnica «gold estándar» para medir la dosis de diálisis. Dada la dificultad de este método se han propuesto otros alternativos como el modelo cinético de la Urea (Kt/V), la medición de la dialisancia iónica o la recogida de muestras representativas del líquido de diálisis total.

El objetivo de este trabajo es comparar la fiabilidad y concordancia de dos dispositivos de medida (dialisancia iónica y recogida parcial de líquido de diálisis) integrados en el mismo monitor de diálisis y compararlos con los propuestos por el modela cinético de la urea (MCU) para la medición de la dosis de diálisis (Kt/V) y otros parámetros de HD.

Para ello se estudiaron 20 pacientes (16V/4M) con una edad media de 64,5 ± 13 años, estables en programa de HD y dializados con el monitor Integra® (Hospal) equipado con los biosensores Diascan (DC) y Quantiscan (QC). El volumen de distribución de urea (VD) se calculó a partir de la fórmula de Watson y por el QC. La generación de urea se calculó a partir del MCU y el Kt/V se determinó por la fórmula de Daurgidas 2ª generación corregida para el rebote (eKt/V), por el DC y el QC.

La transferencia de masa de urea medida por QC fue de 37,2 ± 13,8 g. El VD por la fórmula de Watson y por QC fue de 35,7 ± 6,6 y de 35,06 ± 9,9 L respectivamente (ns) y mostraron una correlación significativa (r: 0,82 p < 0,001). Los valores de aclaramiento (K), mediante DC, y QC fueron similares KQC: 230,3 ± 56,5 ml/min, KDC: 214,05 ± 24,3 ml/min (ns) No se apreciaron diferencias en el Kt/V calculado por DC y el eKt/V (KtVDC: 1,64 ± 0,33 vs *KtVeq; 1,61 ± 0,26). El coeficiente de correlación fue de r: 0,45 (p < 0,05). Por el contrario los valores de Kt/VQC fueron superiores a los calculados por el eKtV (1,67± 0,22 vs. 1,61 ± 0,26). El coeficiente de correlación fue de r: 0,94 (p < 0,001). La generación de urea por el MCU fue de 8,7 ± 3,4 y por QC de 8,6 ± 3,2 g/ 24h (ns) r: 0,94 p < 0,001).*

Podemos concluir que tanto la medición de la dialisancia iónica mediante el DC, como la recogida de muestras representativas del líquido de diálisis mediante el QC, son métodos sencillos, fiables y reproducibles que nos permiten medir de manera rápida la eficacia dialítica y otros parámetros de hemodiálisis. En nuestra experiencia la cuantificación de la dosis de diálisis mediante el QC presenta una mayor concordancia que la realizada con DC.

Palabras clave: ***Dosis de diálisis. Volumen de distribución de urea. Recogida parcial líquido de diálisis. Dialisancia iónica. Generación de urea.***

INTRODUCCIÓN

The Kt/V formula (effective urea clearance by Kt time and standardized for the distribution volume V) is the most frequently used parameter to quantify dialysis dose. This parameter may determined through several kinetic models. Currently, most of hemodialysis units use the formulas derived from the Urea Kinetic Model (UKM) that requires sample gathering at the beginning and at the end of the session, with further corrections that remove the final urea rebound.[1]

Total gathering of dialysis fluid (DF) has been considered the «gold standard».[2] However, this method

entails important difficulties for its routine use in daily clinical practice. Partial collection of representative samples of total dialysis fluid avoids these complications with good reliability and safety.

In recent years, advances in continuous monitoring of dialysis fluid conductance has led to the measurement of effective ionic dialysance, which may be assimilated to effective urea clearance.[3]

The aim of this study was to compare the reliability and agreement of two measurement devices: dialysance and partial continuous collection of DF integrated within the same monitoring device and compared them with formulas derived from UKM.

MATERIAL AND METHODS

Twenty stable patients (16 M / 4 F) with mean age of 64.5 ± 13.8 years, and on a hemodialysis program three times a week and average time on hemodialysis of 41 months (3-242 months) were studied.

Dry weight was 68.9 ± 15.9 kg. Pre-HD weight was 70.8 ± 16 kg, and post-HD was 68.76 ± 15 kg. Session duration was 257.2 ± 35 minutes. Mean ultrafiltration volume per session was 2.8 ± 1.1 liters.

All sessions were done using the same Integra® (Hospal) monitor equipped with Diascan (DC) and Quatiscan (QC) modules. The dialyzer used was made of low-permeability polysulphone of 1.80 m^2 in 5 patients and 2.4 m^2 in 15 patients.

Diascan (DC) is a device that non-invasively measures effective ionic dialysance using the hemodialysis machine's conductivity probes. This module functioning has already been tested in several previous studies.[2,3,4] The average dialysance value was taken throughout the

whole session.

Quatiscan (QC) is a system that allows continuously gathering representative samples of total dialysis fluid used. For that, it incorporates a low-flow peristaltic pump that collects the sample in a single use bag. So, at any time of the dialysis session we are able to collect a few milliliters of dialysis fluid that will allow measuring the kinetics of several solutes. Moreover, it shows total volume of dialysis fluid that has passed through the dialyzer. Several studies have remarked the usefulness of this method to directly quantify urea clearances.[4,5,6,7]

Blood samples were collected for urea measurement at the beginning, end (after decreasing Qb to 50 mL/min for 2 minutes), and at the beginning of the following session. Also, we measured urea in the fluid collected by QC.

The formulas used to quantify the different parameters were as follows:

Urea mass transference

$$MT = Vd \times Cd$$

Cd: Urea concentration in QC sample.
Vd: Total volume dialysis fluid.

Logarithmic mean of plasma urea concentration

$$Cm = \frac{(Co - Cf)}{Ln\ (Co/Cf)}$$

Co: patient pre-HD urea concentration
Cf: patient post-HD urea concentration

Clearance

$$K = (MT/\ Cm \times t) \times 1000$$

t: HD session duration.

Distribution volume (DV) for urea was calculated from Watson's formula[8] and by QC:

Distribution volume

$$DV = \frac{MT - (\Delta\gamma \times Co)}{Co - Cf}$$

$\Delta\gamma$: weight increase

The machine calculates the total volume of dialysis fluid used, and the volume of the sample collected (Qs) is calculated by the following formula:

$$Qs = K \times (Qd + Quf + Qinf\ ) \times 0{,}001$$

Where K = 1 when Qd was 500 mL/min and K = 0.667 when Qd used was 750 mL.

Also, the volume of collected sample (Qs) was directly measured.

Kt/V was determined by the second generation Daurgidas' formula corrected for rebound (eKt/V).[9]

To measure Kt/V by DC the K quantified through ionic dialysance was used, and for Kt/V by QC the K by direct measuring was used.

Urea production was calculated by the urea mass transference in QC and by the formula of urea kinetic model.[10]

Results are expressed as arithmetic mean ± standard deviation. Comparison of quantitative variables

was done by Student's t test for paired data, and by analysis of variance for repeated data. The relationship between numerical variables was determined by Pearson's correlation analysis. In order to assess agreement between measuring systems we used the Bland-Altman method. A p value < 0.05 was considered statistically significant.

RESULTS

Blood urea levels were 126.1 ± 30, 26.6 ± 8 and 117.9 ± 26.8 mg/dL, pre, post- and pre-2, respectively.

Urea concentration in dialysis fluid was 19.05 ± 5.07 mg/dL.

The volume of dialysis fluid used, calculated by QC was 194.8 ± 34 liters.

The volume collected and measured in the sampling bag was 127 ± 22.3 mL, and the calculated to be collected by coefficient was 130.5 ± 18.1 mL (NS).

Urea mass transference by QC was 37.2 ± 13.8 g. Clearance values (K) calculated by DC and QC were 214.05 ± 24.3 mL/min and 223.6 ± 39.6 mL/min, respectively (mean of the difference: 9.5 ± 29.9 mL/min; p = 0.16). Figure 1 shows correlation, differences and agreement limits between both parameters.

DV by Watson's and by QC was 35.7 ± 6.6 and 35.06 ± 9.9 L, respectively (mean of the difference 0.64 ± 5.8 L; p = 0.64). Correlation (r = 0.82; p < 0.001), differences and agreement limits are shown in Figure 2.

There were no significant differences between Kt/V calculated by DC and eKt/V (1.64 ± 0.33 vs. 1.61 ± 0.26). By contrast, the Kt/V calculated by QC was significantly higher than eKt/V (1.67 ± 0.22 vs. 1.61 ± 0.26 p < 0.01). The correlation coefficient between eKt/V and KtVDC was r = 0.51 (p < 0.05), and between eKtV and KtVQC was r = 0.95 (p < 0.001). Correlation, differences and agreement limits are shown in Figures 3 and 4.

As shown, Kt/V QC has a better correlation coefficient and narrower agreement limits than Kt/V DC.

Urea production calculated by the urea kinetic model was 8.75 ± 3.4 g/24h, and that calculated by QC was 8.64 ± 3.2 g/24h. The correlation between both was 0.94 (p < 0.001) (Figure 5).

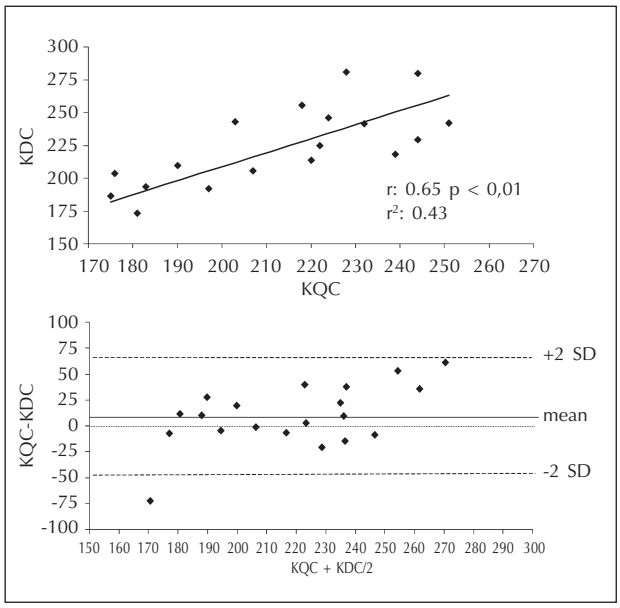

Fig. 1.—Correlation and differences between clearance (K) measured by DC and QC.

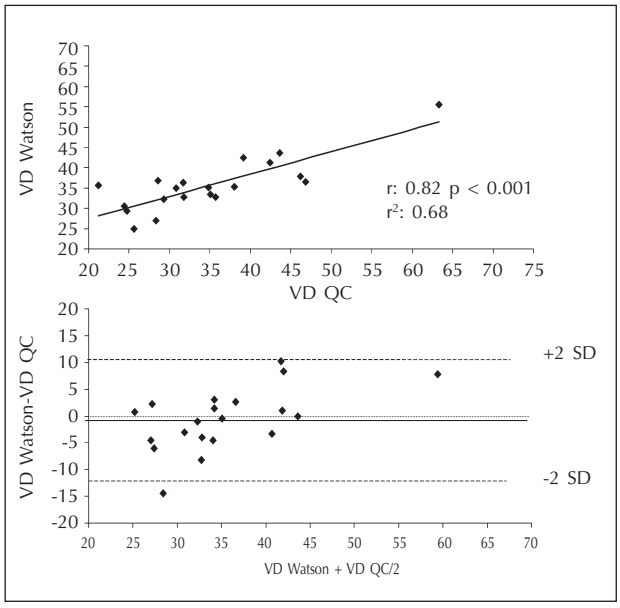

Fig. 2.—Correlation and differences between VD measured by Watson and QC.

DISCUSSION

Morbimortality of hemodialysis patients is clearly related to dialysis dose received. DOQI guidelines recommend measuring dialysis dose through urea fractional clearance according to distribution volume (Kt/V). This parameter may be calculated by the urea kinetic model.[1,10] However, this method requires multiple determinations and complicated calculations to estimate K and V. Each one of these parameters is subjected to error, which inevitably will low the accuracy of Kt/V estimation.

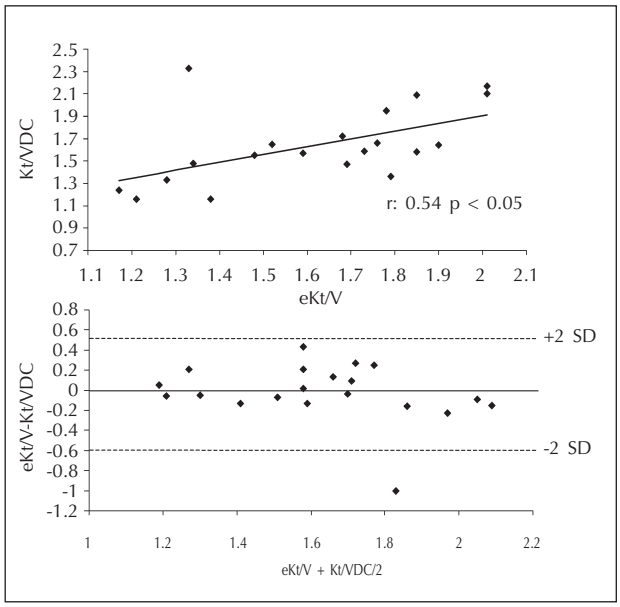

Fig. 3.—Correlation and differences between Kt/V measured by Daug.eq. and DC.

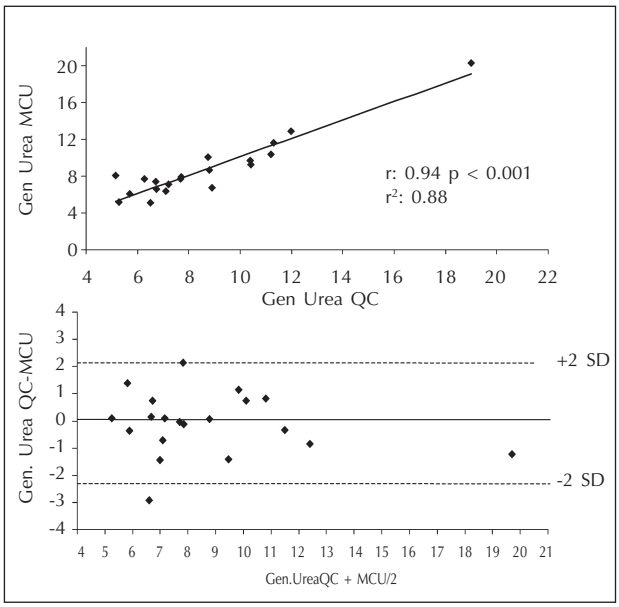

Fig. 5.—Correlation and differences between Gen. Urea measured by QC and MCU.

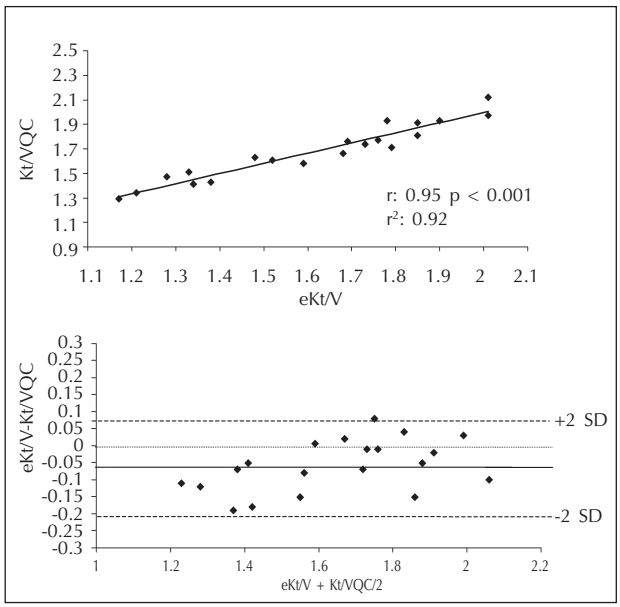

Fig. 4.—Correlation and differences between Kt/V measured by Daug.eq. and QC.

Other alternative methods are based on total dialysis fluid collection techniques. This method has been considered the gold standard for urea kinetic analysis.[2] However, it is difficult to get it into practice in most of dialysis units and is also subjected to multiple errors, both in urea collection and measuting.[11] Other studies have pointed out the advantage of using more simplified methods based on partial collection and of a representative part of total dialysis fluid.[4,5,6,7]

In recent years, it has been proposed the use of direct quantification systems, through sequential online determination of urea by devices built in the machines or by measuring ionic dialysance, which reflects urea clearance.[12,13,14]

The main clinical practice guidelines suggest routinely using the formulas described by Daugirdas, either with single pool or double pool (correction for rebound). Also, they recommend the need for assessing the above-mentioned alternative methods.[1]

In our study, we have analyze the dialysis dose calculated by ionic dialysance (DC) and by partial collection of dialysis fluid (QC). Both methodologies are integrated within the same monitoring device, and we have compared them with the formulas derived from UKM.

Mean urea clearances obtained by the two methods (QC and DC) are similar and have good correlation, although it only explains 40% of the association between them. Also, the wideness of the confidence interval (m ± 2 SD) was relatively large (between +68 mL/min and -49 mL/min). Several studies have pointed out a good correlation between ionic dialysance and urea clearance, although determination of the latter was done by single measu-

rements, either from the blood side or from the dialysis fluid side.[15,16,17,18] By contrast, other authors point out a series of errors that may arise when using this technique, among which there are *in vivo* discrepancies between sodium and urea movement, its interrupted nature, and the need for including another variable such as DV, which is difficult to measure.[19] In our study, both parameters, ionic dialysance and urea clearance, represent a mean value for the whole hemodialysis session. Therefore, the lower correlation and the greater amplitude of confidence interval would be justified.

QC allowed us to directly quantify DV of urea, which showed a good correlation with that calculated through Watson's formula, and regression analysis explained 68% of the association between both. In the study by Manzoni *et al*.[20], urea distribution volume calculated by anthropometrical formulas was 17% higher than that calculated by direct quantification. On the other hand, the study by Filippo *et al*. verified that there was a significant difference of 7.3 ± 3.3 L between direct quantification and anthropometrical methods.[21]

We did not found significant differences between Kt/V calculated by DC and eKt/V, but there did were differences between Kt/V by QC and eKt/V. Manzoni *et al*. found up to 22% differences between Kt/V values obtained by ionic dialysance and direct quantification. In this study, we used DV obtained both by anthropometrical formulas (Watson) and that obtained by assuming that V accounts for 55% of dry weight.[20] By contrast, McIntyre *et al*. demonstrated an excellent correlation and accuracy between Kt/V calculated by ionic dialysance and single pool Kt/V. These authors also used anthropometrical formulas (Watson) to calculate DV.[22]

The study by Di Filippo *et al*. did not find significant differences between Kt/V obtained by ionic dialysance and the urea kinetic model, being both of around 1.14. In this case, the distribution volume used for ionic dialysance Kt/V was calculated by the formula derived from the kinetic model for single compartment distribution.[13] The data obtained from our study show that Kt/VQC has better correlation coefficient and narrower agreement limits when compared with eKt/V, as is shown in Figure 4.

In summary, we may conclude that both ionic dialysance measuring (Diascan) and collection of samples representative of total dialysis fluid (Quantiscan) are simple, reliable, and reproducible methods that allow rapid determination of dialytic efficiency and other hemodialysis parameters.

In our experience, quantification of dialysis dose by Quantiscan has better agreement than that obtained by Diascan.

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