http://www.senefro.org
© 2008 Órgano Oficial de la Sociedad Española de Nefrología

see original article in page 43

Hemodialysis dose. Difficulty in measuring it

J. L. Teruel Briones and M. Fernández Lucas

Ramón y Cajal Hospital

Nefrología 2008; 28 **(1)** 28-29

Standardized urea clearance (Kt/V) and the percentage of urea reduction (PUR) are the parameters currently accepted to calculate the hemodialysis dose. The Kt/V is the quotient between two volume magnitudes: the volume of depurated body fluid throughout the hemodialysis session (Kt) and the urea steady state volume (V), which is equivalent to the volume of body water. The numerator in the equation indicates the hemodialysis dose that the patient has received and the denominator is the anthropometrical parameter selected to correct that dose according to body size.

Observational studies performed on a large number of patients verified that the relationship between dose and mortality described a J-shaped curve: the risk for death increases with the highest Kt/V or PUR values.[1-4] The analysis of these data may be interpreted in two ways: either hemodialysis overdose is harmful for the patients or the measurement method entails some confounding phenomenon.

In 1985, the Kt/V was established as an index to estipulate a minimal hemodialysis dose after a secondary analysis of the data from the National Cooperative Dialysis Study.[5] At that time, it was not known that body size had a prognostic value in dialyzed patients. Further studies observed a direct relationship between survival and several anthropometrical parameters, among which was V.[6-8] The Kt/V is a mathematical construct that may induce to interpretation errors since it is a quotient between two parameters having a positive influence on progression. Pathological decreases of V increase the Kt/V value and are related to poorer prognosis. The PUR presents the same problems: with the same hemodialysis dose, the PUR is negatively proportional to body size.[6] The cause for a higher mortality risk observed in the population with the highest Kt/V or PUR values was clarified when it was verified that that group of patients included those with higher hyponutrition status.[2]

To avoid the interference between hyponutrition and hemodialysis dose, in 1999, Lowrie proposed using the Kt as a new measurement index.[6] The relationship between Kt and survival is always positive and the highest Kt values are not associated to hyponutrition or greater mortality risk.[2,6]

The first problem considered when using the Kt was the procedure to calculate it. Whereas the Kt/V may be calculated from formulas derived from the PUR, and V may be determined by anthropometrical equations, direct calculation of the Kt during a hemodialysis session is difficult to perform due to the complexity that entails «in vivo» determination of K. In the first studies, the Kt was calculated indirectly by dividing the Kt/V obtained from Lowrie's formula (ln UreaPre – ln UreaPost) by the V obtained through Chertow's equation.[3,6] This is a complicated procedure for daily clinical practice since it requires previous determination of Kt/V and V, and this work overload was one of the causes making difficult its applicability.

The advent of monitors measuring ionic dialysance resolved this problem. Ionic dialysance is similar to urea clearance (K). The ionic dialysance monitor automatically provides the Kt at each hemodialysis session. The Kt obtained by ionic dialysance also has a direct relationship with survival at any range.[4]

In the current issue of the Nephrology Journal, Maduell et al. publish the results of the follow-up for three months of the hemodialysis dose through the Kt and the usual Kt/V and PUR indexes.[9] The Kt is obtained at all hemodialysis sessions by ionic dialysance and the other two parameters by means of monthly laboratory work-up. The most relevant outcome is that 100% of the patients received an adequate dialysis dose according to the Kt/V, 90% according to PUR, and however 31% did not reach the required Kt value.

There are three aspects to comment on the Kt values considered acceptable. In the first place, there are no concordance studies between the two procedures used to measure the Kt. The Kt values recommended by Lowrie et al. in their original work (40-45 liters in women and 45-50 liters in men) correspond to a Kt determined from the Kt/V (obtained by laboratory) and the V (obtained by the anthropometrical formula), as it has been previously mentioned.[6] The same authors did not establish the minimal Kt values obtained by ionic dialysance (the mortality progressively decreases as the Kt increases without a tendency of the curve to plateau).[4]

In the second place, we should consider the type of monitor used to measure the Kt by ionic dialysance. There are two types of ionic dialysance monitors: Diascan (Hospal) and OCM (Fresenius). In the works by Lowrie et al.,[4,10,11] the Kt was obtained by using an OCM monitor. In the work by Maduell, both monitors were used. Maduell himself has recently verified relevant differences between both: the Kt values yielded by Diascan are 15-17% lower than those by OCM.[12] The Kt values obtained by Lowrie by ionic dialysance

Correspondence: *José Luis Teruel Briones*
jteruel.hrc@salud.madrid.org
Hospital Ramón y Cajal. Crta. de Colmenar, km. 9,100. 28034 Madrid

KEY CONCEPTS

1. The Kt/V is a quotient between two volume magnitudes having prognostic importance.

2. The Kt/V and PUR values are higher in malnourished patients.

3. The Kt is a marker exclusively of hemodialysis dose and its value is not influenced by hyponutrition.

4. The ionic dialysance monitors automatically provide the Kt at each hemodialysis session.

5. The contribution of the Kt to hemodialysis dosing remains to be established in further studies

came from the monitor yielding higher values, and thus they are not valid if the Diascan monitor is used. The type of monitor used has to be taken into account at the time of establishing the reference values.

Lastly, we should consider that the data by Lowrie et al. have been obtained in a population with anthropometrical parameters different from ours. In the last Lowrie's series,[11] the mean weight for his population was 10 kg higher than that for Maduell's series. In order to achieve similar Kt/V and PUR values, the Spanish population would need lower Kt values than the North American population.

Should we get rid of the standardization of the hemodialysis dose and prescribe fixed doses to all patients? Should a patient with a steady weight of 50 kg with no hyponutrition evidence receive the same dialysis dose than another one weighing 80 kg? Lowrie himself reconsidered that issue and proposed to correct the Kt by body surface area.[10] He established a target Kt for each value from a body surface area scale, ranging from 1.20 to 2.80 m^2.[11] When Maduell et al. corrected the Kt according to body surface area following Lowrie's indications, the percentage of patients not reaching the minimal recommended value went up to 43%.

In order to achieve the minimal Kt values proposed by Lowrie, for both the absolute value and the value standardized by body surface area, the patients have to receive a hemodialysis dose measured by the classical Kt/V and PUR indexes very much higher than those recommended by current Clinical Guidelines.[13] The hemodialysis dose that Maduell's patients receive is high according to usual measurement indexes (mean PUR values: 79.2% and mono-compartment Daugirdas Kt/V: 1.98), but 31%-43 % of them did not reach the target dose required according to the new criteria by Lowrie et al.. The HEMO study, a randomized and controlled trial, failed to show any clinical benefit by increasing the dialysis dose to values not even reaching those suggested by Lowrie.[14]

The excellent work by Maduell et al. contributes to bring data and raises concerns about the unachieved topic of adequate hemodialysis dose and tailored procedure. Until further studies confirm the superiority of the Kt and establish the minimal required values, we should keep on using the classical indexes, always keeping in mind the presence of hyponutrition at the time of interpreting the data.

REFERENCES

1. McClellan WM, Soucie JM, Flanders WD. Mortality in end-stage renal disease is associated with facility-to-facility differences in the adequacy of hemodialysis. *J Am Soc Nephrol* 9: 1940-1947, 1998.
2. Chertow GM, Owen WF, Lazarus JM, Lew NL, Lowrie EG. Exploring the reverse J-shaped curve between urea reduction ratio and mortality. *Kidney Int* 56: 1872-1878, 1999.
3. Li Z, Lew NL, Lazarus JM, Lowrie EG. Comparing the urea reduction ratio and the urea product as outcome-based measure of hemodialysis dose. *Am J Kidney Dis* 35: 598-605, 2000.
4. Lowrie EG, Li Z, Ofsthun N, Lazarus JM. Measurement of dialyzer clearance, dialysis time, and body size: death risk relationship among patients. *Kidney Int* 66: 2077-2084, 2004.
5. Gotch FA, Sargent J. A mechanistic analysis of the National Cooperative Dialysis Study (NCDS). *Kidney Int* 28; 526-534, 1985.
6. Lowrie EG, Chertow GM, Lew NL, Lazarus JM, Owen WF. The {urea x diálisis time} product (Kt) as an outcome-based measure of hemodialysis dose. *Kidney Int* 56: 729-737, 1999.
7. Wolfe RA, Ashby VB, Daugirdas JT, Agodoa LYC, Jones CA, Port FK. Body size, dose of hemodialysis, and mortality. *Am J Kidney Dis* 35: 80-88, 2000.
8. Port FK, Ashby VB, Dhingra RK, Roys EC, Wolfe RA. Dialysis dose and body mass index are strongly associated with survival in hemodialysis patients. *J Am Soc Nephrol* 13: 1061-1066, 2002.
9. Maduell F, Vera M, Serra N, Collado S, Carrera M, Fernández A, Arias M, Blasco M, Bergadá E, Cases A, Campistol JM. Kt como control y seguimiento de la dosis en una Unidad de Hemodiálisis. *Nefrología* 28 (1): 43-47, 2008.
10. Lowrie EG, Li Z, Ofsthun NJ, Lazarus JM. Evaluating a new method to judge dialysis treatment using online measurements of ionic clearance. *Kidney Int* 70: 211-217, 2006.
11. Lowrie EG Li Z, Ofsthun N, Lazarus JM. The online measurement of hemodialysis dose (Kt). Clinical outcome as a function of body surface area. *Kidney Int* 68: 1344-1354, 2005.
12. Maduell F, Serra N, Vera M, Arias M, Blasco M, Bergadá E, Cases A, Campistol JM. Influencia del monitor en la eficacia dialítica y en la determinación del Kt. *Nefrología* 27 (Supl. 4): 57, 2007.
13. Maduell F, García M, Alcázar R. Dosificación y adecuación del tratamiento dialítico. Guías SEN: Guías de Centros de Hemodiálisis. *Nefrología* 26 (Supl. 8): 15-21, 2006.
14. Eknoyan G, Beck GJ, Cheung AK, Daugirdas JT, Greene T, Kusek JW, Allon M, Bailey J, Delmez JA, Depner TA, Levey AS, Levin NW, Milford E, Ornt DB, Rocco MV, Schulman G, Schwab SJ, Teehan BP, Toto R, and Hemodialysis (HEMO) Study Group. Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Eng J Med* 347: 2010-2019, 2002.