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ASSESSMENT OF HEMODIALYSIS ADEQUACY: IONIC DIALYSANCE IN COMPARISON TO STANDARD METHOD KT/V-MAKATI MEDICAL CENTER (MMC) EXPERIENCE

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ABSTRACT

Introduction: **Delivered dose of solute removal (assessed by Kt/v) is an important determinant of clinical outcome in chronic dialysis patients. The gold standard for Kt/v is the direct quantification of the removed urea. A new method, ionic dialysance has been suggested and used over the years. This method is faster, less expensive and non invasive. The objective of this study is to determine the value of Kt/v ID in comparison with the computed Kt/v UR at Makati Medical Center (MMC) setting.**

Methods: **We studied 65 chronic hemodialysis patients, retrospectively on routine Kt/v determination from January 2007 to December 2007. Urea reduction was measured using the formula, and the Kt/v ID value from the dialysis machine were all collated. Data were encoded statistically.**

Results: **Significant differences were noted between Kt/v Ur and Kt/v ID.**

Conclusion: **Kt/v UR gives a higher value than the Kt/v ID hence they are not comparable and significantly different.**

Keywords: **hemodialysis, urea reduction, ionic dialysance**

INTRODUCTION

Morbidity and mortality rates in patients on renal replacement therapy are unacceptably high. Lots of factors contribute to these such as age, comorbidities especially cardiovascular and infectious diseases.[1]

Measurement using delivered dialysis dose using clearance x time/volume (kt/v) index requires multiple blood sampling which is laborious and cumbersome and also expensive. The most commonly used parameter to evaluate delivered dialysis dose is the spKt/V index, where K is the dialyzer urea clearance, t is the duration of dialysis session and V is the patient's urea distribution volume.[1] The Kt/V is derived from a mathematical formula 25 years ago, first proposed by Gotch in the secondary analysis of The National Cooperative Dialysis Study (NCDS).[1]

At present the gold standard for the determination of Kt/v is the direct quantification of removed urea, however, this method requires the total and partial collection of spent dialysate, and is thus inapplicable in everyday clinical practice.[2] New methods for assessment of dialysis dose based on equivalence of ionic dialysance (ID) and urea removal (UR) have been suggested over the last few years. These advances in hemodialysis monitoring based on the conductivity monitoring (using sodium flux as a surrogate for urea) allow repeated and noninvasive measurement of delivered dialysis dose during each session.[1] Because conductivity is related to ion concentration, it is possible to substitute one for the other in further calculations. The transfer characteristics of sodium and urea are similar, hence the ionic dialysance reflects the clearance of urea. The measurement of inlet and outlet dialysate conductivity enables software to measure ionic movement across the dialysis membrane. Online monitoring devices have evolved.[3]

Kt/v can be calculated continuously without blood samples using ionic dialysance method. It is automatic, no need for blood draws, with no extra cost with regular dialysis. Researches have been done comparing these with different methods to assess Hemodialysis adequacy and somehow proved that it is comparable, but using a small sample size of 10-20 patients. In our dialysis unit on the other hand, it is not a common practice to use the OCM/ID of the dialysis machine, but the standard manual computation of Kt/v using Daugirdas equation (UR), since based on MMC experience, and observation, the manual computation is better to assess the hemodialysis adequacy of our patients.

Keywords

Dialysance – the number of milliliters of blood completely cleared of any substance by an artificial kidney of by peritoneal dialysis in a unit of time.

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Ionic dialysance – (ID) an online measured variable available on dialysis monitors to evaluate small solute clearance based on conductivity measurement in the inlet and outlet dialysate.

Adequate dialysis – is the effective dose that is able to achieve the stated objective.

Second generation natural logarithmic formula (daugirdas equation) –

Kt/v = -Ln (R – 0.0008 x t) + (4-3.5 x R) x UF/W
R Pre dialysis BUN/post dialysis BUN
W post dialysis weight or patient's dry weight in kg
UF volume of ultrafiltration in liters

- Hence, the objective of the study is to determine the value of kt/v OCM (ID-ionic dialysance) in comparison with computed kt/v (UR-urea reduction). Specific objective is to assess the correlation of both values in determining dialysis adequacy and to confirm the clinical usefulness of utilizing OCM vs manual computation of kt/v.

MATERIALS AND METHODS

Patient and Hemodialysis Parameters

We studied 65 of hemodialysis patients on routine Kt/v determination in MMC. On chronic hemodialysis dialyzed using 2 needles in native AV fistula or AV graft. All patients were dialyzed at the kidney unit of MMC from January 2007 to December 2007 thrice or twice weekly using dialysis machine 4008S Fresenius Medical Care equipped with on line clearance monitor module and hollow fiber low flux polysulfone/high flux dialysis membrane (F7-F10, HF80s, FX80). Blood flow ranged between 200-350cc/min. Drug therapy schedules were kept constant during the study period. Excluded were patients using temporary dialysis catheters, on hemodialysis due to an acute onset of renal failure, on hemodialysis once a week schedule and patients without a record of the ionic dialysance at the time of Kt/v determination.

Measurement of Dialysis Adequacy

Hemodialysis delivered dose were measured using the standard method of blood sampling and calculation according to the present clinic guidelines. The target normal values of Kt/v used were according to the updated DOQI guidelines minimal adequate dose of Hemodialysis of thrice a week schedule of 1.2 while for the twice a week dialysis patient, using Kt/v value of 1.8 per dialysis to a total 3.6 per week of dialysis treatment. The ID (ionic dialysance) was measured using the OCM module, which is part of the dialysis machine. The quality of Kt/v is automatically calculated by appropriate software.

Analysis of Data

Data were encoded and tallied in SPSS version 10 for windows. Descriptive statistics were generated for all variables, For nominal data frequencies and percentages were computed. For numerical data, mean + SD, the median and the range were generated. Comparison of the different variables under study was done using the following test statistics:

Paired t-test – used to compare two groups with numerical data that are dependent

Pearson Correlation – used to determine correlation between two numeric data

RESULTS

Sample Size Computation

The number of samples to be included was computed based from the previous study by McIntyre *et al*, wherein it was found out that kt/vID underestimated urea reduction on Kt/v by a mean of 2.54%. Taking into account this reduction and utilizing a 95% confidence level of alpha and 5% marginal error, we have for 37 patients only to be included in this study.

$$n = \frac{(Z\alpha)^2 pq}{e^2}$$

Where:
Z_α = 95% confidence level = 1.96
p = underestimation of 2.54% = 0.0254
q = 1-p = 1 – 0.0254 = 0.975
e = allowable error of 5% = 0.05

There were 65 subjects included in the study, 56.9% of whom were females and 43.1% were males. All patients included were diagnosed cases of chronic kidney disease on chronic hemodialysis. Fifty five point four percent were cases of diabetic nephropathy, followed by hypertensive nephrosclerosis 26.2%. The rest were distributed to Chronic Glomerulonephritis (with and without biopsy), CTIN, IgA Nephropathy, NSAID induced nephropathy, RPGN.

Majority of patients (72.3%) had access through native AV fistulas and 27.7% used graft. 55.4%

of patients in this study were on twice a week hemodialysis, 44.6% on thrice a week. Blood flow ranges between 200-350cc/min.

The mean Kt/v was 1.56 ± 0.34 as measured by UR and 1.18 ± 0.19 as measured by ID. The differences between the two values were found to be statistically significant. There was noted correlation with both Kt/v result from Ur and ID as well.

Table I. Distribution of Subjects According to Demographic Characteristics

	Frequency (%)
Sex	
Female	37 (56.9)
Male	28 (43.1)
Diagnosis	
CGN	4 (6.2)
CGN Biopsy proven	2 (3.1)
CTIN	1 (1.5)
DM nephro	36 (55.4)
HPN nephro	17 (26.2)
IgA Nephro	1 (1.5)
NSAID induced CKD	3 (4.6)
RPGN	1 (1.5)
Access	
AVF	47 (72.3)
AVG	18 (27.7)
QB	
200	12 (18.5)
250	36 (55.4)
300	15 (23.1)
350	2 (3.1)
Frequency	
2	36 (55.4)
3	29 (44.6)

Table II. Comparison of the kt/v Ionic Dialysance in MMC with Daugirdas Equation kt/v

	Kt/V (UR)	Kt/v (ID)	P value
Mean ± SD	1.56 ± 0.34	1.18 ± 0.19	<0.001 (S)

Comparing the Kt/v using ionic dialysance (machine) with the computed Kt/v using the value, showed that there was a significant difference noted as shown in this table. It was noted that there was a significant direct correlation between the two results that as the one increases the other increases as well.

This table shows the comparison of the Kt/v ID with Kt/v UR. The results showed that there was a significant difference noted as shown by the p value of <0.01. This means that the Kt/v derived from ionic dialysance is significantly different from the Kt/v derived from the computed UR.

Table III. Correlation of the Kt/v from UR and ID

		Kt_v UR	kt_v ID
Kt_v (UR)	Pearson correlation	1.000	.448 **
	Sig. (2-tailed)		.000
	N	65	65
Kt_v (ID)	Pearson Correlation	.448 **	1.000
	Sig. (2-tailed)	.000	
	N	65	65

**Correlation is significant at the 0.01 level (2-tailed).

This table shows the correlation of the Kt/v measured either by the machine of the actual result. The results showed that there was a significant correlation noted proven by the p values of 0.01. There was a significant direct correlation as shown in the correlation coefficient in that as one variable increases, the other also increases. The scatterplot diagram is depicted below.

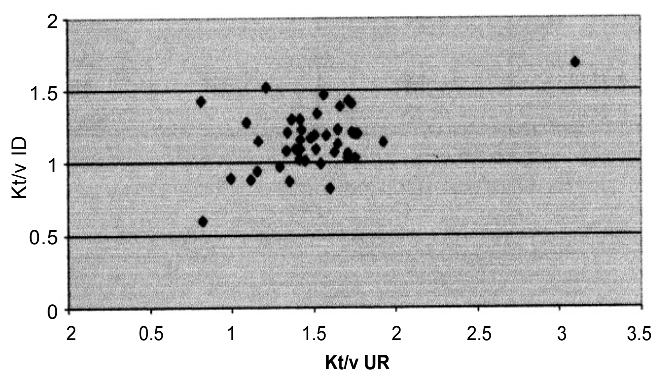

Fig. 1. Scatterplot Diagram for the Correlation Between Kt/v from UR and from ID

Table IV. Distribution of Subjects According kt/v Result

	Frequency	Percentage
Kt/V (UR)		
Adequate	31	47.7
Inadequate	34	52.3
Kt/V (ID)		
Adequate	14	21.5
Inadequate	51	78.5

Table IV and V depicts the distribution of subjects on whether the kt/v result was adequate or not an adequate dose of dialysis. Based on the computed Kt/v, 47.7% of the 65 patients have adequate dialysis (using a normal value of Kt/v 1.2 per session in a thrice weekly and 1.8 for twice weekly), while on the other hand 21.5% were adequate (on the same population) if we are to use the machine computation.

Table V. Comparison of the kt/v UR and ID

UR	ID		Total
	Adequate	Inadequate	
Adequate	13	18	31
Inadequate	1	33	34
Total	14	51	65

P value <0.0001 (Significant) (McNemars test)

There was a significant difference in the comparison of the Kt/v UR with the Kt/v ID as proven by the p value of <0.0001. This means that Kt/v UR and ID was not comparable. (with correlation coefficient 0.448)

DISCUSSION

As was mentioned by Racki *et al*, the spKt/V is derived from a mathematical formulated 25 years ago, first proposed by Gotch in the secondary analysis of The National Cooperative Dialysis Study (NCDS).[1] However, dialysis efficiency has substantially increased over the last 15 years, and postdialysis urea rebound observed, which followed to recent double-pool kinetics. Hence, equilibrated Kt/V (eKt/V), was proposed to assess the dose of dialysis more adequately. Usually, dialysis with sufficient dialysis dose is considered adequate. Based on available evidence, the minimum prescribed HD dose per session for a thrice-weekly schedule should be: urea eKt/V_1.2.[1] Other dialysis-related problems including hypotension episodes, dialyzer microclotting, or vascular access problems may substantionally influence the delivered dialysis dose.

Delivered dialysis dose (Kt/v) has shown a great impact on the morbidity and mortality rate in patients on maintenance hemodialysis. Different methods for quantification of Kt/v have been suggested. Although, if the correct approach is used, the assessment of Kt/v by predialysis and postdialytic blood sampling may give an adequate estimation of dialysis dose.[1] In addition, the use of mathematical calculations may not be the best use of the doctor's time. Although the use of calculators, which are also available on the internet, partly resolves this problem. Hence, the direct quantification of removed urea (the gold standard for determining kt/v) cannot be used on a routine basis. However, there appears to be a need for new methods to assess dialysis adequacy.[2] A practical method for measuring K semi continuously during dialysis using conductivity monitoring has been described. This method relies on the principle that the diffusive properties of sodium and urea are similar and that sodium flux van be measured noninvasively using conductivity measurements in the dialysate. This method estimates K as ionic dialysance within the dialysis machine and requires no reagent, disposable or blood sample. The value of K calculated using this method has an advantage as it represents blood water clearance and includes the effect of cardiopulmonary and any access recirculation.[4]

In our study we also used an appropriate calculation to assess delivered dialysis dose obtained from direct blood sampling and laboratory analysis. Most of our patients achieved target Kt/v as proposed by recent clinical guidelines. Recently, the approach estimating Kt/v from ionic dialysance has been introduced. The high degree of correlation between Kt/v (ID) and Kt/v (UR) show without doubt that the new method of direct dialysis dose quantification could be more frequently used.

The measurement of ionic dialysance is based on two assumptions: (1) ionic transfer through the dialyzer membrane has the same characteristics as urea transfer with a null reflection coefficient and a distribution volume in the blood equal to blood water and (2) The Transfer could be easily calculated from conductivity measurements by probes. Conductivity is the ability of a solution to conduct electrical current. For a solution with a unique electrolyte, conductivity is directly related to the concentration of this electrolyte by a relationship depending on the valence of the ion and its mobility.

This relationship is not strictly linear: conductivity normalized to an ionic equivalent (called molecular conductivity) decreases with the increase of concentration owing to both the decrease of ionic mobility for strong electrolytes and the decrease of dissociation for weak electrolytes. The conductivity of a solution with several electrolytes is more complex because of electrostatic interactions between these ions. Conductivity of plasma and dialysis fluids is mainly under the influence of sodium and chloride, which are predominant. Yet, the domain of nonlinearity in the interval of physiologic concentrations of these ions is of minor concern. Ionic dialysance is not an instantaneous measure but depends on the recording – over a certain time – of the outlet conductivity that is influenced by a recirculation phenomenon.

In this study, the ionic dialysance values were clearly lower in comparison with the urea clearance computed mathematically. Although there was a significant correlation between values, it also showed that there is a significant difference on both. Hence, we can conclude that there is an indirect evidence to suggest that there may actually be a difference between the two parameters. It has been observed that the value of ionic dialysance can decrease during dialytic sessions performed using high ultrafiltration rate, and a correlation has been found between the decrease in plasma water flow at a constant blood flow. On the contrary, no decrease in effective urea clearance has been observed, and blood water flow is not significantly reduced by intradialytic ultrafiltration. Consequently, although the urea and sodium diffusion constants are almost equal, ionic dialysance cannot assimilate to urea clearance because of difference in effective blood flow, which is lower for ionic dialysance and mainly represented by plasma water flow. This is where the Donnan's equilibrium theory gets in which is defined as the state of equilibrium that exists at a semipermeable membrane when it separates two solutions containing electrolytes, the ions of some of which are able to permeate the membrane and the others not. The distribution of the ions in the two solutions becomes complicated so that an electrical potential develops between the two sides of the membrane and the two solutions have different osmotic pressures. Called also Gibbs-Donnan phenomenon. Hence this theory could also explain the reason for the difference on both values.

In our study, we found difference in the two values which were found to be statistically significant. This were in contrast with other studies made by Gotch and Petitclec. But similar with the study made by Manzoni *et al* (NDT 1996). This could be due to inaccuracies in dialysate flow determination, or since sodium is charged and urea uncharged, that the correlation between ID and UR would be dependent on the type of dialyzed. Moreover, according to Racki *et al* (Renal failure 2005) that there are modifiable dialysis parameters which could be changed during the dialysis session for achieving adequate delivered dose, are blood flow, dialysate flow, dialysis membrane surface and dialysis session duration and intrapatient variability could affect the kt/v results.

CONCLUSION

In conclusion, the results clearly suggest that kt/v ID and kt/v UR (on line clearance vs computed kt/v) are not the same. This is based on the statistics presented in the study, assessment of the delivered dialysis dose by ionic dialysance is not comparable with the computed kt/v used by Makati Medical Center Nephrologist. The computed kt/v gives a higher value compared to the kt/v value from the OCM.

RECOMMENDATION

It is recommended that further studies are needed to clarify the relationship between Ionic dialysance and Urea clearance. Also to do comparative study (in vitro vs in vivo) regarding the results of kt/v OCM and computed kt/v in MMC. We further recommend researches on kt/v using a strict inclusion/exclusion criterion in patients all in 3 x a week hemodialysis who are anuric.

It is further recommended to use a different formula of the Kt/v without the variable of UF removed, and compare the Ur and ID.

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