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# Hemodialysis Adequacy: A Comparative Multicenter Study Between OCM and Calculated Kt/V from Two Centers in the Gulf

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## Abstract

**Introduction:** Adequate delivered dose of solute removal (as assessed by urea reduction and calculation of Kt/V) is an important determinant of clinical outcome in chronic haemodialysis (HD) patients. This requires both prescription of an adequate dose of HD and regular assessment that the delivered treatments are also adequate. On line conductivity monitoring Kt/V OCM online clearance measurement (OCM) (OCM) -using sodium flux as a surrogate for urea- allows the repeated non-invasive measurement of Kt/V on each HD treatment.

**Methods:** We prospectively studied 131 (63 males, 68 females) established chronic HD patients over 8 weeks period (1048 treatments). A pre and post dialyzer measurement of the conductivity is performed by two mutually independent temperature-compensated conductivity cells equipped with Fresenius 4008 S® dialysis machines. Urea reduction was measured (once a week) by a single pool calculation using immediate post treatment sampling. No changes were made to any of the dialysis prescriptions over the study period. Values of calculated Kt/V (conventional method with Daugirdas' formula) Kt/V Dau and simultaneously obtained online Kt/V OCM were compared.

**Results:** There was a statistically significant difference between calculated Kt/V DAU and Kt/V OCM over the study period. The mean calculated Kt/V DAU was 1.459 ± 0.31, and mean OCM was 1.139 ± 0.14 ($p = 0.000$), yet there was moderate correlation between calculated Kt/V DAU and Kt/V OCM ($r^2 = 0.59$) ($p = 0.000$) (Figure 1).

**Conclusions:** Online clearance measurement (OCM) results underestimates dialysis efficiency compared to calculated Kt/V DAU values. This difference has to be considered when applying Kt/V OCM to clinical practice (Figure 2).

**Keywords:** Kt/V; Hemodialysis; Online clearance monitoring

## Introduction

Quantification of the dialysis dose is an essential element in the management of chronic haemodialysis treatment because the adequacy of the dose has a profound effect on patient morbidity and mortality [1]. The most useful and widely applied index to prescribe the dialysis dose (as well as to assess the dose which is actually delivered) is the Kt/V DAU formula [1]. It is now well recognized that an adequate delivery of haemodialysis (HD) dose (as measured by Kt/V derived from urea reduction) is a crucial determinant in clinical outcome of chronic HD patients [2]. This requires both prescription of an adequate dose of HD and regular assessment that the delivered treatments are also adequate [3].

The greatest problem we are facing at the moment is to check whether the prescribed dialysis dose has actually been delivered. There is often a difference, sometimes large, between the prescribed and delivered dose [4].

There are many reasons why a discrepancy between calculated and delivered dose of extra-corporeal blood purification might exist. Failure of staff to ensure the pre-determined treatment time is given (usually in the face of variable patient resistance) is a common failing. However, other factors such as suboptimal needle placement, haemodynamic instability and progressive access malfunction all militate against this optimal delivery [5]. Bed-side Kt/V is currently determined using various kinetic models; the most widely used being the single-pool variable volume urea kinetic model (SPVV- UKM) [6].

The European Best Practice Guidelines recommended as minimum treatment dose an equilibrated Kt/V = 1.2 [7], but in clinical practice this value cannot be achieved for every patient [8]. According to the guidelines, dialysis dose should be measured using a validated method [7]. Apart from blood sample-based methods, alternative methods determining dialysis dose have been developed, mostly based on measurements of conductivity [9] or of urea [10], recently also of ultraviolet absorbance in the spent dialysate [11].

On-line clearance monitors measure the difference in conductivity between the dialysate entering and leaving the dialyser with two different dialysate inlet electrolyte concentrations [12].

On-line clearance monitoring (OCM) allows dialysis dose to be monitored at every treatment with virtually no additional overheads. While it is unlikely that these non-invasive measurements of *Kt/V* will replace routine blood sampling, OCM affords staff the opportunity to monitor unstable patients more effectively, identify problems quickly and assess the effect of remedial actions.

Recently, advances in the on-line monitoring of conductivity during HD sessions have made the repeated measurement of Kt/V OCM on all HD treatment sessions a practical proposition [13]. This method has been shown to have an excellent correlation with Kt/V

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measured by urea reduction in a number of small studies [14-15]. However other studies reveal that OCM underestimate dialysis efficacy when compared with calculated Kt/V [16-17].

In view of these contradictory results, the aim of this prospective clinical trial was the comparison over a wide range of dialysis doses of the two methods, Kt/V Dau, Kt/V OCM to test the validity of ionic dialysance in determining Kt/V in comparison with the gold standard direct quantification method using the single-pool variable volume urea kinetic model (SPVV- UKM) in a series of haemodialysis patients from 2 centers in the gulf area.

## Subjects and Methods

### Patients

**Demographic criteria:** We prospectively studied 131 patients (63 males, 68 females) chronic HD patients over 8 weeks (1048 treatments) (Table 1). All patients had been on HD for>3 months (mean 32.13 ± 32.57 months). Patients were allocated from 2 dialysis centers; Princa Salman Center for Kidney Diseases located in Riyadh– the capital of Saudi Arabia and Nephrology unit, Internal Medicine Department, Jahra Hospital, Kuwait.

**Dialysis prescription:** All our patients were on Hemoflow Pn-Series High – Flux (Fresenius polysulphone Capillary dialysers – Pn60 LS and Pn80S), 77 of them were dialyzing via AVF while 45 were dialyzing via permicath and 9 via AVG. Patients received dialysis with Fresenius 4008 S monitors equipped with OCM biosensors (On-line clearance monitoring, Fresenius Medical Care AG). Mean age was 51.5 years (±15.04 years), fifty percent of our patients had blood flow rate was 300 ml/min (range 200-300 ml/min), The mean treatment time was 180 min (range 150-210), and the dialysate flow was fixed at 500ml/min.No changes were made to any of the dialysis prescriptions over the study period.

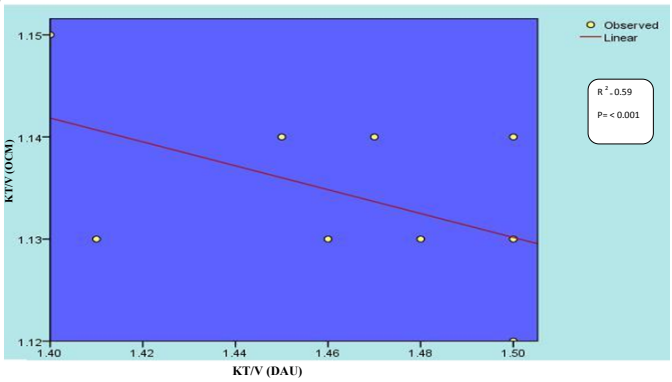


**Figure 1:** Correlation between Kt/V as measured by urea reduction and by ionic dialysance over the study period.

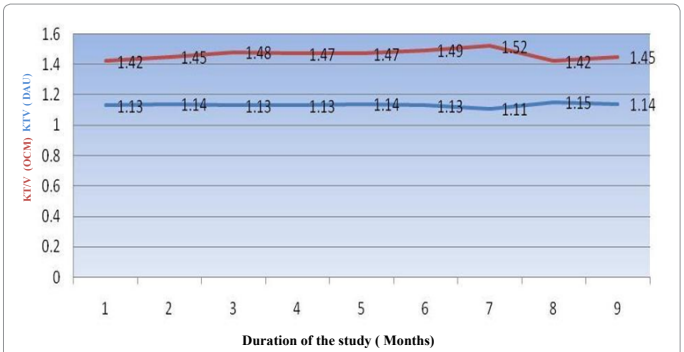


**Figure 2:** Comparison between KT/V(OCM) and KT/V (DAU) over the study period.

| Variable | Value |
|---|---|
| Age (years) | 51.5 ± 15.04 |
| Male/Female | 63/68 |
| Original renal disease (number):<br>Diabetes + Hypertension<br>Diabetes<br>Hypertention<br>Glomerulonephritis<br>Unknown<br>Interstitial nephritis<br>Adult Polycystic Kidney Disease<br>Haemolytic uraemic syndrome | <br>51<br>27<br>10<br>10<br>27<br>4<br>1<br>1 |
| Comorbedities:<br>DM<br>Hypertension<br>Ischemic Heart Disease<br>Cerebrovascular stroke | <br>51<br>65<br>47<br>30 |
| Blood pumb speeds (ml/min) | 356±54 ml |
| Wight (Kg) | 67 ±11 |
| BMI | 26.5±1.4 |
| Mean UF Rate ( kg/session) | 4.5 ±1.5 |

**Table 1:** Demographic criteria for 131 patients included in our study.

### Measurement of dialysis adequacy

Kt/V was measured by two techniques. The first method is the conventional method with blood sampling and calculation (Kt/V Dau). The second technique is effective plasma conductivity that is performed by two mutually independent temperature-compensated conductivity cells equipped with Fresenius 4008 S® dialysis machines ($Kt/V_{ID}$). The Fresenius module changes inlet conductivity every 30 min and records the change in conductivity at a second conductance meter at the dialysate waste. From this change ionic dialysance and plasma conductivity can be calculated automatically. Because the transfer characteristics of sodium and urea are similar, the ionic dialysance reflects the clearance of urea. For each patient and each dialytic session, $Kt/V_{ID}$ is calculated automatically by the dialysis monitor. Total body water, which is assumed to be equal to urea distribution volume, was calculated by the dialysis machine using the empirical formula of Watson et al. [18] for women and men, respectively.

The Research Ethics Board in the 2 centers approved the study protocol and a written consent was signed from all participants.

### Statistical analysis

The values of Kt/V by each of the two methods are expressed as means ± standard deviation. A P value of ≤ 0.05 was considered significant. The Spearman correlation test was used to assess the relationship between the two exploratory methods and the Student´s t test to compare the results obtained by the Kt/V DAU and Kt/V OCM. All data were analyzed using the SPSS for windows software package release 17.

## Results

### Patients' characteristics

Our study included 131 patients (63 males, 68 females); their mean

age was (51.5 ± 15.04 years), mean dialysis duration was 32.13 ± 32.57 months.

### Dialysis prescription

More than 58.8% of our patients were using AVF, about 34.4% only were using permicath and the remaining was using AVG.

### Comparison between Kt/V obtained by the two methods

Mean Kt/V was (1.459 ± 0.31) as measured by the single-pool variable volume urea kinetic model (KT/V DAU) while it was (1.139 ± 0.14) as measured by ionic dialysance (OCM). The difference between these two values did reach a statistical significance (P = 0.000).

### Correlation analysis

This was performed between all obtained online Kt/V DAU and Kt/V OCM. Two values of online Kt/V were used for correlation: simultaneous Kt/V, taken at the same time when OCM measurements were performed, and mean Kt/V representing the mean Kt/V value for both methods. There was positive correlation between calculated Kt/V and online Kt/V ($r^2 = 0.59$) with (P = 0.001).

## Discussion

Dialysis dose quantification by means of Kt/V is of fundamental importance in prescribing and, above all, assessing the adequacy of the dialysis actually delivered, which is strictly related to patient morbidity and mortality. The direct quantification of removed urea (the gold standard for determining Kt/V) cannot be used on a routine basis since it requires the total or partial collection of spent dialysate; and on-line urea sensing devices are too expensive to be a real alternative at the moment [19]. It is well known that the difference between prescribed and delivered dialysis doses greatly affects the morbidity and mortality of dialysed patients. The on-line monitoring of delivered dialysis is therefore of paramount importance. Kt/V is usually calculated monthly from pre- and post dialysis blood samples. A number of factors lead to a lower delivered dose than prescribed, such as cardiopulmonary and access recirculation, compartmental disequilibrium, loss in dialyzer clearance, and actual values of blood flow or effective treatment time being less than prescribed. If Kt/V is measured once per month, important variations in delivered dialysis dose may be missed. Measurement of delivered dialysis dose each dialysis would be desirable if it could be achieved without blood samples [19]. It is therefore not surprising that great interest should be shown in a method which can allow Kt/V to be determined at each session without the need for any blood or dialysate samples, and at no additional cost [20].

The ability to assess Kt/V on each treatment also gives some insight into the significant variability of delivered dose that each individual patient is subjected to [16]. In our study a correlation coefficient between Kt/V obtained online and calculated as SPVV Kt/V with urea measurement in blood probes was about 0.59. This is in agreement with that was reported by Grzegorzewska AE et al. [17]. Who studied 40 patients with total number of sessions involved in his study were 80 for each method, while in our study we included 131 patients with total number of 1048 records for each method.

Results of McIntyre et al. [16] indicate that the significantly greater correlation coefficient between values of SPVV urea Kt/V and online Kt/V can be obtained, when blood sample for urea determination is drawn 30 minutes after the end of the HD session (R2 = 0.92, p < 0.001). But this double-pool measurement of Kt/V is not practical due to difficulty in compliance and inconvenience for many patients. There is 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 a high ultrafiltration rate, and a correlation has been found between the decrease in ionic dialysance and 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 (the solvent for urea) is not significantly reduced by intradialytic ultrafiltration. Consequently, although the urea and sodium diffusion constants are almost equal, ionic dialysance cannot be assimilated to urea clearance because of the difference in effective blood flow, which is lower for ionic dialysance and mainly represented by plasma water flow [21].

For explanation of only moderate correlation between online Kt/V and Kt/V obtained using urea estimations these points should be considered, The whole spent dialysate was not collected in our study, Unlike what is reported by Petitclerc et al. [22] where the whole spent dialysate was collected and used for Kt/V measurement, which could explain a higher correlation coefficient, showing value of 0.94. Collection of the whole spent dialysate is very inconvenient. For this reason, collection of a representative fraction of spent hemodialysate [23], continuous sampling of spent dialysate and total dialysate volume measurement [23] or dialysate sampling at the beginning and at the end of dialysis session [24] were advised. These methods did not find, however, a place in routine clinical practice. And according to the European best practice guidelines on hemodialysis, online clearance should not substitute for monthly measurements using the reference method (equilibrated Kt/V), but it is an acceptable method for calculating haemodialysis on a treatment-by-treatment basis [25]. There are many advantage for OCM technique, First an automatic measurement of the dialysis dose during every dialysis session does no harm to the patient, as no blood samples are taken. For patients with a constant dialysis dose. Second the benefit of an automatic measurement may be moderate, but for patients with varying and lower dialysis doses the risk of an undetected low dialysis dose for longer periods of time are real, and the benefit of continuous surveillance concerning dose delivery seems obvious.

In conclusion, our study show that Kt/V obtained using online monitoring indicates a lower intermittent haemodialysis adequacy than those calculated from urea measurements. So they cannot replace each other without proper correction. Nevertheless the close correlation between the two parameters makes it easy to derive effective urea clearance from ionic dialysance. Since it is reasonable to assume that urea distribution volume is constant in steady-state patients, once this has been exactly determined by means of the measurement of ionic dialysance, it is possible to calculate Kt/V on-line at each session without the need for any blood sampling or laboratory examinations, and at no additional cost.

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