Assessment of Hemodialysis Adequacy by Ionic Dialysance: Comparison to Standard Method of Urea Removal

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Assessment of haemodialysis adequacy by ionic dialysance: comparison to standard method of urea removal

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ABSTRACT

Background. The haemodialysis adequacy is one of the most important issues influencing the survival of patients on maintenance haemodialysis (HD). Assessment of measuring the delivered dialysis dose using Kt/V index requires multiple blood sampling. New methods for assessment of dialysis dose based on ionic dialysance (ID) have been suggested. Online conductivity monitoring (using sodium flux as a surrogate for urea) allows the repeated non-invasive measurement of Kt/V on each HD treatment. In this study we have compared this method with the standard method of estimating Kt/V.

Methods. We studied 24 established HD patients over 4 weeks time period. Patients were dialysed using Fresenius 4008S dialysis monitors, equipped with modules to measure ID. Data were manually collected and analysed using the appropriate statistical software. Urea removal (UR) was measured once a week by a two-pool calculation, estimating an eKt/V.

Results. The Kt/V measured by ID highly correlated with the one derived from the measurement of the UR ($r = 0.8959$, $p < 0.0001$). The ID underestimated UR by the mean of 6%. The ID varied greatly within individual patients with a median of 1.29 ± 0.22. If the eKt/V ≥ 1.2 is considered adequate, 33% of the patients would have been inadequately dialysed. The mean HD duration to achieve an adequate dialysis was 4 hours and 47 minutes with high inter-patient variability.

Conclusion. The ID seems to be an easily obtained measure of the delivered dialysis dose, well correlating with standard UR method. Substantial individual variations

imply that repeated measures (ideally for all treatments) are necessary to obtain a real answer of the mean treatment dose being delivered to the patients.

Right Running Head: Haemodialysis adequacy - ionic dialysance vs urea removal

Introduction

The morbidity and mortality of patients on renal replacement therapy (RRT), especially on the dialysis therapy, are still unexceptably high[1]. There are a lot of factors influencing morbidity and mortality such as age, underlying disease, different comorbidities, especially cardiovascular, infectious and vascular access related. One of the most important factors influencing the morbidity and mortality of patients on maintenance haemodialysis is the delivered dialysis dose[2]. The correlation between lower mortality and higher dose of dialysis has been suggested analysing an US national random sample of over 2300 Medicare ESRD patients. The risk of mortality was 7% lower (p<0.001) with each 0.1 increase of delivered dialysis dose[3]. The most commonly used parameter to evaluate delivered dialysis dose is the spKt/V index, where K is the dialyser urea clearance, t is the duration of dialysis session and V is the patient's urea distribution volume. The spKt/V is derived from mathematical model formulated 25 years ago, first proposed by Gotch in the secondary analysis of The National Cooperative Dialysis Study (NCDS)[4,5]. However, dialysis efficiency has substantially increased over the last 15 years, and post-dialysis urea rebound observed, which followed to recent double-pool kinetics. Hence, equilibrated Kt/V (eKt/V), a two-pool approximation derived from spKt/V, was proposed to assess the dose of dialysis more adequately[6]. 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 (spKt/V≈1.4)[7]. Further increase of proposed dialysis dose is not recomended according to recent findings of the HEMO study[8]. The procedure of estimating delivered dialysis dose requires additional efforts of the dialysis stuff, higher laboratory costs and the results

are obtained after dialysis session. These disadvantages prevent the dialysis dose from being assessed routinely at each dialysis. According to clinical guidelines, the delivered dose of HD should be checked at least monthly[7]. Variability of the delivered dialysis dose estimated by the Kt/V index is affected by the type and surface of membrane, blood flow (Q_B), dialysate flow (Q_D), vascular access and cardiopulmonary recirculation. Other dialysis-related problems including hypotension episodes, dialyser microclotting, vascular access problems may substantionally influence the delivered dialysis dose[9].

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 haemodialysis monitoring based on the conductivity monitoring (using sodium flux as a surrogate for urea) allow repeated and non-invasive measurment of delivered dialysis dose during each session. The measurment of inlet and outlet dialysate conductivity enables software to measure ionic movement accross the dialysis membrane[10,11]. On-line monitoring devices have evolved from "toys" for research to tools for routine clinical application. Conductivity monitoring appears the most versatile tool, as it permits quantification of delivered dialysis dose, potentially at each dialysis session and without extra cost[12].

The aim of this study was to determine the valuability of ionic dialysance (ID) for assessment of delivered dialysis dose (Kt/V) in comparison to standard urea removal procedure (UR).

Patients and methods

Patients and haemodialysis parameters

We studied 24 (12 males and 12 females) chronic haemodialysis patients for a four week period (288 consecutive treatments). All patients had been on HD for more than one year (mean 35±31 months, range 12-123 months). The mean age was 62.8 years (range 32 to 80 years). All patients were dialysed using two needles in native arteriovenous fistulae. All patients were dialysed at haemodialysis unit in the Clinical Hospital Center Rijeka, Croatia, thrice weekly using dialysis machine 4008S-Fresenius Medical Care (FMC), equiped with Online Clearance Monitor (OCM[®]) module and hollow fibre low-flux polysulphone dialysis membrane (six patients using F6 HPS-1.4 m^2 and 18 patients using F8 HPS-1.8 m^2). Blood flow ranged between 200 and 400 ml/min. Dialysate flow was maintained at 500 ml/min. Drug therapy schedule was kept constant during the study period.

Measurment of dialysis adequacy

The HD delivered dose was measured using the standard method of blood sampling and calculating UR according to the present clinic guidelines. The following procedure was used: at the end of HD we set ultrafiltration rate to zero, decreased the blood flow to 100 ml/min for 15 s, than draw the blood sample from the arterial sampling port nearest to the patient. The result was calculated using the following formula: eKt/V=spKt/V-(0.47xspKt/V/T)+0.02[7]. The target eKt/V value was ≥ 1.2.

Calculating urea removal using standard procedure was performed once weekly, in the middle week dialysis session.

ID was measured on every dialysis session using OCM[®] module (FMC). As ID (sodium transport) is similar to transfer characteristics of urea, the ID reflects the clearance of urea (corrected for recirculation)[13]. The quality of Kt/V information content depends on the accuracy of the individual parameters, primarily on the volume of urea distribution (V). Empirical Watson formula is then emloyed to determine V from sex, weight, height and age of the patient. During an OCM[®] measurement, a pre- and post-dialyzer measurement of the conductivity is performed by two mutually independent temperature-compensated conductivity cells. K (ID) is calculated automatically by means of equality of measured dialysate conductivity and the urea removal. The Kt/V (ID) is automatically calculated by appropriate software. In this study we compared those two methods.

Statistical analysis

All data were manually collected and analysed using GraphPad InStat version 4.00 for Windows (GraphPad Software, San Diego, CA, USA; www.graphpad.com). The data were matched using Mann-Whitney test, considering $p < 0.05$ as statistically significant. The correlation was determined using the Pearson correlation.

Results

A total of 24 chronic HD patients were evaluated by ID during the 288 consecutive dialysis treatments. Every middle week dialysis session was measured for adequacy using both methods as described above. The study resulted in 96 comparable measuring of delivered dialysis dose. The mean Kt/V was 1.37 ± 0.02 (0.84-2.06) as measured by UR and 1.29 ± 0.23 (0.61-1.79) as measured by ID. The difference between two values reached statistical significance (p=0.0019). There was a great inter-patient variability in total of 288 measures made by ID, and substantional number of patients did not reach the target Kt/V values (Table 1).

We also found a slight underestimation of ID *vs* UR of 6%, but very comparable values in the whole group.

There was an excellent correlation in the mean patient measurements (r =0.8959; p<0.0001; Figure 1) and satisfactory correlation in the individual patient measurements (r =0.2071; p=0.04; Figure 2) of Kt/V assessed by two methods.

Using the ID method with appropriate software (OCM$^{®}$-FMC) we also estimated a time or dialysis session duration needed for achieving the target Kt/V value. The mean duration of dialysis session in patients with Kt/V <1.2 to achieve the target value was 4 hours and 47 minutes. There was also a great inter-patient variability (from 4 hours and 20 minutes to 6 hours and 16 minutes).

Discussion

Delivered dialysis dose (Kt/V) has shown a great impact on the morbidity and mortality rate in patients on maintenance haemodialysis[2]. Different methods for quantification of Kt/V have been suggested. Some authors suggested a single pool model for non-scientific purposes, while others suggested the two-pool model, which takes the urea rebound into account. However, the practicability of two-pool model is limited due to the 30 minutes delay for equilibration. Therefore, there is suggested an empirical formula to estimate equilibrated Kt/V without waiting for the rebound[6]. Although, if the correct approach is used, the assessment of Kt/V by pre- and post-dialytic blood sampling may give an adequate estimation of dialysis dose. In addition, the use of mathematical calculations may not be the best use of doctor's time. Although the use of calculators, which are also available on the internet, partly resolves this problem. However, there appears to be a need for new methods to assess dialysis adequacy. In our study we also used an appropriate calculation to assess delivered dialysis dose obtained from direct blood sampling and laboratory analysis[6]. Most of our patients achieved target Kt/V proposed by recent clinical guidelines[7].

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) shows without doubt that the new method of direct dialysis dose quantification could be more frequently used[12]. In addition, in our study there was a high degree of correlation between two methods used, which has already been confirmed in other studies[14, 15].

We also found a slight underestimation of values obtained by ionic dialysance according to standard urea removal procedure. This variance has been postulated to be a result of the effect of cardiopulmonary recirculation[15].

The modifiable dialysis parameters, which could be changed during the HD session for achieving an adequate delivered dialysis dose, are blood flow, dialysate flow, dialysis membrane surface and dialysis session duration. Usually the dialysate flow is constant as it was the case in our study. The membrane could be changed only for consequent sessions. Therefore, the blood flow depends on vascular access characteristics and it seems that dialysis session duration can be the only one online modifiable parameter. In our study we found that significant prolongation of dialysis session has to be made in order to achieve an adequate delivered dialysis dose in 33.3% of the patients. It seems to be reasonable to prolong dialysis session in such patients, if center schedule allows. It may be a problem especially in dialysis centers with a great number of patients and limited number of dialysis stations. Our study confirms the importance of online control of the patients, suggests some modifiable factors and a need for an individual patient assessment in order to achieve an adequate dialysis. The importance of such approach has been confirmed by other authors[12].

In conclusion, assessment of the delivered dialysis dose by ionic dialysance seems to be comparable with standard method of urea removal and sufficient to be useful in everyday clinical practice. Due to slight underestimation and some intrapatient variability, we suggest the use of average values for each patient obtained in single session, rather than a single value. Further investigations including more patients are required before confirming this method to be a standard clinical practice. Neverthless, the first results confirmed in our study are promising to be a significant advantage in everyday care of dialysis patients.

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Table 1. Results of Kt/V using ionic dialysance (ID)

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Number of ID measures	288
Minimal Kt/V (ID)	0,61
Maximal Kt/V (ID)	1,79
Mean Kt/V (ID)	1.29±0.225
Patients with Kt/V (ID) <1,2	8 (33,3%)
Target Kt/V	1,2

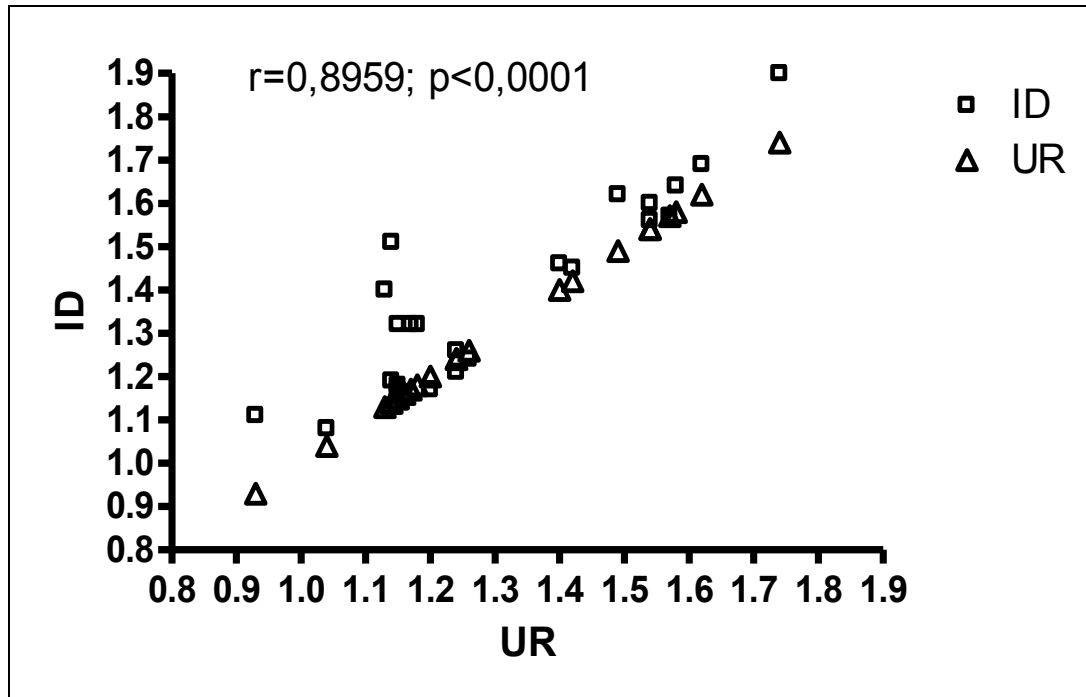Kt/V - haemodialysis adequacy; ID - haemodialysis adequacy as measured by ionic dialysance

Figure 1. Correlation between mean patient measurements of dialysis dose (Kt/V)
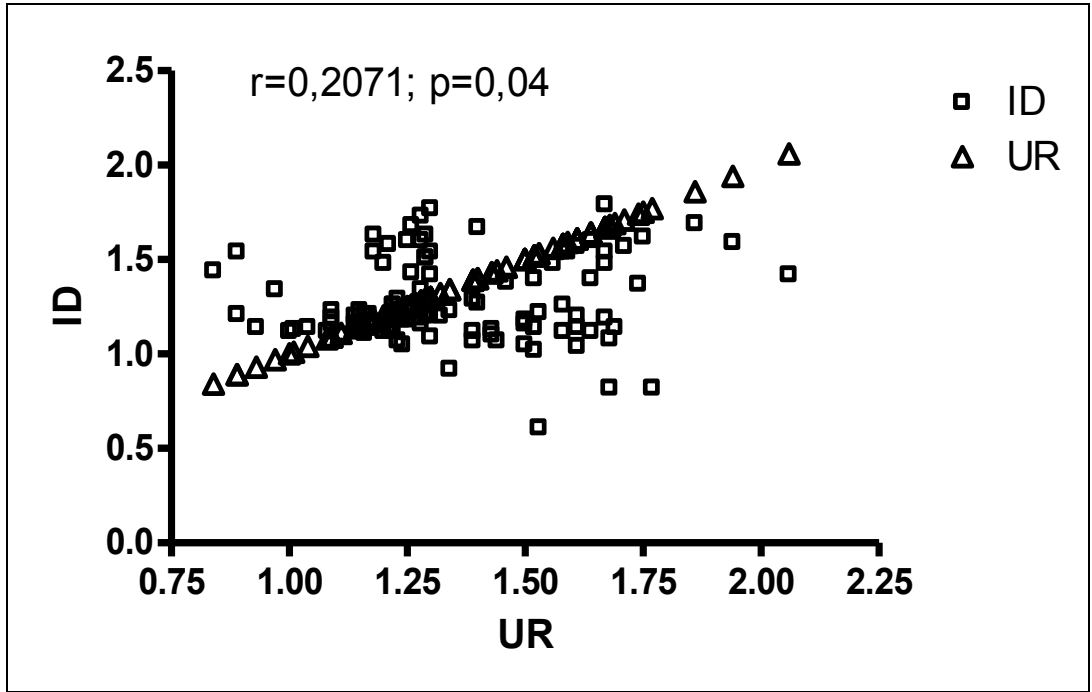assesed by urea removal (UR) and ionic dialysance (ID)

Figure 2. Correlation between individual patient measurements of dialysis dose (Kt/V) assesed by urea removal (UR) and ionic dialysance (ID)