Optical Urea Rebound Estimation during Dialysis

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Abstract— **The aim of the study was to explore the connection of urea rebound and the difference between spKt/V and eKt/V and also the possibility of utilizing UV-absorbance measurements to assess urea rebound. Ten patients of chronic three-times-a-week hemodialysis (HD) were studied. On-line UV-absorbance of spent dialysate was monitored. Single-pool Kt/V (spKt/V), equilibrated Kt/V (eKt/V) and the percentage difference between spKt/V and eKt/V (ΔKt/V) were calculated. Urea rebound was calculated based on urea concentration in blood (R_b) and UV-absorbance in spent dialysate (R_a). ΔKt/V and R_b were not statistically different. Also, R_a and R_b were not statistically different. In summary, the results show that it is possible to assess post-dialysis urea rebound in blood based on UV-absorbance in spent dialysate, which may offer the opportunity to estimate the true dialysis dose and a more personalized approach to the dialysis treatment.**

Keywords— **hemodialysis monitoring, rebound, Kt/V, urea, UV-absorption**

I. Introduction

Urea, a low-molecular weight metabolic end product of the catabolism of proteins, is considered to be the most suitable marker for uremic toxins in the range of low-molecular weight solutes [1]. Urea Kt/V is viewed as a sensitive measure of the overall dialysis dose that characterizes dialysis adequacy [2]. Traditionally, Kt/V is derived from formal urea kinetic modeling (UKM), which is based on blood samples at the start and end of dialysis [1].

If the immediate post-dialysis urea concentrations are used for the calculation of dialysis dose, it can be significantly overestimated because of the increase in blood urea concentration – urea rebound – which occurs after completion of the HD session. Urea rebound is complete within 30-60 min after the cessation of HD, which means that the most accurate way for the calculation of Kt/V would be to wait up to 60 minutes after the completion of HD before drawing the post-dialysis sample. However, this approach is impractical for patients and dialysis facilities.

In order to avoid the delay of waiting for an equilibrated post-dialysis blood sample, algorithms for anticipating post-dialysis rebound of urea have been developed [3, 4]. As the percentage value of rebound relative to the fall in urea concentration during HD approximates the percentage difference between single-single pool Kt/V (spKt/V) and equilibrated Kt/V (eKt/V) [5], this information could be used to estimate the true dialysis dose.

The Smye algorithm [3] estimates the post-dialysis equilibrated urea concentration in blood based on conventional pre- and post-dialysis blood samples and an additional intradialytic blood sample. The drawback of the Smye algorithm is that it suffers from the effects of small urea concentration measurement errors [6]. The Smye algorithm has also been modified for the use together with a continuous urea sensor [7] showing good agreement between the estimated equilibrated urea concentration and urea concentration 25-40 min following termination of dialysis.

There is a need for an instrument capable of directly and easily assessing post-dialysis urea rebound without the need to have the patient wait 30-60 min after the treatment and without repeated blood samples. An optical method utilizing UV-absorbance has been proposed for the monitoring of dialysis adequacy [8, 9]. A good linear relationship has been found between UV-absorbance and dialysate urea concentration in the wavelength range 210-330 nm, with the highest correlation at 280-320 nm [10]. It has been shown that due to the good correlation between UV-absorbance and urea concentration in dialysate, the latter can be estimated from UV-absorbance measurements even if the UV-technique does not measure urea itself [11]. Moreover, urea concentration in spent dialysate is a fixed fraction of arterial urea concentration as long as dialysate flow rate, dialyser clearance and recirculation rate remain unchanged [7].

This study was undertaken to explore the connection of urea rebound and the difference between spKt/V and eKt/V and also the possibility of utilizing UV-absorbance measurements to assess urea rebound.

II. Subjects and Methods

A. Subjects

Ten patients, four females and six males, mean age 60±19 years, on chronic three-times-a-week HD were studied at the Department of Nephrology, University Hospital, Linköping, during a total of 30 sessions. Six patients, i.e. 18 treatments, were dialysed by a low-flux membrane (Polyflux, 17L, Gambro, Sweden) with an effective membrane

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area of 1.7 m^2 and four patients, i.e. 12 treatments, with high-flux membranes (Nephral 300, HOSPAL Industrie, Meyzieu, France and Tricea 150, Baxter Health Care Corp., IL, USA) with an effective membrane area of 1.3 m^2 and 1.5 m^2, respectively. Treatment durations ranged from 240 to 270 min. The dialysate flow was fixed at 500 ml/min and effective blood flow varied between 200 to 350 ml/min. The type of dialysis machine used was Fresenius 4008H (Fresenius Medical Care, Germany).

The Regional Ethics Committee, Linköping, Sweden approved the study protocol and informed consent was obtained from all patients.

B. Sampling and laboratory analysis

Samples of blood were taken at before the start of HD, at the end of HD and 30 min after the end of HD. The blood samples were sent to the laboratory for analysis within 2-4 h. Laboratory's standard sampling procedures were followed. The concentration of urea was determined at the Clinical Chemistry Laboratory at the Linköping University Hospital using a standardized method. The accuracy of the method for the determination of urea in blood was ±5 %.

C. UV-absorbance monitoring

The UV-instrumentation has been described earlier [12]. The wavelength 297 nm was used. The sampling frequency was set at two samples per minute.

The baseline was measured a few minutes before the start of each dialysis treatment on the flowing pure dialysate (reference solution) when the temperature and conductivity had been stabilized and the sodium and bicarbonate level had been preset according to the patient records.

The obtained UV-absorbance values were processed and presented on computer screen by a PC incorporated into the spectrophotometer using Kontron software (UVIKON 943, version 7.0 for Windows; Kontron Instruments, Italy). Data were then transformed to an Excel file at the end of the treatment.

D. Data analysis

Some of the measured values (absorbance or concentration) were excluded from data before analysis. The exclusion criteria were incorrect or illogical values of the measured concentration or absorption, e.g. sampling coexisting with self-tests of the dialysis machine.

Single-pool Kt/V (spKt/V) was calculated according to [1] as

$$spKt/V = -\ln\left(\frac{C_t}{C_0} - 0.008T\right) + \left(4 - 3.5\frac{C_t}{C_0}\right)\frac{\Delta BW}{BW} \quad (1)$$

where C_0 and C_t are blood urea concentrations before and at the end of the dialysis, respectively, measured in mmol/l, T is treatment time in hours, dBW intradialytic weight loss in kilograms and BW end-session body weight in kilograms.

Equilibrated Kt/V (eKt/V) was calculated according to [1] as

$$eKt/V = spKt/V - \left(0.6\frac{spKt/V}{T}\right) + 0.03 \quad (2)$$

The difference between spKt/V and eKt/V (ΔKt/V) was expressed as

$$\Delta Kt/V = \frac{spKt/V - eKt/V}{eKt/V}100\% \quad (3)$$

Urea rebound (R) was expressed relative to C_t as

$$R = \frac{C_{eq} - C_t}{C_t}100\% \quad (4)$$

where C_{eq} is the equilibrium concentration of urea at the end of rebound phase. Rebound was calculated based on urea concentration in blood samples (R_b) and UV-absorbance in spent dialysate (R_a). In case of R_a urea concentrations were substituted by UV-absorbance values.

In order to estimate urea rebound based on UV-absorbance in spent dialysate a substitute value for C_{eq} (A_{eq}) was calculated according to the Smye algorithm [3] where urea concentrations were substituted by UV-absorbance values

$$A_{eq} = A_0 e^{-\lambda t} \quad (5)$$

so that A_0 is the average value of 2 to 6 min from the beginning of HD and t is the duration of HD in minutes. λ was obtained by line fitting based on on-line UV-signal from 60 min to the end of HD session.

Student's t-test for dependent samples was used to compare means for estimated parameters and $p<0.05$ was considered significant. Individual differences in ΔKt/V and R_a compared to R_b were also examined using Bland and Altman analysis [13].

For the analysis Excel (version 2003 for Windows) was used.

III. Results

Average spKt/V was 1.45±0.23 and average eKt/V was 1.27±0.20. Average ΔKt/V was 13.76±1.12 % and it was not statistically different from R_b (p=0.57), which was 13.25±4.95 %. Figure 1 shows the Bland-Altman plot of the differences between R_b and ΔKt/V. The mean difference between R_b and ΔKt/V was -0.57±4.38 %.

Average R_a was 13.20±7.54 % and it was not statistically different from R_b (p=0.79). Figure 2 shows the Bland-Altman plot of the differences between R_b and R_a. The mean difference between R_b and R_a was -0.43±8.15 %.

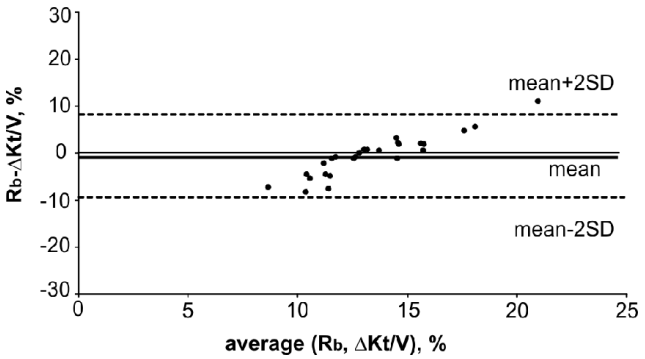

Fig. 1 Bland-Altman plot of the differences between R_b and ΔKt/V (N=26)

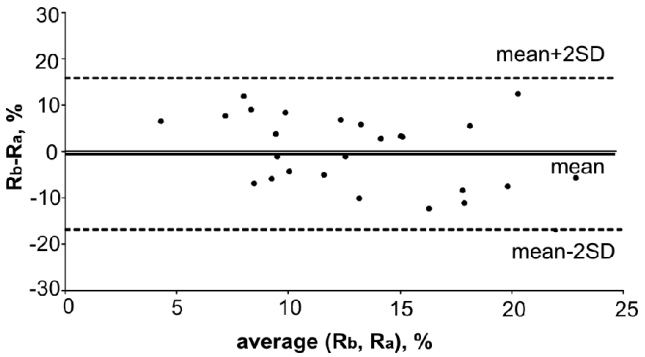

Fig. 2 Bland-Altman plot of the differences between R_b and R_a (N=26)

IV. Discussion

The present study investigated the connection of urea rebound and the difference between spKt/V and eKt/V and also the possibility of utilizing UV-absorbance measurements to assess urea rebound.

The results indicated that: (i) urea rebound percentage value approximates the percentage difference between spKt/V and eKt/V; (ii) it is possible to assess post-dialysis urea rebound in blood based on UV-absorbance measurements in spent dialysate.

It has been suggested previously that the percentage value of urea rebound approximates the percentage difference between spKt/V and eKt/V [5]. The results of this study support this assumption, as ΔKt/V was not statistically different from R_b (p=0.57).

It has been show previously that it is possible to monitor urea concentration in spent dialysate with the UV-absorbance technique [11]. The optical method for monitoring dialysis adequacy [8, 9] offers the possibility to continuously follow the urea elimination profile without the need for disposables of chemicals. As urea concentration in spent dialysate is a fixed fraction of arterial urea concentration as long as dialysate flow rate, dialyser clearance and recirculation rate remain unchanged [7] it is also feasible to estimate urea rebound in blood based on UV-absorbance in spent dialysate. This assumption is supported by the results, as R_a was not statistically different from R_b (p=0.79). Thus, the results of the present study indicate the possibility of assessing urea rebound based on UV-absorbance measurements in spent dialysate.

As the results of this study show that R_b approximates ΔKt/V and the possibility of assessing urea rebound based on UV-absorbance measurements in spent dialysate exist, it can be suggested R_a could be utilized to estimate ΔKt/V. This information could be used to estimate the true dialysis dose and it would enable a more personalized approach to the dialysis treatment.

V. Conclusion

The results suggest that it may be feasible to assess post-dialysis urea rebound in blood based UV-absorbance measurements in spent dialysate, which may offer the opportunity to estimate the true dialysis dose and a more personalized approach to the dialysis treatment. To validate the results using a larger database will be an issue of further studies. The merits of the described method are that it does not need blood samples or the patient to wait 30-60 minutes after the completion of HD before the drawing the post-dialysis sample.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. European Best Practice Guidelines of Haemodialysis, ERA-EDTA. (2002) II.1 Haemodialysis dose quantification: small solutes. Nephrol Dial Transplant 17: 16-31
2. NKF KDOQI guidelines. Clinical practice guidelines for hemodialysis adequacy, update 2006. Guideline 3. Methods for post-dialysis blood sampling at http://www.kidney.org
3. Smye SW, Evans JH, Will E et al. (1992) Paediatric haemodialysis: estimation of treatment efficiency in the presence of urea rebound. Clin Phys Physiol Meas 13: 51-62
4. Daugirdas JT, Schneditz D. (1995) Overestimation of hemodialysis dose depends on dialysis efficiency by regional blood flow but not by conventional two pool urea kinetic analysis. ASAIO J 41: M719-M724
5. Alloatti, S, Molino A, Manes M et al. (1998) Urea rebound and effectively delivered dialysis dose. Nephrol Dial Transplant 13: 25-30
6. Gotch FA, Keen ML (2005) Kinetic modeling in hemodialysis, in Nissenson AR, Fine RN (ed), Clinical dialysis, New York, McGraw-Hill, pp. 153-202.
7. Garred LJ, Canaud B, Bosc JY et al. (1997) Urea rebound and delivered Kt/V determination with a continuous urea sensor. Nephrol Dial Transplant 12: 535-542
8. Fridolin I, Magnusson M, Lindberg L-G (2002) On-line monitoring of solutes in dialysate using absorption of ultraviolet radiation: technique description. Int J Artif Organs 25:748-761
9. Castellarnau A, Werner M, Günthner R et al (2010) Real-time Kt/V determination by ultraviolet absorbance in spent dialysate: technique validation. Kidney Int 78: 920-925
10. Fridolin I, Lindberg L-G (2003) On-line monitoring of solutes in dialysate using wavelength-dependent absorption of ultraviolet radiation. Med Biol Eng Comput 41: 263-270
11. Uhlin F, Fridolin I, Lindberg L-G et al. (2005) Estimating total urea removal and protein catabolic rate by monitoring UV absorbance in spent dialysate. Nephrol Dial Transplant 20: 2458-2464
12. Uhlin F, Fridolin I, Lindberg L-G et al. (2003) Estimation of delivered dialysis dose by on-line monitoring of the ultraviolet absorbance in the spent dialysate. Am J Kidney Dis 41: 1026-1036
13. Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1: 307-310

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