Daily Hemodialysis versus Standard Hemodialysis: TAC, TAD, Weekly eKt/V, std(Kt/V), and PCRn

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Seven patients, mean age 42.57 ± 15.69 years (range 21 – 67 years), on standard hemodialysis (SHD), 4 – 5 hours, three times per week for 11.0 ± 6.63 years (range 1 – 18 years), were switched to daily hemodialysis (DHD), 2 – 2.5 hours, six times per week. For each type of treatment similar parameters were applied, and the total weekly time was the same. Mean duration of DHD was 15.4 ± 4.98 months (range 7 – 20 months). We report here our results of quantification in each method, including time-averaged concentration (TAC), normalized protein catabolic rate (PCRn), equilibrated Kt/V (eKt/V), equivalent normalized continuous standard clearance [std(Kt/V)], equivalent renal urea clearance (eKRn), and time-averaged deviation (TAD).

With DHD, urea TAC was reduced from 19.09 ± 3.47 to 15.16 ± 3.21 mmol/L (p = 0.026), urea TAD diminished from 4.76 ± 1.04 to 2.52 ± 0.57 mmol/L (p = 0.000 53), PCRn increased from 1.11 ± 0.23 to 1.42 ± 0.24 g/kg/day (p = 0.001), weekly eKt/V increased from 4.11 ± 0.31 to 4.74 ± 0.43 (p = 0.000 25), std(Kt/V) rose from 2.17 ± 0.06 to 4.02 ± 0.25 (p = 0.0001), and eKRn increased from 12.96 ± 0.60 to 21.7 ± 3.09 mL/min (p = 0.000 45).

On DHD the most important quantitative variation is the decrease of urea TAD (closer to that of a healthy kidney), due to the increased frequency of dialysis; std(Kt/V) practically doubled and represents 30% of that of normal renal function. These changes are probably the main explanation for the clinical improvements, but it is difficult to dissociate the effects of increased dialysis dose from the effects of decreased TAD.

Key words

Daily hemodialysis, time-averaged concentration, normalized protein catabolic rate, equilibrated Kt/V, standard Kt/V, equivalent renal urea clearance, time-averaged deviation

Introduction

Thrice-weekly hemodialysis is considered as standard hemodialysis (SHD). The criteria for SHD adequacy are established, but the limits and unphysiology of SHD are also well recognized [1]. Frequent hemodialysis, more than three times weekly, has been used in the past [2–4], but daily hemodialysis (DHD), more than five times per week, is a relatively new development [5]. The clinical benefits of DHD are well known: excellent intradialytic tolerance, optimal blood pressure control, decreased left ventricular hypertrophy, correction of anemia, and better overall quality of life [6–8].

This study reports on the quantifiable markers that may account for the clinical improvements. These include urea retention [measured by the urea time-averaged concentration (TAC)], the degree of dialysis unphysiology [measured by time-averaged deviation (TAD)], dialysis dose [indicated by fractional urea clearance per dialysis Kt/V, equivalent renal urea clearance (eKRn), equivalent normalized continuous standard clearance std(Kt/V)], and nutrition [normalized protein catabolic rate (PCRn)].

Material and methods

This study was performed on 7 patients, mean age 42.57 ± 15.69 years (range 21 – 67 years). Three patients had chronic glomerulonephritis; two had chronic interstitial nephritis; one had nephroangiosclerosis; and one had nephronophthisis. All patients were anuric. They had been treated on SHD for 11.0 ± 6.63 years (range 1 – 18 years). Three dialyzed at home and 4 in a self-dialysis unit. The SHD treatment parameters were 4 – 5 hours (4.64 ± 0.38 hours), three times per week. Bicarbonate dialysate was used, and the dialysate flow rate was 500 mL/min. In 5 patients polysulfone dialyzers (1.3 – 1.8 m²) were employed; in one patient a polymethylmethacrylate dialyzer (1.6 m²) was used, and a polymer caprin dialyzer (2 m²) was used in the remaining one. The blood access used for dialysis was a native arteriovenous fistula with double puncture, and the average blood flow rate was 275 mL/min (range 250 – 300 mL/min).

These patients were switched to DHD, 2 – 2.5 hours (2.36 ± 0.2 hours), six times per week at the beginning of 1997. The mean time on DHD was 15.4 ± 4.98 months (range 7 – 20 months). For each patient all parameters of hemodialysis (total weekly time, dialysate composition and flow, blood flow, and dialyzer) remained the same.

All samples were taken at midweek sessions. Predialysis (C_0) and postdialysis (C_f) plasma urea levels (mmol/L) were measured each week in patients treated in the self-dialysis unit or every two weeks in patients treated at home. The postdialysis sample was drawn using a stop pump technique. The urea reduction ratio (URR) was calculated from the pre- and postdialysis samples.

Urea TAC is the mean plasma urea concentration averaged over the whole weekly cycle, and urea TAD is the mean deviation of plasma urea concentration from the TAC value.

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We calculated these with simplified and approximate equations:

$$\text{urea TAC (mmol/L)} = (C_0 + C_f)/2,$$

considering that the mean value of the pre- and postdialysis concentrations at the midweek dialysis session is close to the time-averaged concentration.

$$\text{urea TAD (mmol/L)} = (C_0 - C_f)/4,$$

considering that the mean deviation at the midweek dialysis is equal to the total area of all triangles with bases at TAC line over time, and that the height of each triangle is approximately half the difference between C_0 and C_f.

Hemodialysis quantification was performed once a month during the midweek session using the Biostat 1000 on-line urea monitor (Baxter Healthcare, Deerfield, IL, U.S.A.) and a spent dialysate sampler (Quantispal-Hospal, France). Kt/V was measured by direct dialysate quantification, which avoids the problems associated with postdialysis blood sampling, use of the double pool model, and postdialysis rebound.

The concept of an equivalent renal urea clearance was introduced by Casino [9] and designated EKR, or EKRc if corrected for V urea of 40 L. Depner [10] redesignated it as eKRn, which is the continuous clearance necessary to achieve the urea TAC. We used the formula proposed by Depner:

$$\text{eKRn} = 40 \times (\text{PCRn} - 0.17)/5.42 \times \text{TAC},$$

where eKRn is measured in milliliters per minute, TAC is in milligrams per deciliter, and PCRn is in grams per kilogram per day.

Gotch used the equivalent normalized continuous standard clearance [std(Kt/V)], which represents the continuous clearance required to maintain a constant urea value equal to the predialysis level (C_0) at the midweek hemodialysis session [11]:

$$\text{std(Kt/V)} = 7 \times 1440[0.184 \times (\text{PCRn} - 0.17)]/C_0 \text{ weekly},$$

where PCRn is in grams per kilogram per day, and C_0 is the predialysis blood urea nitrogen in milligrams per deciliter. From the Borah formula [12],

$$G = 0.154 \times \text{PCR} - 1.7,$$

where G is the urea nitrogen generation rate in grams per day, and PCR is the protein catabolic rate in grams per day.

We have calculated PCRn according to the following equation:

$$\text{PCRn} = 0.0260 \times (\text{MT/BW}) + 0.17,$$

where MT is the weekly mass transfer in millimoles per liter, body weight BW is in kilograms, PCRn is in grams per

kilogram per day, and where weekly MT is determined by direct dialysis quantification at the midweek session, multiplied by 3 for SHD and 6 for DHD.

The data were expressed as means and standard deviations; Student's paired *t*-test was used to determine the significance of differences, and α was set at 0.05.

Results

The predialysis blood urea concentration was 28% lower in DHD than in SHD (20.73 ± 5.25 mmol/L vs 28.67 ± 7.10 mmol/L). The postdialysis blood urea concentration was slightly higher in DHD than in SHD (10.46 ± 2.5 mmol/L vs 9.56 ± 1.87 mmol/L), but was not significantly different. Urea TAC decreased significantly ($p = 0.026$) from 19.09 ± 3.47 mmol/L in SHD to 15.16 ± 3.21 mmol/L in DHD (Fig. 1). Urea TAD showed an important regression ($p = 0.000\,53$) of 47% from 4.76 ± 1.04 mmol/L in SHD to 2.52 ± 0.57 mmol/L in DHD (Fig. 2).

With DHD, the mean URR dropped from 66.6% to 49.5% and Kt/V from 1.35 ± 0.10 to 0.79 ± 0.07. Weekly Kt/V significantly increased from 4.11 ± 0.31 with SHD to 4.74 ± 0.43 with DHD (Fig. 3). The eKRn increased from 12.96 ± 0.60 with SHD to 21.7 ± 3.09 mL/min with DHD ($p = 0.000\,45$), and the std(Kt/V) almost doubled ($p = 0.0001$) from 2.17 ± 0.06 with SDH to 4.02 ± 0.25 with DHD (Fig. 4).
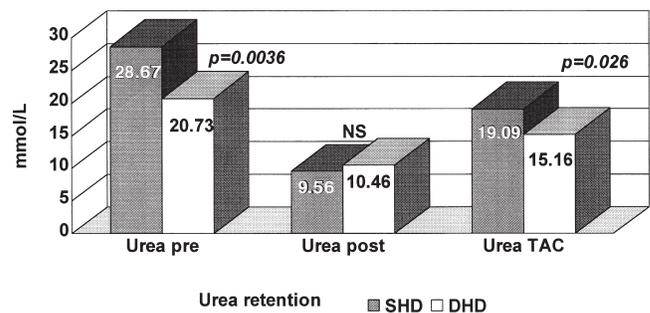

FIGURE 1 Comparison of urea retention in standard hemodialysis (SHD) and daily hemodialysis (DHD).
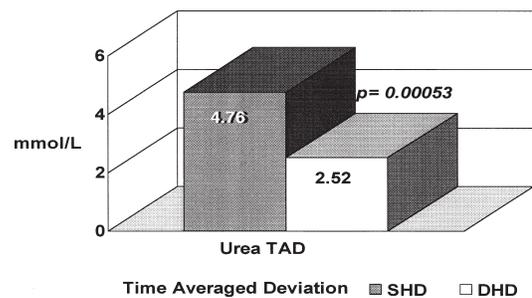

FIGURE 2 Comparison of urea time-averaged deviation (TAD) in standard hemodialysis (SHD) and daily hemodialysis (DHD).
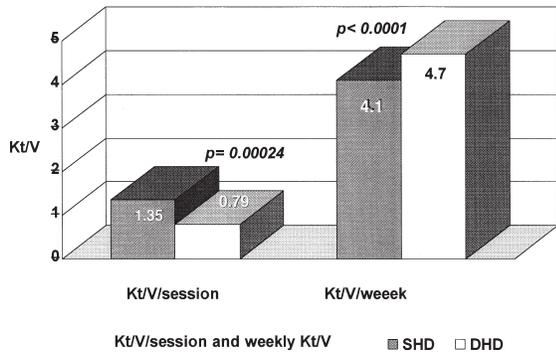
FIGURE 3   Comparison of Kt/V per dialysis session and Kt/V per week in standard hemodialysis (SHD) and daily hemodialysis (DHD).
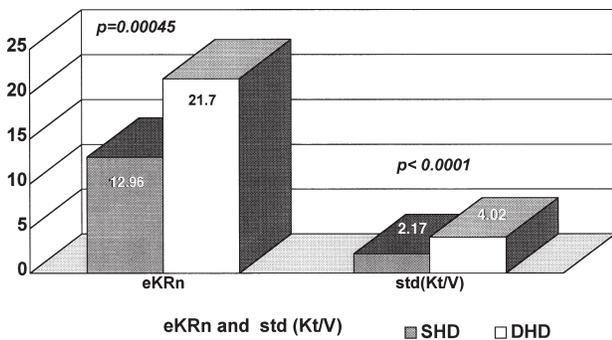

FIGURE 4   Comparison equivalent urea clearance and standard Kt/V in standard hemodialysis (SHD) and daily hemodialysis (DHD).

PCRn significantly ($p = 0.001$) increased from 1.11 ± 0.23 g/kg/day with SHD to 1.42 ± 0.24 g/kg/day with DHD. Dietary protein intake (DPI), measured by seven-day food records, also increased from 1.3 ± 0.27 to 1.62 ± 0.57 g/kg/day (Fig. 5). Dry body weight gain at one year was 2.78 ± 1.55 kg ($p = 0.045$).
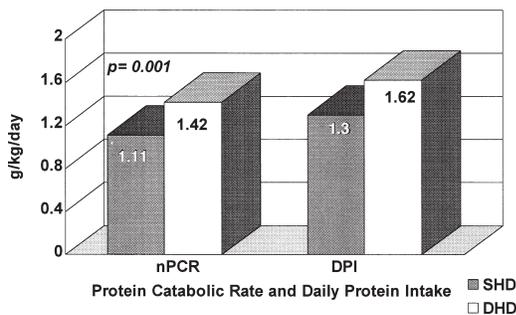

FIGURE 5   Normalized protein catabolic rate (nPCR) and dietary protein intake (DPI) in standard hemodialysis (SHD) and daily hemodialysis (DHD).

Discussion

Our results show an important improvement in DHD as compared to SHD in all quantifiable markers. The postdialysis urea, sampled by a "stop pump technique," excludes the angioaccess recirculation, but doesn't take into account the rebound. This "nonequilibrated" C_f underestimates the TAC value and overestimates the TAD value, and certainly more in DHD than in SHD; however, there is no error in the measurement of Kt/V, std(Kt/V), and PCR because these were calculated from direct dialysis quantification. The reduction in predialysis urea and urea TAC reduces the uremic intoxication. Reduction of urea TAC can be also obtained by increasing the dialysis dose by increasing dialyzer clearance (K) or the length of the dialysis session (t) without increasing the frequency (*N*); however, K is flow, membrane, and patient tolerance limited, and the increase in time results in reduced efficiency toward the end of the treatment. More frequent dialysis allows lower TAC even when the weekly Kt/V value is the same [10].

The "unphysiological" characteristic of intermittent hemodialysis was described by Kjellstrand *et al.* [1]. Lopot proposed that the "unphysiology" of intermittent dialysis could be measured by TAD [13]. In DHD the decrease of urea TAD makes this method more physiological. TAD depends on urea generation rate, total body water (V), and the duration of the interdialytic period. The increase of the dialysis dose has no influence on urea TAD; only increased *N* allows its decrease. The lowest urea TAD may be achieved with continuous blood purification as in continuous ambulatory peritoneal dialysis or with a wearable artificial kidney.

The PCRn showed an important increase that corresponds to the increased DPI (Fig. 5) and dry body weight (+2.78 kg at one year), but this may also have minimized the reduction of TAC and TAD. In DHD the URR was 26% lower and Kt/V per session was only 42% lower, despite a 50% reduction in dialysis time. Weekly Kt/V was 15% higher with the same total weekly time and the same treatment parameters. The influence of the first-order logarithmic decline in plasma urea concentration on dialysis efficiency is diminished when dialysis is more frequent [10]. Other explanations have been offered for the increase of weekly Kt/V with DHD, such as the increase in the ultrafiltration volume per week on DHD compared to SHD, and the better blood pressure stability on DHD, reducing flow-related disequilibrium and local recirculation [14].

Kooistra *et al.* [15] adjusted time of dialysis, without changing dialyzer clearance to preserve the same weekly Kt/V, calculated as the weekly sum of individual dialysis session Kt/Vs in both methods. In their study, after switching from SHD to DHD, urea TAC was lower only at week 8 and essentially unchanged at week 24. Weekly Kt/V, if calculated as a sum of individual hemodialysis session Kt/Vs, is not a good tool to compare different schedules. At this time, the only way to compare the dialysis dose in all therapies is eKRn or std(Kt/V). We determined the std(Kt/V) according to the

formula proposed by Gotch [11], as shown in the Methods section, using direct dialysis quantification; however, we didn't use Gotch's diagram (Fig. 3 in Ref. 11) to estimate std(Kt/V) from single pool Kt/V (spKt/V). This diagram compares the effects of frequency on std(Kt/V) as related to an individual spKt/V of the same duration (3.5 hours) regardless of the frequency of dialysis. We kept the total weekly time of dialysis constant. In our study, std(Kt/V) in DHD practically doubled (4.02 vs 2.17) and amounted to almost 30% of that of normal renal function. Our calculations indicate that for Tassin patients [16] dialyzed three times weekly for 8 hours with Kt/V of 1.85 and PCRn of 1.41, std(kT/V) is only 2.7. Thus it is virtually impossible to obtain a std(Kt/V) of 4.02 in SHD. Finally, the std(Kt/V) is not validated, and the optimal std(Kt/V) is not known.

Only the increase in dialysis frequency permits the amelioration in all quantification markers, but for clinical improvements, it is difficult now to dissociate the effects of increased dialysis dose from the effects of increased frequency.

Conclusion

On DHD, the most important quantitative variation is the decrease of urea TAD (closer to that of a healthy kidney), due to the increased frequency of dialysis; std(Kt/V) practically doubled and represents 30% of that of normal renal function. These two changes probably account for the clinical improvements, but it is difficult to dissociate the effects of increased dialysis dose from the effects of decreased TAD. Thus DHD is more efficient [lower TAC, higher std(Kt/V)] and more physiological (lower TAD); it will be perhaps, tomorrow, the standard hemodialysis.

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