

Daily Hemodialysis: Is It a Complex Therapy with Unproven Benefits?

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Introduction

Daily hemodialysis in the form of both short daily hemodialysis and nocturnal hemodialysis is used more frequently as an alternative to conventional hemodialysis and the interest in these modalities has intensified. The argument for their wider use will be defended.

Definitions and History

The typical prescription of daily short hemodialysis is 2 h daily, 6 days a week, using high blood and dialysate flows to achieve the highest clearance possible. It has been used either at the dialysis unit or at home. Nocturnal hemodialysis is performed nightly at home, for an average of 8 h 6–7 nights a week, at variable blood and dialysate flows. Peripheral accesses as well as central venous catheters have been used for both methods. The buttonhole cannulation technique [1] has been used by many centers for the cannulation of AV fistulas. The use of short daily hemodialysis was described first by DePalma et al. [2] in 1969, but the Italian experience of more than 18 years has generated the best known publications, mainly by Buoncristiani's group in Perugia [3]. Several reports from The Netherlands [4], France [5], USA [6, 7] and elsewhere have been published and recently Woods et al. [8] published retrospective data from several centers. Nightly (nocturnal) hemodialysis was started by Uldall [9, 10] in Toronto in 1994. Several centers in North America [11,

12] and elsewhere [13] have experience with nocturnal hemodialysis with more than 100 patients currently on the treatment. The history of daily hemodialysis has been published by Kjellstrand and Ing [14].

Results

Short Daily Hemodialysis

Quality of life (QOL): Most of the published studies are controlled, comparing the QOL of the same patients prior to and after the conversion to short daily hemodialysis. All studies were consistent in describing improvement of uremic as well as dialysis-related symptoms and remarkable hemodynamic stability. Although some of the older studies did not quantitate the improvement or used their own instruments for the quantitation [15], the more recent articles used previously validated instruments [4, 6]. The improvement in QOL and decrease in symptoms in unstable and symptomatic patients for whom the method was used as 'salvage', has been impressive.

Blood pressure control: Improvement in blood pressure control has been uniform in all studies with an average decrease in antihypertensives by 50% [8]. Buoncristiani et al. [16] as well as Traeger et al. [17] reported decrease in left ventricular hypertrophy after conversion to short daily hemodialysis.

Anemia control and EPO dose: A decrease in EPO dose has been described by most studies on average by about 50% [8, 18]. Kooistra et al. [4] did not detect significant

difference but in most studies the results are confounded by the lack of control for adequate iron administration.

Nutrition: Improvement in nutritional parameters in the form of increase in serum albumin and weight gain has been reported by most of the studies [8].

Hospitalization rates: Decrease in hospitalization rates after conversion to short daily hemodialysis has been reported [7] but prospective studies have not yet been published.

Vascular access: Despite the use of peripheral accesses daily, a decrease in the complication rate has been reported by Woods et al. [8] in their retrospective study. The complication rate decreased from 0.28 to 0.005/patient/year after the conversion to short daily hemodialysis. Similar results were reported by Ting [19].

Nocturnal Hemodialysis

Small molecule clearance is higher than all the other hemodialysis regimens with a Kt/V of 1–2 nightly [10, 20].

Quality of life: significant improvement in QOL was documented by using several validated instruments including SF-36 [21, 22], Beck Depression Index and Sickness Impact Profile [21]. Personal patient testimonies have been very positive, especially by patients with previous co-morbid conditions.

Hemodynamic stability of the patients is very high, as a result of the long and frequent dialysis as well as the recumbent position during the treatment. Therefore, dialysis partners have not been necessary.

Blood pressure control: Improvement in blood pressure control has been impressive. In most patients all antihypertensives were discontinued [10]. Data on LVH are not yet available.

Phosphate control has been excellent without the need for phosphate binders. Despite a high phosphate diet, addition of phosphate in the dialysate is required in 75% of the patients [23, 24]. The calcium phosphate product normalized in all patients.

Middle molecule removal four times higher than conventional hemodialysis has been reported, exemplified by β_2 -microglobulin [25].

Bone disease is easier to control with effective PTH suppression with phosphate control and the use of high dialysate calcium. Extraosseous tumorous calcifications have dissolved [26].

Sleep apnea is prevalent in ESRD and is an independent predictor of mortality [27]. Nocturnal hemodialysis has been found to correct sleep apnea in the affected individuals [28].

Anemia control improved with decrease in EPO dose by about 40%. The confounding effect of intravenous iron infusion has not been dissected out [24].

Nutritional studies done by our group showed increase in the serum amino acid levels [29] and increase in the total body nitrogen in 75% of the patients [30]. Weight gains have varied with some patients gaining more than 10 kg after the conversion to nocturnal hemodialysis.

Why Is Daily Hemodialysis Better than Conventional Hemodialysis?

Kinetics

The three times weekly hemodialysis regimen is characterized by wide fluctuations of biochemical parameters as well as intravascular fluid volume, described as ‘unphysiology’ by Kjellstrand et al. [31]. Daily dialysis is smoother, closer to the native kidney function. Since continuous ambulatory peritoneal dialysis (CAPD), the ultimate example of a physiological dialysis regimen, offers comparable patient survival with hemodialysis despite the lower weekly Kt/V, it was deduced that lower weekly Kt/V and therefore less total time on dialysis is adequate for daily hemodialysis. This is consistent with the good clinical results described by Buon cristiani [3] in the early 1980s in patients dialyzed with daily Kt/V of 0.23. Gotch [32] proposed the concept of the standard Kt/V (stdKt/V) to allow comparison of the different dialysis modalities. An stdKt/V of 2 per week (current level of adequacy) corresponds to single pool Kt/V (spKt/V) of 1.2 (or eKt/V of 1.05) delivered three times a week (3.5 h each) or a spKt/V of 0.53–0.56 (or eKt/V of 0.38) delivered six times a week in the form of short dialysis. A review of this and related concepts was published by Gotch [32, 33]. This concept assumes that all dialysis regimens having the same predialysis BUN have the same outcomes.

Casino and Lopez [34] described the concept of the equivalent renal urea clearance and used it for the comparison of the different modalities as well as native kidney function. The assumption was made that regimens with similar time average concentration (TAC) have similar outcomes. Following this concept, the amount of dialysis necessary for daily dialysis is higher than Gotch’s model predicts.

Clark et al. [35] using computer simulation found that relative to a standard three times weekly hemodialysis regimen, a daily/short-time regimen results in a 3–6% increase in effective small and middle molecule removal. They also found that a daily low-flow/long-time regimen

(low-flow nocturnal hemodialysis) substantially increases the effective removal of all solutes. The existence of the different approaches shows the difficulty when comparing the different regimens based on urea kinetics alone.

Beyond Urea Kinetics

The improvement in the condition of most of the patients after the conversion to daily hemodialysis is often impressive, more than one would predict from the increase in the dialysis dose, especially when it involves patients with small body size and already high Kt/V. Furthermore, there is doubt if outcomes improve with increasing Kt/V >1.4 [36, 37]. Another explanation for the improved results on daily hemodialysis is that the increased dialysis dose may improve the outcomes on daily hemodialysis more than on conventional hemodialysis or that the improvement is not related to the increase in the Kt/V but to other factors.

Effect of Dialysis Time

The importance of time on dialysis has been hotly debated. The difficulty lies in the fact that increased dialysis time increases the delivered Kt/V and therefore the effect of the two parameters is difficult to separate. The impressive results from the long dialysis practiced in Tassin [38] were ascribed to the long dialysis regimen. Interestingly, Kt/V did not correlate with patient survival in this group [39]. If time is the most important parameter, what can explain the improvement of patients on short daily hemodialysis? Early studies by Twardowski [40] suggested that frequency of dialysis is more important than time. Are then both time and frequency important? Do these methods have anything else in common?

Importance of 'Unphysiology': A Unifying Hypothesis?

The so-called 'unphysiology' of dialysis could be a significant cause of morbidity and often mortality. Frequently patients are rendered unconscious during hemodialysis and still these events are not taken into account in the evaluation of the dialysis modality. Despite some attempts to quantitate 'unphysiology', no correlation with outcomes exists. The best known parameter is the time average deviation (TAD) [41]. Unfortunately this value does not include time on dialysis and therefore the rate of change of the different parameters. The Tassin regimen, short daily hemodialysis and nocturnal hemodialysis, have as a common characteristic the decreased rate

of change in biochemical and hemodynamic parameters during dialysis. We hypothesize that the 'unphysiology' of dialysis could be as important as the dialysis dose, especially in the smaller patients with co-morbidities. Improvement of the outcomes could be achieved by increase in dialysis dose or decrease in 'unphysiology'. In the case of CAPD, improvement of outcomes will be achieved by providing higher dose of dialysis. This could be possibly achieved by the continuous flow peritoneal dialysis [42–44]. Hemodialysis outcomes can improve mainly by decreasing the 'unphysiology' of dialysis, while increasing the dialysis dose of the three times a week regimen may not be as effective. The larger patients are known to be better outcomes [45]. It is conceivable that the better outcome of this group is related to the lower level of 'unphysiology' relative to their size. Conversely, the poor outcomes of the small patients could be partially related to the higher level of 'unphysiology'.

Is Daily Hemodialysis a Complex Therapy?

When it comes to the notion that daily hemodialysis is complex, one can ask the obvious question: In whose eyes? Despite the perceived complexity, none of the 50 patients that we have trained in nocturnal hemodialysis in our center requested to switch to conventional hemodialysis. Some of the patients insist on receiving dialysis 7 nights a week and a few requested that their transplantation be put on hold. Similar is our experience with 13 patients on in-center short daily hemodialysis over 2 years. Home daily/nocturnal hemodialysis is not unduly complex since it is done happily by the patients at home, who visit the hospital only infrequently. In-center short daily hemodialysis is indeed more complex but the only result of the complexity is the increased expense. Is it then justified to fund daily hemodialysis with the current level of evidence?

Finances: The direct cost of daily dialysis is obviously higher than that of conventional hemodialysis when done in the center, but in the case of home hemodialysis, labor cost is decreased. In a multicenter retrospective analysis, Mohr et al. [46, 47] calculated yearly savings of about USD 6,400 by the in-center short daily hemodialysis and about USD 9,500 for home short daily and nocturnal hemodialysis. The main reason for the financial benefits of daily hemodialysis was the decreased hospitalization rates [7] as well as the lower cost of medications, mainly EPO, antihypertensives and phosphate binders in the case of nocturnal hemodialysis. The data need to be documented in a prospective fashion.

Are the Benefits Unproven?

Although there is little doubt about the significant improvement in the QOL of the patients on daily/nocturnal hemodialysis shown by both data and patient preference, we do not have sufficient data on patient mortality to this point. Woods et al. [8] have reported a very high survival rate of 93% over 2 years on short daily hemodialysis. Similarly, Mastrangelo et al. [48] have described high survival of 55% over 10 years on a four times a week regimen. It is important that prospective controlled studies be done to document the benefits of daily hemodialysis in the areas of patient survival, hospitalization rates and cost. On the other hand, the improvement in QOL and the rest of the parameters outlined above, as well the

strong endorsement by the patients would dictate that daily hemodialysis should be used as an alternative dialysis regimen. In the case of in-center hemodialysis, short daily dialysis should be offered. Preference should be given to the smaller size patients as well as patients with dialysis-related or cardiovascular symptoms. At home, both short daily hemodialysis and nocturnal hemodialysis should be offered with preference to nocturnal hemodialysis in view of its several added advantages, including phosphate control, free diet and better hemodynamic profile.

I will end on a philosophical note. Although not using critical scientific thinking in the practice of medicine is a mistake, ignoring the very obvious because of the lack of well-validated studies could be an even bigger mistake.

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