Hemodialysis at Home
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Short Daily Hemodialysis and Nocturnal Hemodialysis at Home: Practical Considerations

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ABSTRACT

There are currently over 350,000 patients in the United States on dialysis, with more than 90% receiving conventional in-center thrice-weekly hemodialysis (HD). Less than 1% of patients receiving HD are at home, and of these approximately 1500 patients receive more frequent and usually longer dialysis sessions. This article provides a historical perspective of HD at home, followed by practical considerations for short daily HD (SDHD) and long nocturnal HD, contrasting the strengths and limitations of these modalities. Finally, frequent and longer dialysis therapy is put forth as the best way to improve patient outcomes. It suggested that the optimal location in the present dialysis delivery system for more frequent and longer dialysis is in the home.

In the United States today, there are more than 350,000 patients on maintenance dialysis. More than 90% receive in-center hemodialysis (HD) thrice-weekly and < 1% are on conventional thrice-weekly home HD (1). In addition, there are approximately 1500 patients at home performing some form of SDHD, including home HD with the NxStage System One (NSO), and nocturnal daily HD (NDHD), at a frequency of five or more times per week. The annual mortality rate of prevalent patients on conventional thrice-weekly in-center HD has slowly declined from 22.5% in 1993 to 20.7% in 2004. However, HD patients continue to require on average two hospitalizations per patient per year. This figure has remained unchanged from 1993 to 2004 with the average number of hospital days improving only slightly from 16.3 to 14.4 days per patient-year (1).

The landmark HEMO study showed that no further improvement in mortality could be attained for standard vs. high dose conventional in-center thrice-weekly HD, suggesting major limitations of the therapy in its current delivery format (2). In 2006, the Kidney Disease Outcomes and Quality Initiative (K/DOQI) clinical practice guidelines on dialysis adequacy defined the minimal dialysis dose for conventional thrice-weekly HD as a single pool *Kt/V* (sp*Kt/V*) of 1.2, equivalent to a weekly standard *Kt/V* (std*Kt/V*) of 2.0 (3). The guidelines also suggested that for more frequent and longer dialysis, as there was no adequate information concerning the appropriate dose, the minimal requirement for such alternative therapies should be calculated based on a weekly std*Kt/V* of 2.0. It is also worth noting that although the K/DOQI clinical practice guidelines recommend that serum phosphate levels be maintained between 3.5 and 5.5 mg/dl, fewer than 50% of patients on in-center HD in the United States achieve this goal. This is due to the fact that phosphate removal by dialysis is markedly time-dependent secondary to its slow transfer from the intracellular to the vascular compartment (4).

Historical Trends in Home HD

The current standard of care, thrice-weekly HD, was established very early in the clinical development of maintenance HD, at a time of severe cost and resource restraints. At the time of inception of HD, there was no scientific rationale for settling on three treatments per week, except that early experience with stepwise increments in the frequency of treatment showed that it produced better results than dialysis once or twice per week (5). The frequency of dialysis was therefore incremental from one to three based on patient well-being, and once thrice-weekly became the norm there was little investigation of more frequent dialysis. By the time the United States Congress mandated Medicare reimbursement for dialysis for end-stage renal disease in 1972, thrice-weekly

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dialysis had become the accepted standard of care. At that time, there were 11,000 patients on dialysis, and 40% were doing home HD (6). It should also be noted that the early experience with thrice-weekly dialysis in the US was, by modern standards, of low-efficiency with long dialysis times (5)—more like the Tassin regimen of 8 hours three times per week (7) than current US practice.

In 1969, DePalma et al. (8) was the first to systematically explore "daily" dialysis. Patients dialyzing at home were switched from 8 to 10 hours three times a week to a regimen of 4–5 hours five times per week using the Ultra-flo 100 coil dialyzer (Travenol Laboratories, IL, USA). Again this was by current standards long, low-efficiency dialysis, with a urea clearance of just over 100 ml/minute. In this original description, 57% of the total urea and creatinine removal took place in the first 3 hours of a 7-hour low-efficiency dialysis session with either a coil or Kiil dialyzer. Therefore DePalma (8) concluded that, "a 2–3 hour five times a week coil dialysis might equal the results obtained with a Kiil dialyzer 4 hours three times a week."

The current format of SDHD was first reported by Bonomini et al. (9) in 1972. The treatment regimen consisted of 3–4 hours of dialysis five times per week, with the use of low blood flow rates (200 ml/minute) and cuprophane coil dialyzers with low urea clearance (100 ml/minute). This author demonstrated marked improvement in several clinical parameters including anemia, hypertension, heart failure, and osteodystrophy. It is noteworthy that these improvements were observed in patients who had transferred from thrice-weekly 10-hour treatments with the same dialyzers.

In 1994, Uldall in Canada initiated a program of frequent (6–7 treatments per week) nocturnal HD in the home (10). The 3-year experience with 13 patients was reported in 1997, demonstrating significant improvement in quality of life (QoL) measures, improved blood pressure control with fewer antihypertensive medications, better anemia control, and normalization of serum phosphorus level with no phosphate binder requirement (10).

These encouraging reports led a few centers around the world to develop programs with more frequent dialysis in the home, offering short daily and long nocturnal HD (11–15). In the US, the nephrology community, in response to the unacceptably high mortality rate of dialysis patients and the outcome of the HEMO study, has recently exhibited renewed interest in increasing HD frequency, with or without increasing treatment length.

Three types of more frequent and longer dialytic approaches being performed in the world today are SDHD, including SDHD with the NxStage System One Machine (NSO, NxStage, Lawrence, MA, USA) and NDHD. Table 1 defines the typical treatment parameters of conventional HD as compared to the three aforementioned therapies. Table 2 provides the urea weekly std*Kt/V* values for the various dialysis therapies (16).

TABLE 1. Typical treatment parameters for the various hemodialysis modalities

Treatment parameters	CHD	SDHD	SDHD with NSO	NDHD
Number of treatments/week	3	6	6	5–6
Treatment time (hours)	4	2–3	2–3.5	7–8
Shortest interdialytic period (hours)	44	21	20.5	17
Longest interdialytic period (hours)	68	45	44.5	41
Blood flow rate (ml/minute)	400	400	400	200
Dialysate flow rate (ml/minute)	500	800	130	300

CHD, conventional hemodialysis; SDHD, short daily hemodialysis; NSO, NxStage System One™; NDHD, nocturnal daily hemodialysis.

TABLE 2. Target weekly urea std *Kt/V* target values according to the various dialysis treatment regimens

Dialysis treatment regimen	Dialysis treatment frequency	Weekly urea std*Kt/V*
Peritoneal dialysis	Continuous	1.7–2.0
Conventional hemodialysis	Three times/week	2.1
	Four times/week	2.6–2.9
Short daily hemodialysis	Six times/week	2.7–3.2
Short daily hemodialysis with the NxStage System One™	Six times/week	2.1
Nocturnal hemodialysis	Six times/week	4.6–5.0

Reproduced from reference (16).

Short Daily HD

Most clinical experience with SDHD has been with the use of conventional machines, either in-center or in the home. It has generally been assumed that the results are equivalent, but there are no formal validation studies. The evidence that exists indicates that SDHD offers many benefits compared to thrice-weekly dialysis. A comprehensive review of studies of SDHD has recently been published (17). In general, the studies suffer from a small sample size and short follow-up period. In terms of study design, only one study was randomized (18), two short-term studies have crossover designs (19,20), and the remaining reports are single arm cohorts of patients switching from thrice-weekly dialysis to SDHD five or six times per week. While the limitations of the variable study designs must be recognized, it is also striking that improved clinical results are uniformly reported, particularly, blood pressure control, which is markedly improved in all studies. Some studies have found better control of serum phosphate level and reduced need for phosphate binders, but this is not a consistent finding. Similarly a reduction in the erythropoietin requirement is found in some but not all studies. QoL measures do not consistently improve by the usually administered instruments, and based on one of the authors' (JM) experience (and that of his patients), this might be due in part to limitations in the instruments rather than a true failure of improvement in QoL. The best objective measure as to whether QoL is improved is the choice that the overwhelming majority of patients make to continue therapy 5 or 6 days per week even though they are free to revert to thrice-weekly dialysis at any time.

Prescription of SDHD should follow the 2006 update of the K/DOQI guidelines of minimal requirement for

TABLE 3. Minimum single pool *Kt/V* per dialysis session required to achieve weekly standard *Kt/V* of 2.0

	T_d (hours)		
Number of treatments per week	2.0	3.5	8.0
K_r = 0 ml/minute/1.73 m^2			
2	–	–	3.00
3	–	1.22	1.06
4	0.87	0.77	0.68
5	0.64	0.57	0.51
6	0.51	0.45	0.40
7	0.42	0.38	0.34
K_r = 2 ml/minute/1.73 m^2			
2	–	1.93	1.68
3	0.94	0.85	0.77
4	0.62	0.56	0.52
5	0.46	0.42	0.39
6	0.37	0.34	0.31
7	0.31	0.28	0.26

T_d, treatment time; K_r, residual renal urea clearance.
Reproduced with permission from reference (3).

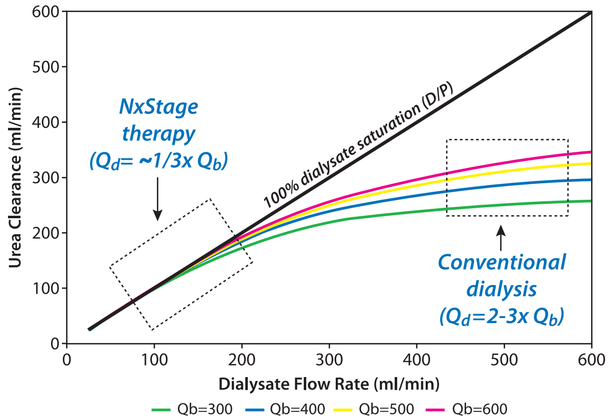

FIG. 1. Saturation of dialysate with urea and clearance of urea at different dialysate flow rates.

adequacy (Table 3) (3). The Daugirdas formula (21) should be used to calculate the daily *Kt/V*. As suggested in the K/DOQI guidelines, the minimum weekly standard *Kt/V* (22) should be 2.0. The standard *Kt/V* can easily be calculated (16). As with routine HD the prescribed and delivered dose must be tracked and adjusted according to the patient's symptoms.

Patients who transfer from conventional thrice-weekly dialysis to SDHD six times per week report a rapid improvement in well-being, with improved appetite and energy. The blood pressure improves within the first 2 weeks, and antihypertensive agents need to be monitored and reduced as required. Patients also universally report that they have a short or absent postdialysis recovery period. Finally, with the lack of travel time to an in-center dialysis facility, most patients readily accept the time commitment required for daily dialysis.

Home HD using the NSO Machine

The NSO is the only machine purpose-built for home HD on the market in the US, but is not yet available in other markets. As of March 2007, 1295 patients were dialyzing at home on this machine. The machine was designed to meet the desirable requirements for home: small size, portability, and ease of use. This machine will be described in some detail since it is novel and is operated differently from conventional machines.

Whereas in conventional machines, a high dialysate flow rate (Qd) of 500–800 ml/minute is utilized to maximize the transmembrane solute gradient, thereby maximizing solute removal (at the cost of using large amounts of dialysate), the NSO machine runs at a much lower dialysate flow rate of 100–150 ml/minute resulting in a solute concentration in, the dialysate approaching that of blood (depending on solute size). Blood flow rates (Qb) are kept at conventional levels (around 400 ml/minute) so that there is a 3:1 to 4:1 Qb:Qd ratio. The rationale for these changes is shown in Fig. 1. Typically, the dialysate is over 90% saturated with urea, so that urea clearance essentially equates with dialysate flow. As originally designed for the NSO machine, the ultrapure lactate-based dialysate was supplied in 5-l bags and patients would use 15–30 l/day, depending on body size. NxStage now supplies a device, the PureFlow, to generate a batch of 60 l of ultrapure lactate-based dialysate, which can be used for 72 hours; thus patients can use a dialysate batch over two or three treatments, depending on their daily volume requirement. The dialysate is used at the same volume and flow rate as when using dialysate bags. For patients who do not travel the PureFlow dialysate-generating device is easier to use than bags; bags can still be provided for travel.

Dialysis prescription with the NSO machine is simple. Fortunately, the 2006 K/DOQI guidelines of minimal requirement for adequacy (3) match-up with our empirical practice since first using the NSO machine in 2003. These guidelines state that for a given patient without residual renal function who is on a 6-day/week dialysis regimen, 3.5 hours of treatment time would be required to achieve a daily *Kt/V* of 0.45 (Table 3) (3). For the NSO machine, we define a simple initial prescription by calculating the total body water (equating it to the urea distribution volume, V) using the Watson formula and multiplying this volume by 0.4; since dialysate flow approximates urea clearance, the result provides the daily dialysate volume. Since the dialysate flow rate is set at 100 ml/minute, the dialysis time is also fixed.

For example, at one of the authors' home dialysis programs (JM), a patient weighing 99 kg with a calculated V (by the Watson formula) of 49 l was initiated on SDHD with a (49 × 0.4) 19.6-l dialysate volume; since the Qd is 100 ml/minute, the initial dialysis treatment time was 196 minutes. Consonant with the authors' experience, the delivered sp*Kt/V* calculated by the Daugirdas equation (21) is approximately 0.05 higher than the prescribed *Kt/V*, since the Watson formula overestimates the urea distribution volume (23). In this patient, the delivered sp*Kt/V* was 0.45, consistent with minimal adequate dialysis for a patient without residual function being dialyzed six times per week (3). Once a patient is stabilized on the starting dialysis prescription, the dialysate volume is adjusted upwards, if required, according to patient's needs. Currently, after 3.5 years on SDHD and prescription adjustments to alleviate symptoms of uremia, the aforementioned patient is using 25 l of dialysate 6 days/week, achieving a delivered sp*Kt/V* of 0.63.

Some dialysis centers, including one of the coauthors (JM), are exploring the use of the NSO machine for NDHD in the home. The current practice is to use a similar volume of fluid as in SDHD, with a slower dialysate flow rate to allow the patient to sleep for 7–8 hours. The use of the PureFlow device to provide larger volumes of dialysate that are closer to those used in conventional NDHD is an area for further investigation.

Nocturnal HD

Following the introduction of daily long nocturnal HD by Uldall and Pierratos et al. (10) in 1994, several centers around the world have established such programs (11–15). A typical patient on nocturnal dialysis runs 7–8 hours with a Qb of 200–300 ml/minute and a Qd of 200–300 ml/minute for five to seven nights per week depending on the sleep pattern and desires of the patient. Studies have consistently reported significant improvement in patients' well-being and ability to function. In addition, consistent observations include less fatigue and fewer uremic symptoms, including fewer or no episodes of headaches, nausea, vomiting, and hypotension during and immediately postdialysis, and most importantly, less psychosocial stress, with the patient often returning to full-time employment.

As recently summarized by Finkelstein et al. (24) in this miniseries on "Hemodialysis at Home," nocturnal HD improves QoL measures consistently. Using psychometric testing, NDHD also improves cognitive ability (25) and corrects sleep apnea (26). Serum phosphate level is most consistently controlled among patients who convert to NDHD, with liberalization of the diet and elimination of phosphate binders in most patients (10–13,15,27). NDHD also provides better blood pressure control with reduction of blood pressure medications; this is not related to a reduction in extracellular fluid volume (28). In patients on NDHD, there is a notable reduction in the left ventricular mass index and improvement in left ventricular function (28); total peripheral vascular resistance is decreased with endothelium-dependent vasodilatation restored (29). Some but not all studies have demonstrated a decrease in erythropoietin requirements among patients converting from thrice-weekly HD to NDHD (30,31). A review of erythropoietin utilization at the University of Virginia Lynchburg Dialysis Facility demonstrated that the dose is reduced from a weekly average of 16,094 units for patients on conventional HD, to a weekly average of 7608 units for those on NDHD (R.S. Lockridge, personal observation). Observational studies of patients on NDHD have also reported improved survival (32,33), reduction in hospitalizations (32,34), and health-care-related cost savings (34,35).

Concluding Remarks

Daily HD appears to be the optimal form of dialysis currently available, and has the potential to improve the vexing poor outcomes of patients currently receiving conventional in-center thrice-weekly HD. Where possible, this is best delivered in the home, for reasons of flexibility and cost. There are some notable differences between SDHD, including SDHD delivered with the NSO, and NDHD. The apparent cause for these differences is related to the amount of renal replacement delivered to the patient, which is based on the weekly frequency and length of treatment time.

In a traditional urea-centric approach, a dialysis regimen that delivers a weekly std*Kt/V* of 2.0 translates into a urea equivalent renal clearance (EKR) of 10–11 ml/minute (36). If one assumes that urea clearance is on average 50% of creatinine clearance, the glomerular filtration rate (GFR), which is the mean of creatinine and urea clearance, would be calculated at 15–17 ml/minute. Thus, according to the K/DOQI guidelines on classification of chronic kidney disease (37), a dialysis therapy delivering a weekly std*Kt/V* of 2.0 would maintain the patient without residual renal function in stage-5 chronic kidney disease (CKD). Based on these principles, one could argue that conventional in-center thrice-weekly HD provides enough renal replacement only to maintain patients in stage-5 CKD, while not providing continuous control of the extracellular fluid volume and serum phosphate level. SDHD with the NSO using 15–30 of lactate-based liters per treatment 6 days/week, and delivering a weekly std*Kt/V* of 2.0, provides a GFR of 15 to 17 ml/minute and maintains anuric patients in stage-5 CKD, but offers the clear advantage of volume control on a more continuous basis, while not optimizing phosphate clearance due to the short length of treatment. SDHD using a traditional dialysis machine and delivering a weekly std*Kt/V* of 2.75, provides a GFR of 19–22 ml/minute and maintains anuric patients in stage-4 CKD, but offers the clear advantage of volume control while not optimizing phosphate clearance. NDHD five or six times per week, has been shown to provide a weekly std*Kt/V* in excess of 4.0, which translates into a urea EKR of greater than 20 ml/minute (36). This level of delivered dialysis therapy is the equivalent to a GFR of 30 or greater, which would be consistent with regression from stage-5 to stage-3 CKD for anuric patients. In addition, NDHD provides the best volume and phosphate control.

When patients are offered the choice between SDHD, including SDHD with the NSO machine and NDHD in the home setting, the primary issues that influence decision-making are the patient and helper's comfort with the equipment, the issue of self-cannulation, the fear of inability to sleep while on dialysis, and of dialysis circuit disconnect during sleep. At one home HD program offering both modalities (JM), patients tend choose SDHD at home, particularly with the NSO, currently the only nonconventional dialysis machine available in the United States. This is driven in part by the ease-of-setup and take-down, equipment portability for perceived travel needs, and overall flexibility. Once patients have successfully and safely performed SDHD at home with the NSO, they are often willing to switch to NDHD with the same machine.

When offering only NDHD using conventional dialysis machines in the home setting, the concerns of the patient and helper can be overcome. At an experienced home HD program specializing exclusively in NDHD (RSL), these issues are addressed through intense training and proper coaching of the patient and helper during their initial experience at home. Use of the buttonhole technique in-center before starting training, use of catheters as vascular access with locking boxes to prevent disconnect, taping the fistula needles in place using the chevron method, covering the fistula needles with a netting and taping the bloodline, and fistula line connection have been successful methods in creating a safe experience for the patients dialyzing at night while they sleep. The complexity of the conventional dialysis machines and needle disconnection remain the most important clinical obstacles to adoption of NDHD by physicians and patients. If this particular safety issue is solved, and if a dialysis machine is able to deliver long slow runs of dialysis safely in the home setting, the authors believe that many more patients would accept and benefit from this optimal form of renal replacement therapy at home.

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