Nephrol Dial Transplant (1999) 14: 2835–2840

Nephrology
Dialysis
Transplantation

Dialysis and Transplantation News

Nocturnal home haemodialysis: an update on a 5-year experience

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Introduction

Nocturnal haemodialysis, done nightly at home was started by our group about five and a half years ago in an effort to provide a high-quality, low-cost haemodialysis devoid of all the major handicaps of in-centre haemodialysis done three times a week [1]. In this review, I will present our updated experience.

Background

Dialysis treatment for end-stage renal disease is characterized by high morbidity, mortality, low quality of life and high cost. Despite the recent encouraging trends (USRDS) in the US [2], patient mortality is still unacceptably high. The excellent long-term survival results reported by the Tassin group on patients haemodialysed for 8 h three times a week have been the yardstick of successful haemodialysis. Their success was ascribed to both increased length and quantity of dialysis [3]. The separate effect of these two parameters is difficult to decipher, but duration of dialysis seems to be a major factor at least in the excellent blood pressure control reported by the group [4]. Despite the long dialysis, phosphate control still required oral calcium supplements, salt and phosphate restriction were necessary and amyloidosis was not prevented [5].

Considerable experience has been collected with short daily haemodialysis mainly practised in Italy [6] and recently expanded elsewhere [7,8]. Buoncristiani has pioneered the method, which in its current form involves high intensity haemodialysis for about 2 h daily six times a week. Recently Woods *et al.* [9] reported a retrospective multi-centre analysis of the experience. Despite the unavoidable weakness of the design of the study, the survival rate was very high at about 80% over 5 years. Significant improvement in blood pressure control, decrease in erythropoietin (Epo) dose as well improvement in quality of life have been reported [10]. Short daily haemodialysis addressed issues related to the 'unphysiology' of the three times a week dialysis [11]. Despite the advantages, short daily dialysis does not achieve phosphate control and at the usual prescription may not be adequate for larger patients.

Rationale for nocturnal haemodialysis

Patients on conventional haemodialysis three times a week are plagued by significant symptoms and complications. Some of them are related to low dose of dialysis and others to the nature of the dialysis process itself. Dialysis related symptoms are linked to the rapid rate of change in the body's 'internal milieu'. Shorter and infrequent dialysis regimens are characterized by more significant symptoms. Therefore the ideal dialysis should provide high dose but also be frequent and long. In-centre haemodialysis is more expensive. Therefore haemodialysis should best be done at home. Long dialysis during the day is intrusive to patients' life. Therefore the ideal dialysis should be long, frequent, be done at home at night during sleep. This rationale was used to design nocturnal haemodialysis.

History

Nocturnal haemodialysis in its current form (nightly) was conceived by Dr Robert Uldall and the project was funded by the Ministry of Health of Ontario, Canada. The first patient was trained in April 1994. Dr Uldall died 1 year later in June 1995. The project was further funded to include 30 patients.

Technique description

Nocturnal haemodialysis involved long haemodialysis for the duration of sleep nightly, six or seven nights a week. A typical regimen was 8 h six nights a week. Obviously, the length of dialysis varied nightly. No partners were required. Blood flow varied from 180 to more than 400 ml/min. The relatively low blood flow of about 200 ml/min provided by a 'single needle system' was adequate to provide excellent clearance on nocturnal haemodialysis. Dialysate flow was originally kept low at 100 ml/min to minimize the probability for

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'overdialysis' and deficiency syndromes. Since no deficiency syndromes have been identified, the flow has been increased up to 800 ml/min to provide excellent dialysis in patients of large body size. Most patients use dialysate flow of 200 or 300 ml/min. We used polysulfone dialysers, initially Fresenius F40 and currently F50 to F80. The Fresenius 2008H machine was used for its ability to provide low dialysate flow. Furthermore, it became the machine for which we created software for 'live' remote monitoring. In view of the current use of higher dialysate flows and the fact that remote monitoring is optional, all dialysis machines can be used for nocturnal haemodialysis. Safety features include two inexpensive liquid sensors placed strategically under the dialyser and the dialysate areas to detect possible leaks of blood or dialysate.

Dialysate prescription

Sodium was set at 140 mmol/l in all but one patient, who gains up to 7 kg daily, in whom dialysate sodium of 147 ml/l was used to prevent dilutional hyponatraemia. No sodium ramping became necessary. Potassium concentration was kept at 2 mmol/l in all patients but one who is on 1.5 mmol/l. In view of the high K diet of these patients, Na/K resonium (Kayexalate®) has been provided to the patients at home in case they stay off dialysis for more than one consecutive night. Dialysate bicarbonate levels were lower than conventional haemodialysis usually at 32 mmol/l. Ultrafiltration ramping was not necessary but a small number of patients prefer to ultrafiltrate at high rates for the initial hour while still awake.

Eighty three percent of the patients needed addition of phosphate into the dialysate to maintain normal serum phosphate levels [12]. This was achieved through the addition of Na phosphate (Fleet enema®) into the 'acid' dialysate concentrate. The dose was continuously adjusted by the patient following our recommendations based on the monthly pre- and post-dialysis phosphate levels. Usual dose is 30 ml of liquid into a 4.2 l concentrate.

Initial dialysate calcium concentration was 1.25 mmol/l to which all patients added a variable dose of calcium chloride powder according to the pre- and post-dialysis serum concentration of calcium. We aimed for normal pre-dialysis and high post-dialysis levels of calcium. Most patients use calcium concentration of 1.75 mmol/l. The precipitation of calcium with phosphate in the acid concentrate is minimal due to the acidic environment.

Access

Initially, we used a central venous catheter as the dialysis access (Uldall–Cook) mainly for safety purposes, as it was assumed to be less prone to accidental disconnection. The InterLink connection system [1] was used to prevent air embolism and bleeding from the catheter. A locking box was added to prevent disconnection and bleeding from the blood tubing. There have been no incidences of disconnection or bleeding from the catheter/tubing connection. A significant advantage of nocturnal haemodialysis is that despite their occasional poor flow, central venous catheters provide excellent clearance in view of the long duration and high frequency of dialysis. Therefore they can be used as long-term accesses. One of the patients has been using the same venous catheter for 5.5 years without a single episode of infection or clotting.

We have started using AV fistulas for nocturnal haemodialysis for the last 10 months. The buttonhole technique has been used [13]. Instead of dialysis needles, plastic cannulas (16 or 17 gauge, $1\frac{1}{4}$ inch) have been used (Clampcath, Medikit, Tokyo). This particular cannula has a soft part, which could be clamped temporarily, allowing for an easy connection without the risk of bleeding. The cannulas were taped properly and the blood tubing was anchored to a Velcro® wristband. Ten out of the 30 current patients use an AV fistula access. Most patients have been able to insert the cannulas and start dialysis on their own. One patient uses a 'single needle system' thereby requiring smaller number of punctures.

Remote monitoring

We have been using the DAX software developed by Cybernius Medical (Edmonton, Alberta) with our collaboration, allowing 'live' remote monitoring of all functions of the Fresenius machine. An observer (previously unskilled individual, trained by the group) called the patients who were not awakened by machine alarms, by using a second telephone line. For the last 1.5 years, patients for whom long distance telephone charges would have been incurred have been connected using the Internet, thus establishing a similar 'live' connection. The number of the alarms has decreased from an average of 1.7 per night (usually in clusters) while using venous catheters, to about one per 10 nights in patients using an AV fistula access. Although the main function of the remote monitoring was to alert the patients of alarms, it has been also used to ensure compliance as well as for data collection. It is not expected that remote monitoring would prevent life threatening problems and therefore we consider its use as optional.

Dialyser reuse

In order to decrease the cost of nightly dialysis to levels similar to CAPD, we reused dialysers for an average of six times. The used and unprocessed dialysers were refrigerated by the patients and were exchanged weekly with reprocessed dialysers at the local outlet of a collaborating laboratory network. Dialyser reuse was practised for about 3 years.

Patients

We have successfully trained 37 patients. Three were transplanted, three died and one was removed for poor compliance. Thirty patients have been on nocturnal haemodialysis for up to 65 months as of September 1999 with 820 months of cumulative experience. Patient training was done while on conventional haemodialysis three times a week, although recently training was done while on daily haemodialysis. The length of training varied from 1 day for patients already on home haemodialysis to 6 or more weeks, especially for patients using new fistulas. Typical training lasted for 6 weeks. During the last week the patients performed nocturnal haemodialysis at night in the hospital. The patients were also taught how to take and centrifuge blood samples and infuse iron or antibiotics intravenously.

The patient selection criteria were not rigid. Any patient who could be trained for home haemodialysis, had no contraindication to systemic heparinization, had adequate space at home and spoke English (because of the need to communicate with the observers overnight) was eligible. Presence of co-morbidities was not a contraindication, neither was remote residence of the patient from the centre. A common question is which patients should be targeted for nocturnal haemodialysis at home. Although we believe that every patient would benefit from nocturnal haemodialysis, certain groups are more likely to opt for this modality. These are patients who are unlikely to be transplanted, patients with significant symptoms and co-morbidities, large patients who do not receive adequate dialysis and lastly patients who have not been on dialysis yet. The last group should be recruited during the pre-dialysis stage and be prepared for training as soon as they need dialysis. Adequate numbers of training nurses should be available so that there is no waiting time for training. Some of the patients who start on in-centre haemodialysis, because of improvement in some of their symptoms tend to become complacent and passive. Often they are unwilling to proceed with training for home haemodialysis.

Clearance (urea/phosphate/β_2 microglobulin)

Using dialysate collection, the measured urea Kt/V was about 1 per session or 6–7 per week when using dialysate flow of 100 ml/min. By increasing blood and dialysate flow Williams *et al.* [14] calculated a weekly Kt/V of above 12 akin to normal kidney function. Therefore, the ability of nocturnal haemodialysis to provide small molecule clearance is unparalleled. One of our recent patients with large body mass uses a blood flow of 400 ml/min and dialysate flow of 800 ml/min. His pre-dialysis serum creatinine dropped from about 1500 μmol/l on conventional to less than 500 μmol/l on nocturnal haemodialysis. Although we do not routinely calculate Kt/V values, since there is no specific goal, we arbitrarily aim for post-dialysis creatinine of less than 200 μmol/l.

Phosphate control has been uniformly excellent. Patients discontinue phosphate binders usually within 1 week of initiation of nocturnal haemodialysis. Despite the increase in phosphate intake, most of the patients need phosphate addition into the dialysate. No patient is hyperphosphataemic. Weekly phosphate removal is twice as high as on conventional haemodialysis [15].

β_2 microglobulin (β_2m) removal is four times as high as on conventional haemodialysis and long-term serum β_2m levels are lower than during conventional haemodialysis [16]. The increased β_2m removal corresponds to the fourfold increase in the weekly duration of haemodialysis.

Quality of life

All patients reported significant improvement in well-being and level of energy. The changes were apparent sometimes within days in significantly symptomatic patients. Within a month, at the first clinic appointment, the patients reported softer skin, improved appetite and in many there was a noticeable and at times impressive change in their complexion with disappearance of the uraemic look. Another impressive change was the haemodynamic stability with disappearance of hypotension episodes, cramping and shortness of breath. Return to conventional haemodialysis even for 1 week for holiday purposes has not been popular among the patients. One of the patient's unsolicited comments was: 'Conventional haemodialysis is like riding in a Volkswagen on a dirt road, while nocturnal haemodialysis is like riding in a Rolls on a freshly paved surface'. Quality of life questionnaires in the form of MOS SF-36, Sickness impact profile (SIP) and Beck depression index showed significant improvement of quality of life in several of the measured parameters [17]. There was improvement in vocational rehabilitation of the patients with most of the patients assuming full time employment. Even patients with frequent alarms declined offers to return to conventional haemodialysis. Five out of six patients who were temporarily switched to short daily dialysis were anxious to convert back to nocturnal haemodialysis. Seven patients elected to dialyse 7 nights a week either because they felt better or they wished to maintain their liberal fluid intake.

Sleep

Tolerance of dialysis during the night was much better than expected. Within one to two weeks almost all patients and their spouses adjusted well and the presence of the dialysis machines and the water purification systems did not seem to disturb their sleep. Sleep studies were done prior and several weeks or months after the conversion to nocturnal haemodialysis in

eight patients. Four out of eight patients were found to have sleep apnea and all improved on nocturnal haemodialysis [18]. Only one patient had difficulty sleeping due to significant number of alarms and was on nocturnal haemodialysis only four nights per week until her catheter was replaced. She currently uses an AV fistula.

Cognitive function

Psychological studies were done prior and after conversion to nocturnal haemodialysis on the same eight patients described above. These studies showed significant improvement in the cognitive function upon conversion to nocturnal haemodialysis [19].

BP control

Blood pressure control has been impressive on nocturnal haemodialysis. Most of the effect has been achieved by decrease in the 'dry weight'. This has been very well tolerated without significant symptoms. Very few of the patients needed antihypertensives. Out of the current 30 patients only six are on a small dose of a beta-blocker. Only in two of these patients the medications is given for hypertension control. Most patients come off most of their medications within one or two weeks on nocturnal haemodialysis even if they had been on multiple medications. We have observed the 'lag phenomenon' described by the Tassin group [20] in few patients who were able to stop their last antihypertensive medication only several months later. Blood pressure control worsened in several patients during stressful periods. Conversion of three patients to daily haemodialysis (3 h daily) because of haemorrhagic complications, resulted in poorer BP control and re-institution of antihypertensives, even though their dry weight was unchanged. BP control improved when nocturnal haemodialysis was re-instituted.

Epo use

No significant improvement in haemoglobin or decrease in Epo use was found during the first year of the study. Upon institution of intravenous iron administration there was a significant decrease in the Epo requirements by about 40%. It is difficult at this point to differentiate the effect of the intravenous iron from the effect of the method. It is interesting that in several cases of patients who were iron replete as a result of intravenous iron administration, there was a decrease in the iron indices accompanied by increase in haemoglobin upon conversion to nocturnal haemodialysis. All patients self-administer iron hydroxide-sucrose (Venofer®) on a regular basis usually every 2 weeks.

Calcium/phosphate control/bone disease

Addition of phosphate into the dialysate became necessary in most patients within the first one or two weeks of treatment. The dose of dialysate phosphate at times was increased higher than 1 mmol/l to normalize a low pre-dialysis phosphate. The obvious explanation was the presence of an anabolic state or active bone mineralization, which usually lasted for few weeks. Good control of phosphate allowed increase in the dialysate calcium safely. Parathyroid hormone (PTH) levels were suppressed variably, depending on the levels prior to the conversion to nocturnal haemodialysis. PTH levels as high as 200 pmol/l were suppressed to almost normal (8 pmol/l) at the expense of asymptomatic hypercalcemia post-haemodialysis. The rule we have followed was to increase dialysate concentration of calcium so that while the serum pre-dialysis calcium was normal, the post-dialysis calcium was usually in the hypercalcaemic range. This was especially important in patients in whom the volume of ultrafiltration was relatively high with unavoidable calcium loss into the ultrafiltrate. This issue is particularly important in nocturnal haemodialysis patients since they are on no oral calcium supplements. Indeed, in some patients dialysate calcium was raised to 2.25 mmol/l. The addition of calcium powder into the dialysate by the patients made the adjustments easy. The role of calcitriol in this population is unknown. In most patients we avoided calcitriol in order to maintain lower pre-dialysis calcium allowing positive calcium balance during dialysis when using high dialysate calcium. We found that this strategy was more effective in decreasing alkaline phosphatase. In most patients alkaline phosphatase increased initially on nocturnal haemodialysis. When we adopted the policy of maintaining a high dialysate calcium and added phosphate into the dialysate, alkaline phosphatase normalized in most patients. We have been following bone densitometry 6 monthly and the results have been useful in guiding the calcium/phosphate levels into the dialysate. Lack of patient compliance with the dialysate dose of calcium, led to increase in alkaline phosphatase. Long-term effect of nocturnal haemodialysis on bone density is not fully known yet and we have no information on bone histopathology. In view of the relative ease in suppressing moderately elevated PTH (5–10 times normal) it is likely that nocturnal haemodialysis can prevent or reverse renal osteodystrophy of at least moderate severity. At this point it is unclear if it can reverse every case of advanced tertiary hyperparathyroidism.

Nutrition

Diet is completely free on nocturnal haemodialysis. Patients are encouraged to maintain high phosphate and protein diet. Potassium intake was free but patients were encouraged to maintain relatively consistent K intake. Salt and water intake was unrestricted to the extent that one patient continues to gain up to 7 kg

daily. In this case high salt intake was also prescribed to decrease the magnitude of the resulting dilutional hyponatraemia. The most significant challenge was to convince the patients to increase protein, phosphate and dairy product intake since these products were significantly restricted before. Improved appetite as well as consultation with our dietician was useful in that respect. Amino acid losses were substantial on nocturnal haemodialysis in the range of 10–15 g per day. We quantitated serum amino acid levels. Both essential and non-essential serum amino acids increased on nocturnal haemodialysis [21]. Most patients were followed with total body nitrogen and potassium measurements using in vivo neutron activation analysis. We found that most patients were anabolic [22].

Complications

Most of the complications of nocturnal haemodialysis were related to the dialysis access. They included infections and catheter malfunctions. Systemic infections occurred at a frequency of one infection per 25 patient months and in most cases caused only minimal morbidity. There were three episodes of more severe systemic infection, one leading to myocardial abscess and death. The typical case included fever, usually at the beginning of dialysis at night, often associated with chills. Following our current protocol, the patients sampled blood for cultures through the dialysis catheter (culture bottles are kept at home) and self-administered one dose of vancomycin and tobramycin. Dialysis was not performed especially in the presence of chills. The antibiotic regimen was adjusted following the results of the cultures. Highly concentrated antibiotic solution was dwelled into the catheter for part of the day. If the infection recurred (usually 1 month later), antibiotics were restarted and the catheter was replaced over a guidewire. Unless there was a severe exit site infection the site was rarely lost. Only rarely did infections lead to hospital admissions. We believe that the use of the Interlink system has provided extra protection against infections although we have no hard data to support this assertion. Exit site infections were rare. Catheter malfunctions were related to poor placement, intraluminal clotting or fibrin sheath formation. We treated clotted catheters successfully with local urokinase or TPA instillation or systemic urokinase infusion. The patients were placed on low dose warfarin after the first episode of catheter malfunction. With each subsequent episode the dose of warfarin was raised slightly till there is no recurrence. Haemorrhagic complications included three GI bleeds and a subdural haematoma after a soccer game. Three patients had uterine bleeds aggravated by the treatment with warfarin. All the patients with bleeding complications were switched temporarily to heparin-free 3-h daily haemodialysis. Other complications, not seemingly related to the dialysis procedure, included one case of spinal osteomyelitis and one case of prosthetic hip staph aureus infection treated with intravenous antibiotics administered by the patient at home. The survival of the catheters in this population was significantly better than in the in-centre haemodialysis group [23].

Finances

The most expensive component of nocturnal haemodialysis is the disposable supplies. The personnel cost is significantly lower than in-centre haemodialysis. The improvement in the well being and the relatively infrequent encountered problems can allow the nurse to patient ratio to decrease to one per 30–50 or more patients. Depending on the patient selection criteria, some of these patients are expected to be on nocturnal haemodialysis for many years and therefore the initial cost of the dialysis machine and the training costs can be amortized over a longer period of time. The operating cost of nocturnal haemodialysis in Canada is similar to home peritoneal dialysis. The cost of nocturnal haemodialysis is lower than the cost of in-centre haemodialysis. Other financial advantages of nocturnal haemodialysis include the decreased dose of Epo, antihypertensives as well as the anticipated decreased rate of hospitalization. Improved vocational rehabilitation of the patients provides social financial benefits through increased productivity. The difference in cost between the in-centre and nocturnal haemodialysis may not be as significant in all countries depending on the cost of labour versus the cost of supplies and dialysis machines. Lastly, the system of the reimbursement of the expenses for the care of the patients can influence the attractiveness of nocturnal haemodialysis. A single payer system or a capitated environment where a single payer is responsible for all costs including hospitalization is the environment where the financial motives to adopt nocturnal haemodialysis would be the strongest.

What does the future hold?

There are two main factors that will affect the penetration of the different dialysis regimens especially in relationship to home haemodialysis: the system of reimbursement of the dialysis costs and the availability of simpler haemodialysis machines.

In countries where the direct cost of daily (or nightly) dialysis at home is higher than of in-centre haemodialysis (as in the US), several centres may opt for nocturnal haemodialysis either in-centre or at home, three times a week (the Tassin regimen) or every other night. If the direct cost of home daily (or nightly) dialysis is lower than of in-centre dialysis, as is the case in Canada, home dialysis mainly in the form of nocturnal haemodialysis may become the preferred choice in view of the added benefits, followed by daily short haemodialysis.

If (or when) frequent dialysis regimens are funded, many patients may opt for daily short haemodialysis as the preferred method for in-centre haemodialysis

followed by in-centre overnight haemodialysis on conventional or alternate day regimen. In terms of home haemodialysis, nightly nocturnal haemodialysis could be the most popular choice at home followed by short daily haemodialysis. Decisions regarding funding of the high frequency regimens will be based on the expectation or data showing lower overall cost of care for the dialysis patients or data from controlled studies showing decrease in morbidity and mortality. Such studies are urgently needed.

Beyond finances, the current lack of easy-to-use haemodialysis machines for the home haemodialysis patients is another significant disincentive for patients from dialysing at home. This is particularly true for short daily haemodialysis, since the current length of preparation for dialysis represents a significant part of the total length of dialysis.

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