# Nocturnal hemodialysis

#### D. Ranganathan, G. T. John

Department of Renal Medicine, Royal Brisbane and Women's Hospital, Herston, Queensland, Australia

## ABSTRACT

Patients receiving conventional hemodialysis have high hospitalisation rates, poor quality of life and survival compared to the general population. Many centres around the world are providing longer hours of hemodialysis - short daily hemodialysis and nocturnal hemodialysis - with a view to improving patient survival and quality of life. Studies have shown that nocturnal haemodiaysis is more effective than conventional hemodialysis in clearing most small, middle and larger molecule toxins and suggest nocturnal dialysis enhances patient survival and quality of life. Concerns include patient acceptance, vascular access related complications and increased cost. The purpose of this review is to examine the advantages and drawbacks of nocturnal dialysis, with a focus on applicability to India where the renal physician has to face cultural and economic barriers, erratic power supply and poor water quality.

Key words: Australia, India, nocturnal hemodialysis

# Introduction

End stage renal disease (ESRD) is a major health problem. Renal replacement therapy (RRT) places a considerable burden on health care resources. The survival and quality of life on dialysis have not improved commensurate with the technological advances. The reasons include patients' underlying illness, co-morbidities and the mode of delivery of RRT.

Conventional hemodialysis (CHD), though meeting targets of urea clearance, removes the uremic toxins suboptimally.<sup>[1]</sup> With the assumption that increasing hours on HD would improve the 'uremic milieu', many centres practise short daily dialysis or longer treatment at night the so-called "nocturnal hemodialysis (NHD)". This article will review whether nocturnal dialysis, either

#### Address for correspondence:

Dr. Dwarakanathan Ranganathan, Senior Consultant Nephrologist, Head, Home and Independent Dialysis Services, Royal Brisbane and Women's Hospital Herston, Queensland, Australia. E-mail: dwarakanathan\_ranganathan@health.qld.gov.au

Access this article online				
Quick Response Code:	147 - L - M -			
	Website:   www.indianjnephrol.org   DOI:   10.4103/0971-4065.103905			

in-centre (INHD) or at patients' home – nocturnal home hemodialysis (NHHD), significantly improves the 'uremic milieu', well-being and survival.

# **Conventional HD and its Drawbacks**

The 'uremic syndrome' is characterised by non-specific symptoms such as increasing tiredness, nausea, loss of appetite and or organ specific illness such as pericarditis or encephalopathy.<sup>[2]</sup> The pathophysiology of this syndrome is partly due to the retention of nitrogenous waste products from the underlying renal illness; further compounded by co-morbidities.<sup>[3,4]</sup> These patients are often unwell, find it difficult to carry out daily activities and will die without RRT.

The principle of dialysis was first described by Graham from Glasgow in 1854.<sup>[5]</sup> The modern era of dialysis began in 1960 when Wayne Quinton and Belding Scribner showed long term dialysis is possible, using an arterio-venous (AV) shunt.<sup>[6]</sup> HD has been provided to ESRD patients with the sole view of improving survival since then. In the 1960's HD sessions were long and impractical. In 1972 thrice weekly HD sessions were approved and launched in the United States of America (USA) which has become the bench mark for the subsequent programs.<sup>[7]</sup>

The National Cooperative Dialysis Study (NCDS), a land mark study<sup>[8]</sup> supported thrice weekly dialysis,

showing time –averaged urea concentration was the most important determinant of patient hospitalisation or withdrawal from the study. There was no correlation of longer time on dialysis with hospitalization rates, withdrawal from the study or death. Subsequently maintenance HD sessions were shortened with high flux, high efficiency haemodialysers to prolong patient survival with reduced costs and improved life-style.<sup>[9]</sup> Dialysis was delivered to achieve an adequate urea clearance (measured as equivalent Kt/V of 1.2).

The 'Hemodialysis' (HEMO) trial did not find any difference between high Kt/V (single pool Kt/V of 1.71) and standard dose of Kt/V. Also, the use of high flux membrane vs. low flux membrane dialyser did not alter the outcome.<sup>[10]</sup> However, patients using a high flux membrane could have a survival advantage if they were on dialysis for more than 3.6 years. This study suggested that increasing solute clearance during dialysis may not affect patient outcome. Further, the adequacy of dialysis measured by small solute-urea clearance was indeed less than 15% of clearance that is achieved by normal kidneys. Other factors such as cardiovascular (CV) complications, malnutrition and deranged calcium and phosphate metabolism play a significant role in patient outcomes.<sup>[11]</sup> It is difficult to maintain euvolemia with CHD resulting in high blood pressure (BP) and related complications including left ventricular hypertrophy. On the contrary the intermittent nature of CHD leads to hemodynamic instability due to excess fluid removal in a short duration. Post hoc analysis of the HEMO study revealed ultrafiltration rate in excess of 13 ml/hour/ kg was associated with an increased all cause and CV mortality.<sup>[12]</sup> The hypotensive episodes during HD induce repeated myocardial stunning resulting in an ischaemic myocardium.<sup>[13]</sup> It is therefore not surprising that in dialysis patients CV related mortality is over 40%.

# **Reasons to Look for Alternative HD Modalities**

The survival of patients on dialysis has not improved in the past two decades. The expected survival of a 55-year old who is on dialysis is five years and with a functioning allograft, 15 years<sup>[14]</sup> while an average American would live for another 26 years. It was presumed that increased mortality in dialysis patients was due to inadequate clearances of uremic toxins and poor volume control. Improved patient related outcome is seen in dialysis patients from Tassin, France where patients undergo longer HD sessions, eight hours in a day, thrice weekly.<sup>[15]</sup> Studies have shown that removal of toxins alone is insufficient for improving well-being of a dialysis patient; the procedure has to be well tolerated with the least hemodynamic disruption. Finally, dialysis must improve the hard end-points namely, quality of life and long-term survival. Australia New Zealand DATA on survival outcome of patients who were on HD from 1997-2006 showed longer hours on dialysis had a clear dose-response relationship with survival.<sup>[16]</sup> Recent DOPPS data shows longer treatment time on HD is associated with a survival benefit.<sup>[17]</sup> In view of better survival of patients on longer hours of HD, different modalities have been attempted by the dialysis community including frequent or nocturnal HD. This review focuses on nocturnal dialysis, its advantages and drawbacks.

# **Different Modalities of Dialysis**

CHD is usually performed three times a week. Quotidian dialysis is defined as dialysis that is performed daily or more than thrice weekly. Dialysis modalities can be classified as shown in Table 1.

## The prevalence of nocturnal hemodialysis

The practice of Nocturnal Hemodialysis (NHD) was reported even in the 1960s.<sup>[18]</sup> Subsequently there was a lack of interest until early 1990s when the Toronto nephrologists reported their success with NHHD.<sup>[19]</sup> In the late 1990s another group from Montreal reported, their experience with INHD.<sup>[20]</sup> All over the world, gradually interest has grown and now many HD programs offer NHHD or INHD. In 2004 the 'International Quotidian Dialysis Registry (IQDR) was formed with three Canadian and two US centres to study practices and outcomes associated with more intensive HD prescriptions (http:// www.quotidiandialysis.org/) and the first report showed that 70 were on NHD and 8 patients on short-daily HD.<sup>[21]</sup>

#### Table 1: Classification and characteristics of the various hemodialysis modalities

Modality	Sessions/ week	Duration/ session (hours)	Blood flow (ml/mt)	Dialysate flow (ml/mt)	Vascular access
Day time dialysis					
Conventional HD	3	3-5	300	500	Any
Long day time intermittent HD	3	6 - 9	300	500	Any
Short daily HD	6-7	1.5 - 3	400-500	500-800	Any
Nocturnal HD (NHD)					
In-center NHD (INHD)	3	8	300-400	500	Any
NHHD – 'Daily'	5-7	6 - 10	200 -350	200-300	Preferably AV fistula/graft
NHHD – 'Alternate days'	3	8	300	500	Preferably AV fistula/graft

This registry currently captures data from the dialysis registries of Australia-New Zealand, France, in addition to Canada and dialysis providers of USA. Still, it does not represent a widespread international participation. By March 2010, 2400, 327, 306 and 1175 patients, from Australia, Canada, France and US respectively were receiving short daily or nocturnal HD. The largest number of patients in the registry were from Australia and New Zealand and 68.3% of those patients were on NHHD. Majority (about two thirds) of Canadian patients were on NHD and 93.5% dialysed at home. In the US only 7.2% of patients were on NHHD.<sup>[22]</sup> There is no registry based information about dialysis of longer duration from Asia.

# Procedure

# Selection criteria

The patients should be motivated and able to self administer HD. In our centre a multidisciplinary team including a psychologist assesses the patients before accepting them for the nocturnal program. Serious comorbid conditions such as terminal cardiac failure (CF), diabetes mellitus with intractable coronary artery disease are not contraindications for NHHD or INHD. At our centre 11% of dialysis patients are on home HD and 20% of this group are in the NHHD program.<sup>[23]</sup>

# **Training and modality**

Patients are given training for four- six weeks in a dialysis centre before they can perform NHD independently at home. Training period is tailored to the individual's learning skills. Patients who are on self-care (day time home HD) can be transferred to NHD program earlier whereas an inexperienced patient will need a longer duration of training. If required, the partner or a family member can be trained to assist with the dialysis procedure but this is not essential. Electrical supply and water connections at patient's home may have to be modified to connect the dialysis equipment. There has to be sufficient space to accommodate the dialysis machine and the water treatment trolley.

# Equipment

Standard dialysis machines and dialysers can be used at home. Higher concentration of calcium is required in the dialysate and many patients on NHD require phosphate supplementation.

## Access

Central venous catheters, arterio-venous fistulas (AVF) and grafts have been used.<sup>[24]</sup> Many centres use single needle devices for NHHD. Both rope / step ladder and buttonhole techniques are used to puncture AVF. There are conflicting reports regarding the use of the buttonhole

infectious complications with buttonhole technique while Quinitaliani<sup>[26]</sup> *et al*, report no significant increase in adverse effects. In our centre, we predominantly use button-hole technique without major complications. Each centre has to choose the technique best suited to their patients.

technique. Van Eps et al,[25] report increased incidence of

# Safety alarms

A blood leak detector alarm [Figure 1] is taped around the AVF needles to detect blood leak. Moisture sensing device is placed under the machine, on the floor to detect blood or dialysate leaks. Commercially available clip –lock 'connector boxes' over central venous catheters can be used to prevent accidental disconnection and air embolism. 'Back slabs' can be used to protect and stabilise the AVF needles. Currently we do not use any of these devices excepting blood leak detector alarm. We generally avoid using central venous catheter for NHHD patients.

Some centres monitor their patients from remote locations 'live' either by internet or via telephone while their patients perform NHHD.<sup>[27]</sup> Our patients use a bedside telephone and have a nurse on call for troubleshooting. Generally patients are advised to terminate HD if they encountered problems at night and to contact the centre the following morning.

# Water treatment unit

The water treatment unit is dependant on the purity of the source water. At regular intervals water has to be tested to maintain the standards of quality as advocated by the Association for the Advancement of Medical Instrumentation.<sup>[28]</sup> The unit that we use in our NHD program contains a five micron particle filter, two carbon filters, one micron filter, reverse osmosis (RO) system and a Diasafe<sup>®</sup> filter (Fresenius Medical Care), all connected



Figure 1: 'Blood leak detector': 'Enuresis pad' between cannulas to detect blood leak. DRI-Sleeper(TM) [flexible], Alpha Consultants, Nelson, New Zealand (http://www.dri-sleeper.com/)

in series. Water is filtered first by the 5 micron filters and then passed through carbon filters, one micron filter, RO system [Figure 2] and finally through the Diasafe® connected at the back of the HD machine. The five micron filter eliminates dirt from the water before going through the carbon filters while the one micron filter removes finer material and bacteria before the water enters the RO unit. Water filters have to be changed monthly. The aim is to keep the slit density index (SDI) to less than five as most RO membrane manufactures recommend that feed water SDI should not exceed a value of 5.0 (http://www. reverseosmosischemicals.com). Carbon filter gets rid of excess chloramines, some pesticides and plant particles but it needs to be backwashed monthly and changed annually. The RO system removes pyrogens, bacteria, excess salts such as sodium and aluminium and Diasafe, endotoxins.

Water testing is done every three months. Chlorine and chloramine are tested before and after the carbon filter; bacterial counts at the RO unit and at the venous port of the dialysis machine; endotoxin assay is performed from the water at the venous port while the tests for heavy metals and trace elements is done from the inlet supply and the post RO water source.

## Advantages of nocturnal hemodialysis

#### **Small solute clearance**

Small solute clearance in CHD is traditionally measured by a urea kinetic modelling-'Kt/V'. This modelling measures the urea clearance with an assumption that urea is generated at a constant rate. In nocturnal HD the urea generation rate at night time is shown to be lower than the day time.<sup>[29]</sup> Further the urea falls significantly by about 75% in first two hours of HD and then on falls slowly through the rest of the treatment. This implies that although NHD sessions are longer, they may not have an advantage in urea clearance compared to CHD. Therefore the method to measure urea clearance is not optimised and validated in nocturnal HD. However many studies have shown that NHD significantly improves small solute clearance (measured as percentage reduction in urea (PRU) or equilibrated Kt/V (eKt/V)). A single centre study from Toronto has shown that PRU increased from 74 to 89% when they converted 39 patients from conventional HD to INHD (P < 0.001).<sup>[30]</sup> A multicentre study has compared single session eKt/V of 655 INHD patients to matched 15,334 conventional HD patients. The single session eKt/V of conventional HD patients was  $1.46 \pm 0.32$ whereas that of nocturnal HD group was  $2.21 \pm 0.56$ .<sup>[31]</sup> Lindsay et al. from Ontario, Canada has demonstrated that a group of NHHD patients who received nocturnal HD -six sessions in a week, had weekly e Kt/V 8.11  $\pm$  0.46



Figure 2: Water treatment equipment

compared to  $4.26 \pm 0.17$  in the conventional group (*P* < 0.001).<sup>[32]</sup> These studies highlight that nocturnal HD, either INHD or NHHD improves small solute clearance. However, the ideal measurement of small solute clearance in NHD is yet to be established.

#### Middle and large molecule clearance

The diffusive clearance of middle and large molecules depends on the duration of dialysis as there is a gradient maintained between the vascular and dialysate compartments for these substances. It is therefore expected that NHHD and INHD are effective in removing larger molecules in addition to a better clearance of small molecules. Studies have suggested that a longer duration of HD results in a greater clearance of  $\beta_2$  microglobulin.<sup>[33]</sup> Advanced Glycated End products and homocysteine levels decrease with nocturnal dialysis compared to conventional dialysis.<sup>[34]</sup> The effect of INHD or NHHD on the removal of highly protein bound substances such as hippuric acid, indoxyl sulphate, indole 3 acetic acid, methyl guanidine and guanadino-succinic acid, 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid has not been examined in depth.

Middle molecules can be better removed by using a convective technique using high flux membranes without extending the duration on dialysis. Hemodiafiltration (HDF) combines high flux HD with ultrafiltration of large amounts of plasma water, needing near-equivalent volumes replaced with an appropriately constituted fluid. In 'Online HDF' (OL-HDF), the substitution fluid is generated online that is safe, free of pyrogens and toxins. This therapy is well tolerated but there is no survival benefit.<sup>[35]</sup> A recent study has shown OL-HDF on alternate nights is better compared with 4-5 hr thrice weekly OL-HDF in improving the dialysis dose, BP, nutrition and occupational rehabilitation.<sup>[36]</sup>

## Calcium, phosphorous and PTH

Studies have consistently shown improved phosphate control in patients on IHND or NHHD. A randomised controlled trial has shown NHHD group had significantly more decrease of phosphate compared to CHD patients, despite the marked reduction in the use of phosphate binders in NHD group.<sup>[37]</sup> Further, many patients require the addition of phosphate into the dialysate concentrate commonly as sodium phosphate.<sup>[38]</sup> Low bone turn over is demonstrated in bone biopsies of NHD patients. Dialysate calcium has to be kept at a higher level to minimise the decline of bone mineral density.<sup>[39]</sup> High dialysate calcium is prescribed to reduce PTH levels in NHD although this is not a proven strategy.<sup>[37,39]</sup>

## Haematological effects

NHHD patients self-administer erythropoietin and intravenous iron during dialysis. The majority report either an increase in haemoglobin or a decreased requirement of erythropoietin.<sup>[40]</sup> There is an increase in the number of early-outgrowth endothelial progenitor like hematopoietic cells in nocturnal dialysis.<sup>[41]</sup> In contrast, a recent report has failed to show improvement of haemoglobin in NHD patients.<sup>[42]</sup> The inconsistent results with treatment of anaemia may be due to diverse populations and varied targets for iron replenishment.

## **Cardiovascular effects**

Many studies have evaluated various CV changes in patients undergoing NHD. This includes BP and volume control, and reduction in left ventricular mass (LVM). The studies with patients undergoing NHD have shown that there is good BP control with minimal requirement of antihypertensive drugs.<sup>[42,43]</sup> The BP control in NHD patients depends on other factors in addition to volume control. Nesrallah et al, showed improved control of BP in their groups of 11 patients on SDHD and 12 patients on NHD but the reduction in extracellular fluid volume was mainly seen in SDHD group only.[44] In NHD patients reduced levels of catecholamines and endothelium dependant peripheral vasodilation play a role in BP control.<sup>[45,46]</sup> In NHD patients studies have shown not only improved BP control, but also better LV function. Culleton from Alberta was the first to conduct a randomised trial to study the effects of NHD on LVM. This randomised controlled trial comparing 26 NHHD patients to 25 CHD patients found regression of LVH.<sup>[42]</sup> He demonstrated a reduction in LVM in NHD group when compared to CHD group (reduction in LVM 13.8  $\pm$  23.8 g vs. increase in LVM in CHD group  $1.5 \pm 24.0$ g; *P* 0.004). The limitations of this trial were a small sample size and a short follow up period of six months only. In patients on NHD who had cardiac failure improved LV ejection fraction was demonstrated.<sup>[47]</sup> Frequent Hemodialysis

Network (FHN) trial on daily in-centre HD has shown significant reduction in LVM as measured by magnetic resonance imaging.<sup>[48]</sup> In this study 125 and 120 patients were randomised to undergo intermittent HD 6 times per week and CHD (three times per week) respectively. At the same time the 'Frequent Hemodialysis Nocturnal Network (FHNN) trial' did not demonstrate significant reduction in LVM in NHD patients having randomised 45 patients to the nocturnal arm and 42 to the conventional arm.<sup>[49]</sup> The reasons for different outcomes in these studies are multifactorial as discussed below.

## Nutrition

NHD improves appetite and eliminates the need of dietary restrictions. NHD increases intake of protein, as measured by normalised protein catabolic rate and dietary intake.<sup>[50]</sup> Total body nitrogen improves in NHD patients even though there is loss of amino acids into the dialysate.<sup>[51]</sup> It also improves intake of other nutrients such as lipids, phosphorous with preservation of calcium, phosphorous and potassium levels in blood.<sup>[52]</sup> Nevertheless, despite improved nutrition, overall survival is yet to be demonstrated.

#### **Sleep disturbances**

Sleep disturbance in ESRD patients is considered as one of the indicators of suboptimal dialysis.<sup>[53]</sup> Sleep disorders such as sleep apnoea, restless legs while asleep and daytime sleepiness predict mortality in HD patients.<sup>[54]</sup> It has been shown that NHD improves sleep apnoea though it may not improve day time sleepiness or periodic limb movements. It is hypothesised that the cross sectional luminal area of pharynx increases when patients are shifted from CHD to NHD, reducing sleep apnoea.<sup>[55]</sup> Sleep disorders in NHD patients need further study.

## **Endocrine and reproductive functions**

Fertility is adversely affected in patients with ESRD and does not improve with CHD. Nocturnal HD improves fertility and reduces foetal and maternal complications.<sup>[56]</sup> NHHD reduces prolactin levels and may help re-establish regular menstrual periods in women and improves testosterone levels in males.<sup>[57]</sup>

## **Quality of life**

The results on assessment of Quality of life (QOL) measurements in NHD are conflicting. Many studies have demonstrated improved QOL measures.<sup>[30,32,58]</sup> The Toronto group demonstrated that IHND patients had improved overall QOL score.<sup>[30]</sup> Fresenius group showed no improvement in mental component of SF-36 score but showed better physical component of SF-36 score in INHD patients.<sup>[32]</sup> QOL score of patients on NHHD also observed to be better than the patients receiving CHD.<sup>[58]</sup>

A recent study did not show improved QOL score in NHD patients.<sup>[59]</sup> However IHND and NHHD are better than CHD in improving overall QOL in particular with the poorly performing CHD patients.<sup>[4]</sup>

# Hospitalisation

Hospitalisation rates are lower in patients on NHD. A casecontrol study from North America compared 655 patients who were on thrice-weekly INHD with 15334 CHD patients from the same geographic area. IHND patients were reported to have fewer annual hospitalisation rates (48 vs. 59%). They had fewer normalized hospitalization events at 1.26 vs. 1.74 hospitalization events per patient-year, and a lower normalized rate of 9.6 vs. 13.5 hospital days per patient-year (P < 0.0001).<sup>[60]</sup> Studies in NHHD patients also have demonstrated decreased hospitalisation rates.<sup>[61]</sup>

# Survival

Survival benefit is considered as the most important outcome of dialysis therapy. A number of reports on nocturnal dialysis have addressed this issue. A study from Canada, 'CAN-Sleep' involving 247 patients did not find a significant relationship between frequency of dialysis and mortality.<sup>[61]</sup> A group from USA analysed the data from United States Renal Data System (USRDS) in both NHD and CHD patients. They found the mortality rate in 94 NHD patients was a third of that in 940 CHD patients. (P = 0.0001).<sup>[62]</sup> Another group of investigators compared survival of 171 NHD patients who were on NHD from 1994 to 2006, to 1062 living and 1062 deceased donor transplants. This data derived from USRDS revealed that the survival of NHD patients is comparable to deceased donor transplant (hazard ratio 0.87, 95% CI 0.50-1.51, P = 0.61) though not as good as living donor transplants (hazard ratio 0.51, 95% CI 0.28-0.91, P 0.02).<sup>[63]</sup> Three randomised controlled trials, Alberta Study, FHN and FHNN trial were designed to determine the beneficial changes of LVM associated with longer hours on dialysis.<sup>[42,48,49]</sup> The FHN trial demonstrated that frequent daily dialysis improved coprimary outcomes (hazard ratio for death or increase in LVM, 0.61; 95% confidence interval (CI, 0.46 to 0.82). [48] The FHNN trial did not show any survival advantage or decrease in LVM with NHD compared to CHD.<sup>[49]</sup> The nocturnal group received 1.82-fold higher mean weekly standard Kt/V urea compared to conventional group. Further, this study failed to show improvement in many of the secondary outcomes including markers of nutrition, hospitalisation rate, haemoglobin, physical health composite score and self-reported depression. The study showed only improvement in control of BP and phosphate. There are certain issues involved in the design and methodology of FHNN study.<sup>[64,65]</sup> This study has detected (mean) 10.9g (CI -23.7 + 1.8) reduction in LVM. The reduction in LVM in this study is similar to the observations found in the study done by Alberta study though it was not statistically significant. Further there were baseline differences between these two studies: patients were younger, longer on dialysis and LV mass of conventional group is  $137.1 \pm 45.7$ g in FHNN study compared to relatively older and baseline LV mass of  $181.5 \pm 92.3$ g in the CHD arm of Alberta study. These findings suggest the patients of Alberta study have chronic disease of the heart and thereby benefit shown with NHD. Further FHNN study is underpowered as they could randomise only 87 patients though the target was 250 patients. Secondly, the time on dialysis is not significantly different between the patients in the two arms. Patients in the CHD arm received an average of 256 minutes of HD per session, about 45 minutes more than the US HD patient whereas the patients in NHD group received about less than 10 hrs of HD per week than the standard NHD patients. In the nocturnal group only about three fourths of the patients could complete the prescribed dialysis time. The next question is why FHNN did not demonstrate the improvement in LVM or survival benefit when daily FHN study showed benefits in both co-primary outcomes. The daily FHN trial had more power to detect the difference as the number of participants recruited into this study was three-fold that of FHNN study. The FHN trial though did not show a significant reduction in LVM but there was still a possibility of a large treatment effect. This is shown by a 19 gm reduction in LVM with a 95% confidence interval. One cannot therefore conclude that frequent nocturnal HD is inferior to frequent daily in-centre HD.[66] It is important to point out that no study has assessed the impact of NHD on CV mortality.

# **Cost Effectiveness**

Cost estimates in dialysis involve actual (dialysis equipment, dialysate, dialyser, water, water treatment unit, electricity, medication) and hidden expenses. Hidden expenses include wages of the multidisciplinary team, cost of training and follow up, hospitalisation, establishment and maintenance of the dialysis centre. The cost difference depends on the site of dialysis – home vs. in-centre and or nocturnal vs. conventional. If a patient is undergoing HD at home and in particular longer hours on dialysis, the cost on infrastructure and labour may be avoided but the cost may increase due to training, requirement of one HD machine per patient and extra- supplies. However studies from Australia and Canada have shown the cost involved with IHND or NHHD is less than CHD.<sup>[67,68]</sup>

# **Barriers**

The main roadblocks to NNHD are either with dialysis providers' attitude toward funding or patients' perceptions regarding the difficulties of the procedure. Service providers may be reluctant to pay for escalating direct costs of longer and daily HD. Further, the lack of training and experience with instructing patients to perform HD at home could impede the program. Patients are hesitant to adopt the nocturnal program due to lack of motivation, missing the comfort of in-centre dialysis, fear of self-cannulation, poor confidence and family support, inadequate home facilities or water supply, increasing electricity and water bill and fear of adverse consequences.<sup>[69]</sup> The advent of patient friendly HD machines would attract both the patients and the training staff to expand this program.

# Future

The main drawbacks of NHD are the barriers listed above and also a trend towards increasing vascular access related problems.<sup>[21,49,69]</sup> However nearly 44% of the vascular access related complications observed in FHNN study occurred in patients who used CV catheters, which are generally not encouraged by NHD centres.<sup>[49]</sup> The FHNN study showed improved BP and phosphate control in the nocturnal arm though it did not show survival benefit due to multiple factors as discussed before. In addition the Alberta study and many observational studies have shown improvement in many clinical parameters with INHD or NHHD as discussed earlier. A Clinical Trial of IntensiVE (ACTIVE) study, currently in progress may shed more light on QOL with longer hours on HD. Randomised controlled studies have to be conducted comparing OL-HDF and CHD and NHD. It would be difficult to perform OL-HDF at home due to complex nature of the HDF machine. In future, NHD machines have to be compact, portable and needing fewer consumables, allowing patients to travel for work or leisure with their machines. In the meantime one should continue to support the NHD program but with careful selection of motivated patients.

# **Our Experience**

Our unit advocates the policy of 'First Home Therapyeither PD or home hemodialysis (HHD)'. The patients opting to HHD are identified and educated on HHD even before they enter the dialysis program. All our patients who enter NHHD were initially trained on HHD for four to six weeks and perform HHD for few months. Then patients who opt to undergo NHHD perform three sessions of nocturnal dialysis using Fresenius 4008 B machines in the training centre programmed with target 'dialysis parameters' as shown in Table 1. Our patients use the dialysate as shown in Table 2 and for an eight hours session of NHHD, a five litre of Part A concentrate and 950g of Bibag (Part B –Bicarbonate concentrate) are required. The dialysate flow is reduced to 300 ml/minute and therefore five litres of Part A concentrate is sufficient to complete eight hours of HD. In an alternate day protocol of 8 hours NHHD, the dialysate is run at 500ml/minute. The patient has to change the container or decant  $2 \times 5$  litres of concentrate into a 10 litre jerry can, late into the night.

Of the 17 patients on NHHD, six patients subsequently underwent deceased donor transplantation. Currently six patients continue on NHHD and one of them has been on NHHD for the past 75 months. Two patients who trained in our program then transferred to a neighbouring district. In our 400 patient months of experience on NHHD, we came across only one blood leak from accidental disconnection of AV fistula needle. Two patients had infection related to vascular access and one improved with antibiotics. The second patient had infective endocarditis following access infection, had to undergo mitral valve replacement and is on in-centre HD. One patient had a thrombosed fistula due to high haemoglobin, and was transferred to PD. Another patient died of bronchiectasis.

# **Applicability to India**

Is it possible to expand the NHD program for dialysis patients in India? In 1963 one of the patients trained by Dr. Scribner returned home to Chennai and became the first to be on home HD in the country.<sup>[70]</sup> However home HD programs are not popular in India and currently few centres offer home and nocturnal dialysis. (http://news. indiamart.com/story/nephroplus-brings-out 'nocturnal-dialysis'working-patients-160921.html). There is no registry or published data on NHD from India. A program aiming to start NHD in India has to address issues such as cultural barriers, water quality and erratic electrical power supply. One of the major problems is the quality

Table 2: Comparison of 'dialysate' used in CHD vs. NHD	
at Royal Brisbane and Women's Hospital <sup>[22]</sup>	

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	CHD	NHD	
Sodium (mEq/L)	135-140	140	
Potassium (mEq/L)	1.5-3	2-3	
Calcium (mg/dl)	5-6	6-7	
Bicarbonate (mEq/L)	35-40	28-32	
Phosphate	-	Supplement (Fleet Enema) is usually required for NHD 5-7 nights/ week. Add 5 ml into the dialysate concentrate and titrate up depending on phosphate levels	
Supplement of Phospha	te <sup>.</sup> Fleet en	ema® C. B. Eleet: Each 118 ml. contains	

Supplement of Phosphate: Fleet enema® C. B. Fleet: Each 118 mL contains sodium phosphate monobasic 19g and sodium phosphate dibasic 7g; each mL contains 1.86 mg/dl of phosphate and 4 meq/l of sodium

#### Table 3: Road Map to NHD

Item	Action required	Comments	
Convince the fund providers	A business case has to be provided; highlight the advantages of NHD; cost efficient.	3 months.	
Establish a multidisciplinary training unit –Nephrologist, Dialysis Nurse and Technician; include psychologist, medical social worker and a dietician.	Liaise with centres that have experience with NHD program. Send these personnel to the collaborating centre/s to observe NHD training program.	Training for 4 weeks if feasible.	
Identify suitable patients	Multidisciplinary team has to identify suitable patients.	First few patients have to be 'the best patients' from the conventional program or preferably from HHD program.	
Assess suitability and modify the patient's home	Identify a bed room and make modifications for water connection and electrical supply if required.	4 weeks.	
Training	Train to perform NHD with 'User-friendly' dialysis machines; e.g. Fresenius 2008 B or Gambro AK20 using all safety precautions.	4 -6 weeks.	
Follow up	Review of Blood Tests (Renal, Liver functions, Full Blood Count, Kt/V) and modify the medications accordingly. Adjust the dry weight.	Once a month.	
	Review by the nurse and nephrologist; review by allied health if and when required	Once every 2 months.	
	Home visit by the nurse.	Once every three months.	

of feed water, in particular during monsoon. Water filters may have to be changed fortnightly or even weekly instead of monthly. Continuous power supply with a stable voltage in sine wave is essential. An online UPS with sufficient capacity to run the dialysis machine with a backup for at least 30 mins is recommended. The use of surge protectors is necessary to protect electronics of the dialysis machine. (http:/: www.isn-india.com/ images/Image/HD standards Draft.pdf.). A generator with a capacity of two KW/hour is recommended as the electrical requirement for an hour of hemodialysis is 1.5 KW. Dialysis care provider has to brief the patient on HHD regarding the electrical safety requirements and the risks of use of other equipment in the area. If these concerns are attended to, NHD can be offered to selected patients with a favourable cost-benefit ratio. Table 3 provides a suggested roadmap for starting NHD services.

# Acknowledgment

Jock Howes, Anne Salisbury, Sally Goodwin, Rebecca Russo and all nursing staff, Home HD Program, Department of Renal Medicine, Royal Brisbane and Women's Hospital.

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How to cite this article: Ranganathan D, John GT. Nocturnal hemodialysis. Indian J Nephrol 2012;22:323-32. Source of Support: Nil, Conflict of Interest: None declared.

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