Nocturnal haemodialysis in Australia and New Zealand

JOHN WM AGAR

Renal Unit, The Geelong Hospital, Barwon Health, Geelong, Victoria, Australia

SUMMARY: Although early experience in Australia and New Zealand confirmed home haemodialysis to be well tolerated, effective and with lower morbidity and mortality compared with centre-based haemodialysis, the advent of ambulatory peritoneal dialysis and 'satellite' haemodialysis has led to a steadily declining home haemodialysis population. However, the emergence of nocturnal haemodialysis, as a safe and highly effective therapy, has added to the modality choices now available and offers a new, highly attractive home-based option with many advantages over centre-based dialysis. For the patient, nocturnal haemodialysis means fluid and dietary freedom, less antihypertensive medication, the abolition of phosphate binders, the return of daytime freedom and the capacity for full-time employment. Potential biochemical benefits include normalization of the blood urea, serum creatinine, albumin, \( \beta_2 \) microglobulin, homocysteine and triglyceride levels and other nutritional markers. Improved quality of life and sleep patterns and a resolution of sleep apnoea have been shown. Left ventricular function has also shown marked improvement. For the provider, nocturnal home haemodialysis offers clear cost advantages by avoiding high-cost nursing and infrastructure expenditure. Although consumable and equipment costs are higher, the savings on wage and infrastructure far outweigh this added expenditure. These combined factors make nocturnal haemodialysis an irresistible addition to comprehensive dialysis services, both from a clinical outcome and fiscal perspective.

KEY WORDS: Australia, haemodialysis, home, New Zealand, nocturnal, review.

INTRODUCTION

In Australia and New Zealand, home dialysis has always been an integral part of the dialysis landscape – whether haemodialysis or peritoneal dialysis. This has largely been due to the geographical isolation of many regional dialysis patients and the unique urbanization of the majority of the population into a handful of seaboard cities, leaving in Australia in particular, a vast tract of sparsely populated inland without well-developed dialysis services. Historically, home haemodialysis (HHD) programmes were first developed concurrently during the mid 1960s by Blagg et al.\(^1\) in Seattle, by Merrill and coworkers in Boston\(^2\) and by Shaldon\(^3\) in the United Kingdom. So successful were these early attempts at HHD that the practice rapidly spread, including to Australia and New Zealand. In New Zealand, HHD was embraced particularly in the South Island where HHD programs remain the primary haemodialysis modality to this day. By the late 1960s, many patients had been established at home on Kiil dialysers while centralized training programs had been set up in most Australian states. Indeed, at this time, HHD patients outnumbered in-centre haemodialysis (icHD) patients.

The preference for and training of patients for HHD continued strongly through the 1970s such that by 1979, still 49% of all dialysis patients were based at home.\(^4\) These were predominantly HHD, as at that time only a handful of peritoneal dialysis patients had appeared. In 1979, 51% of all patients were dialysing in-centre (Fig. 1). The future for HHD at the end of the 1970s seemed assured and strong.

THE DECLINE OF HOME HAEMODIALYSIS

Two concurrent developments at the end of the 1970s had a rapid and lasting impact on home therapy and the distribution of home-based modalities. First, the advent of continuous ambulatory peritoneal dialysis (CAPD) in 1978 and its subsequent rapid uptake by both countries as it replaced the less successful, high cost, in-centre inter-
mittent peritoneal dialysis (IPD), led to an overall rise in the percentage of home-based patients on both modalities. This rise in the popularity of CAPD clearly occurred at the expense of HHD where it seemed the ‘eye was off the ball’.

Concurrently, as equipment availability, simplicity and reliability increased and the price per unit costs decreased, it became clear that many patients previously dialysing in-centre could quite safely dialyse in self- or limited-care facilities located in community-based centres distant from and without direct on-site medical supervision. The term ‘satellite haemodialysis’ (SHD) was coined to encompass such centres and rapidly developed throughout suburban metropolitan Australia. Broadly, New Zealand retained CAPD as the preferred therapy and did not fully embrace SHD until the 1990s (Fig. 2). The trends in home-based and satellite dialysis shown in Fig. 2 depict the interrelationships between HHD, SHD and all-modality peritoneal dialysis (then including both CAPD and IPD) at 5 yearly intervals over 25 years from 1979 to 2004.

Despite the wealth of data then confirming HHD as the optimum modality to achieve good clinical outcomes, reduced hospitalization and greater self-reliance and increased usability, SHD burgeoned along with an enthusiasm for ‘corner store’, nurse-supervised, community-based care. In Australia, the impact on HHD was significant. HHD numbers fell from >35% in 1979 to 11% in 2004. The impact in the United States, however, was even more devastating to the modality, such that HHD now accounts for <0.5% of all dialysis in the United States.

THE RISE AND RISE OF SATELLITE HAEMODIALYSIS – GOOD OR BAD?

Retrospectively, the real question was whether these rapid modality changes were truly advantageous – were
In 1993, Uldall about to change. HHD seemed doomed to wither further. All that was HHD became ever less central to the core effort and over home care seemed ongoing. For many renal services, improved outcomes, the enthusiasm for satellite care advantages of HHD and the data attesting to its maintaining it in the home. Sadly, despite the clear cost with providing one-on-one equipment and installing/installing of both in-centre infrastructure and nursing costs in HHD has always outweighed the additional costs associated with providing one-on-one equipment and installing/maintaining it in the home. Sadly, despite the clear cost advantages of HHD and the data attesting to its improved outcomes, the enthusiasm for satellite care over home care seemed ongoing. For many renal services, HHD became ever less central to the core effort and HHD seemed doomed to wither further. All that was about to change.

A NEW MODALITY – NOCTURNAL HOME HAEMODIALYSIS

In 1993, Uldall and Pierratos first formally structured a programme in Canada based on HHD, but performed during sleep, and coined the modality term ‘nocturnal home haemodialysis’ (NHHD). Overnight dialysis had in fact been introduced by Baillod et al. as early as the mid-1960s but, although it continued to flourish in some centres like Seattle until well into the 1970s, new technology and disposable dialysers gradually biased towards daytime and centre-based programs.

The Canadian NHHD program, which emerged in 1993, was based on that of Charra in Tassin where, since the early mid-1970s, patients had dialysed by long, slow, overnight in-centre dialysis 3 nights/week. The Canadian programme, however, was developed as a 6 nights/week programme. Charra’s results, both for survival and clinical outcome, had long been extraordinary but, sadly, had been largely ignored.

Not only was the safety of overnight home-based haemodialysis confirmed but also clear, sustained biochemical, social, rehabilitation and lifestyle benefits were shown. In addition, although the Canadian programme provided 6 nights/week therapy compared with the 3 times/week programs for conventional icHD or SHD, comparative cost data showed that the NHHD programme was cheaper. This was despite the one-on-one equipment requirements and a doubled consumable expenditure. These added home-based costs were far outweighed by the infrastructure and staffing costs of satellite and in-centre care.

One aspect of NHHD and other recently popular dialysis advances, which espouse greater frequency, longer duration or combinations of both, and that deserves clarification, has been the nomenclature. Several terms have arisen over the past decade to describe the various options in frequency and duration. ‘Nocturnal’ dialysis simply means dialysis conducted during sleep. ‘Nightly’ dialysis has been applied to nocturnal dialysis conducted at a frequency usually of 6–7 nights per week. Many nightly programs allow one night ‘off’ per week, although some patients in these programmes still prefer to dialyse every night. ‘Alternate night’ nocturnal dialysis is, as it implies, overnight dialysis every second night but typically this occurs on a rolling basis such that the ‘long break’ associated with conventional dialysis regimens is avoided. As seven treatments are provided every fortnight, this regime is often abbreviated to nocturnal dialysis 3.5 nights/week. ‘Quotidian’ dialysis refers to dialysis ‘every day’ but does not specifically distinguish between daytime, waking-hour treatment or overnight nocturnal therapies. ‘Hemeral’ dialysis is a term that applies specifically to daytime, waking-hour therapy and has thus become associated with the modality of short daily haemodialysis, whether in-centre or at home. Clarification of these terms is needed as there appears to be growing confusion from the proliferation of new terminology.

WHY NOCTURNAL HOME HAEMODIALYSIS?

The reported patient benefits of the Uldall and Pierratos programme were profound and sparked the immediate interest of many groups. The extension of dialysis time to 6 nights/week and to >50 h of membrane contact/week was a major contrast to the icHD and SHD routines of 12–15 h/week. This allowed total dietary and fluid intake freedom for patients, as well as the restoration of full daytime freedom and re-employability.

The ability to reduce the ultrafiltration rate by long, slow therapy, as was used by Charra in the Tassin programme, and which had been the norm in the Seattle programme from the very beginning, abolished the occurrence of intradialytic hypotension. This made dial-
YSIS both safer and less symptomatic for the patient. The removal of this risk also opened the way for home therapy to be considered for un-partnered patients, a previous taboo for HHD and a significant limiting factor for suitable HHD patients.

Previously, HHD was only thought possible if an alert, on-site and trained partner was present during the dialysis run to respond to the episodic hypotensive ‘flats’ associated with rapid ultrafiltration. The 44 h (short break) or 68 h (long break) gap commonly associated with the standard icHD and SHD regime of three ± 4 h treatments/week had been routinely complicated by high interdialytic weight gains, hypertension requiring antihypertensive treatment and episodic acute pulmonary oedema and commonly forced high ultrafiltration rates during dialysis. High ultrafiltration rates, in turn, were known to stimulate thirst and promote excessive postdialysis fluid consumption resulting in further interdialytic weight gain – the vicious cycle of standard dialysis regimes. The ability to increase both the frequency and duration of dialysis by NHHD has been shown to blunt and abolish this destructive cycle and its clinical consequences. This core dialysis principle has recently been highlighted again by the Christchurch group who recently published a randomized cross-over study confirming a reduction in hypotensive episodes with longer dialysis.19

NOCTURNAL HOME HAEMODIALYSIS IN AUSTRALASIA

Although occasional home-based haemodialysis patients had long been known to ‘nod off’ during home therapy and a few had even been known to dialyse while asleep, this practice had always been officially discouraged and/or ignored in Australasia with the exception of the home dialysis programme in Christchurch, New Zealand, where several patients were known and accepted to dialyse during sleep. However, a formal structured programme to enrol patients for planned NHHD did not begin until the Geelong NHHD pilot programme commenced in July 2001. With the support of the Department of Human Services, Victoria, and with the assistance of Fresenius Medical Care, a pilot NHHD programme was established, its subsequent progress being followed with keen interest by the dialysis communities of Australia and New Zealand. The early results of this pilot programme have been published elsewhere,20,21 and have been made public through the internet.22

Immediate participation in similar programmes has followed in most major centres in both countries, such that by the end of December 2004 more than 120 known NHHD patients were dialysing in Australia and some 25 in New Zealand (various personal communications) with the Geelong programme contributing a mere 20 to the Australian pool.

THE BENEFITS OF NOCTURNAL HOME HAEMODIALYSIS

The advantages of NHHD over current haemodialysis modalities have been well reported elsewhere but the salient and important benefits include the following:

Dialysis-related symptoms

The frequently encountered dialysis-related symptoms of intradialytic hypotension, nausea, vomiting, cramp, postdialysis headache, postdialysis hypotension and cyclical high weight gain threatening thirst, lethargy and prolonged postdialysis recovery time all make the experience of conventional dialysis difficult for many patients. These symptoms largely result from the tendency towards high interdialytic weight gain, the subsequent need for high ultrafiltration rates and the consequent disturbance of intra- and extra-vascular volume equilibration. The rapid removal of solutes and volume from the intravascular space distorts trans-compartmental equilibration kinetics and is known to be exacerbated by shorter, more aggressive dialysis treatment.

The long, slow, frequent treatment of NHHD has been invariably reported to abolish these symptoms. Not only is the potential for volume expansion reduced, particularly in programmes where NHHD occurs nightly as opposed to alternate nightly, but the duration of dialysis is doubled, effectively reducing the required ultrafiltration rate by a factor of four.

Cardiac performance

Largely due to the improvement in volume control, many authors have reported both an improvement in blood pressure control and a reduction in blood pressure medication in NHHD patients,23 while regression of left ventricular hypertrophy,24 improvement in left ventricular systolic function,25 improved ejection fraction26 and an overall improvement in haemodynamic status27 have all been reported. In addition, more responsive endothelial-mediated vasodilation has been shown with NHHD,28 while an improvement in lower extremity peripheral arterial disease has also been reported.29

Biochemistry and nutritional status

One of the most easily apparent features of NHHD is the normalization of blood urea where, in all reported series of 6 night/week NHHD, urea levels oscillate within the normal range. Significant reductions in creatinine towards normal are also seen. Serum β2 microglobulin
levels also fall towards normal but, to do so, require the combination of a high flux dialyser.\textsuperscript{30}

Many authors have noted an improvement in nutrition with NHHD, a review of which was published by McPhatter and Lockridge.\textsuperscript{31} Improved triglyceride and HDL levels have also been reported.\textsuperscript{32,33} Improvement in serum albumin has been noted.\textsuperscript{34,35}

**Sleep disturbance**

Sleep apnoea and poor quality sleep have long been associated with dialysis. Significantly fewer patients have sleep apnoea in the NHHD-treated group, while its severity is reduced in those still requiring continuous positive airway pressure.\textsuperscript{36–39}

**Quality of life**

Numerous studies have examined quality of life using a range of qualitative assessment tools. All have documented improvement,\textsuperscript{15,40,41} while cognitive function has also been shown to significantly respond to NHHD, although whether this is due to an improvement in quality of life or to an improvement in the quality of sleep – or a combination of both – remains uncertain.\textsuperscript{42}

Central to the improvement in quality of life has been the return of daytime freedom and, in combination with improved well-being, the capacity and will to rejoin the workforce. This has been a key element of both the Canadian\textsuperscript{12} and Australian\textsuperscript{21} experience. Workforce re-entry has been paralleled by a reduction in social security dependence and has carried significant weight with governments struggling with the budgetary burden of expanding dialysis services.

**Calcium, phosphate, calcium/phosphate product and bones**

One of the most contentious areas in NHHD relates to calcium and phosphate metabolism and the integrity of bone. What is clear is the need for an increased dialysate calcium concentration for patients undergoing NHHD. Dialysate calcium concentrations of 1.75 mmol/L are generally used.\textsuperscript{43}

All authors have reported the ability to withdraw all phosphate binders in NHHD patients. So effective is phosphate removal, the control of the serum phosphate and the calcium/phosphate product, that phosphate replacement is required particularly in those patients on 6 nights/week NHHD.\textsuperscript{44,45} In alternate night NHHD, phosphate control appears ideal with minimal if any requirement for phosphate binders, but also little or no requirement for phosphate replacement.\textsuperscript{46} Whether the remarkable reductions seen in the calcium-phosphate product in NHHD translate in time to less vascular calcification, less peripheral vascular disease and a reduction in coronary artery disease remains to be seen, although the resorption of calcium deposits from peripheral non-osseous sites\textsuperscript{47} and from coronary arteries\textsuperscript{48} has already been reported. It is tempting to speculate, however, that a low-normal phosphate level and a calcium-phosphate product routinely <3.0 might offer a significant vascular morbidity advantage to NHHD in the longer term.

**Safety**

Debate continues regarding the advisability of or need for on-line modem or trans-internet methods of real-time dialysis parameter monitoring. Some programmes routinely monitor,\textsuperscript{49,50} while others do not.\textsuperscript{51} Our unit’s experience has been that patients can dialyse safely without the need for complex and expensive monitoring techniques.\textsuperscript{18} HHD patients have not been externally monitored despite more than 40 years of accepted HHD and, as NHHD treatments are both longer in treatment duration and up to twice as frequent as in conventional HHD, the haemodynamic stresses of dialysis are effectively reduced by a factor of two (alternate night NHHD) to four (6 nights/week NHHD). As a result, we have not pursued modem monitoring and few new programmes now appear to do so.

**Cost**

As previously noted, all programmes where expenditure has been documented note NHHD to be consistently cheaper than conventional dialysis methods, ICHD and/or SHD. The cost savings depend upon the frequency of NHHD, alternate night programmes being highly cost efficient. However, 6 nights/week programmes still undercut the cost of conventional haemodialysis methods,\textsuperscript{18,52–54} although it is recognized that, for the first few patients in a new NHHD program, expenditure exceeds that of conventional HD due to programme establishment costs.

**Other benefits**

Other benefits to hormonal status,\textsuperscript{55} amino acid profiles,\textsuperscript{56} and solute clearance\textsuperscript{11} have been reported. The effectiveness of NHHD in children,\textsuperscript{57,58} a reduction in homocysteine levels\textsuperscript{59} and an improvement in anaemia profiling and management\textsuperscript{60} have all been referred to in the extensive literature now available on NHHD.

Although most authors have noted a fall in erythropoietin (EPO) usage in their NHHD populations, this was not the case in the report of the Geelong experience.
by Agar et al.21 This group suggested that the fall in EPO usage noted by earlier authors might have corresponded to concurrent improvements in iron supplementation methods in those programmes, while the failure to show a reduction in EPO use by the Geelong group was due to a well-established intravenous iron programme at that institution prior to their introduction of NHHD.

**Reduction in hospitalization**

Several authors have recorded similar reduction rates in hospitalization for NHHD populations,21,51,52 although again it is hard to refute the criticism that NHHD patients arise from a selected group where lower hospitalization rates might be otherwise expected. However, Bergman et al. reported comparative data in a cohort converting from 2 years conventional SHD to 2 years NHHD where the hospitalization rate fell from 0.40 ± 0.12 to 0.17 ± 0.06 admissions/patient per year (P = 0.001) after conversion to NHHD.61 The reduction in hospital days and the cost benefits associated with this widely and uniformly reported feature in NHHD programmes is a potent weapon with funding agencies when arguing the advantages of a NHHD programme on a cost-effective basis.

**POTENTIAL PITFALLS IN NHHD**

Several potential and actual problems have arisen in NHHD programmes. First, the potential for overdialysis has been suggested; in particular, the loss of measured or unmeasured solutes and/or minerals and trace elements. To date, there has been no evidence to support this contention despite more than 10 years of several 6 nights/week NHHD programmes.

It had been suggested that a greater/longer exposure to heparin might increase the incidence of heparin-induced thrombocytopenia syndrome and/or osteoporosis, but neither of these potential risks have been reported to date.

The effect of increased use of the arteriovenous fistula has been the greatest concern. Recognizing this concern and to both minimize fistula trauma and assist home patients in self-needling, the buttonhole technique62,63 is now used in many NHHD programmes. In addition, it has been shown to safely and reliably seal following needle withdrawal.64 To date, no evidence to support increased trauma to the fistula has been reported. Indeed, in one study of daily haemodialysis patients, the access failure rate in daily haemodialysis was recorded at 0.05 episodes/patient per year versus 0.28 episodes/patient per year for standard 3/week HD treatment.65

The risk of increased infection, either due to the prolongation of the intravascular ‘dwell-time’ of the access needle and/or to subtle movement of a poorly stabilized needle during sleep has raised anxiety of an increased infection rate. An increased infection rate related to patient ‘corner-cutting’ during needle insertion has been recently reported,66 although these authors noted that ongoing, recurrent reinforcing of the correct needling technique and needle stabilization procedures resolved the infective problems.

**WHO IS SUITABLE FOR NHHD**

The long-held views of many that home haemodialysis is only for the young, fit and comorbid-negative patient and, as a result, is relegated to a niche dialysis modality is, in the view of the author, outmoded and incorrect. The availability of improved dialysis equipment, which has simplified set-up and break-down procedures, has opened home dialysis, and NHHD in particular, to a far wider potential dialysis population. In addition, the newer third generation dialysis machines now emerging look likely to add a further dimension of simplicity and speed of connection and disconnection for the home patient.

Many patients currently sequestered in satellite units are suitable candidates for home training for NHHD. The capacity to dialyse un-partnered at night expands enormously the potential for NHHD. For too long, the soft option has been satellite care. The new option of NHHD takes energy and commitment to engage and establish – yet conservative estimates are that 30–40% of all current haemodialysis patients are potential candidates.21 The social networks that patients establish in satellite services are strong, however, and many current patients who are medically and intellectually capable of NHHD might not realistically be ‘shaken free’ from the satellite systems. Incident patients are another matter. If renal services adopt a ‘home-first’ approach and promote NHHD to new patients and their families as they approach dialysis and governments take a proactive attitude to home supports and subsidies, then the future of NHHD as a prime home therapy looks assured.

Age itself is not a barrier to home haemodialysis, although dexterity and vision are the two key factors that might limit NHHD in the elderly. These can be easily assessed prior to entering the training programme. In support of home haemodialysis for the elderly, the Dunedin group have shown better than comparable survival for elderly patients in both home peritoneal and home haemodialysis techniques when compared to the national average in New Zealand.67 It is our unit’s experience that, although older patients might take a longer time to train, they not only assimilate the techniques well but they pay closer attention to the details needed to secure safe home therapy.

Although an adequate arteriovenous access is essential and, as an access option, a well-functioning arteriovenous native fistula is clearly the optimum choice, it
should also be remembered that the successful early Toronto experience was entirely with catheters.

**WHICH FREQUENCY: ALTERNATE NIGHT OR SIX NIGHTS/WEEK?**

The vexed question of ‘how much is enough?’ as regards both extended dialysis time and/or increased dialysis frequency remains both hotly debated and yet to be answered. What does seem clear, however, is that the Kt/V-driven practice of shorter dialysis time countered by increased blood and dialysate flow rates and larger and leakier dialysers was associated with unacceptable mortality rates. Although dialysis adequacy is still appropriately monitored by either Kt/V or urea reduction ratios, it is clear that true adequacy is more complex than just small solute clearance and that the extension of dialysis time and/or frequency has been a prime step towards more optimal treatments and outcomes.

Although most of the early NHHD work was with 6 nights/week therapy, clear benefits also accrue from alternate night (3.5 nights/week) NHHD. Although dietary and fluid freedoms for the patient are less with alternate night regimes, phosphate control seems close to dietary and fluid freedoms for the patient are less with alternate night (3.5 nights/week) NHHD. Only one report to date has attempted to compare alternate night NHHD with ‘full’ 6 nights/week NHHD. Although this report points to the dietary and improved blood pressure control of 6 nights/week NHHD, it also notes the more efficient achievement of phosphate balance and the clear cost benefits of alternate night treatment. It concludes that the choice between the two chief frequency options of NHHD will ultimately be a balance between cost imperatives versus optimum patient benefits and recommends both options be supported and encouraged according to patient wish and unit capacity.

**SUMMARY**

HHD remains alive and well in Australia and New Zealand with interest and commitment having been reinvigorated by a surging enthusiasm for NHHD. Whether the rapidly increasing contingent of NHHD patients throughout both countries simply reflects a ‘roll-over’ of current conventional regime HHD patients into NHHD rather than a true increase in all HHD from a new patient uptake of NHHD remains to be seen. Nevertheless, the clear and rapid rise in numbers of patients on NHHD, whether by alternate night/week or 6 nights/week options suggests that HHD has been reinvigorated by the new modality of NHHD.

There appears to be a clear patient-driven demand to ensure NHHD services are available. In addition, there is a clear cost imperative to the overall national dialysis budget to ensure cost-effective programmes are sustained and encouraged. The cost benefits of NHHD must impact on programmes throughout Australasia, if for no other reason than to ensure maximum dialysis dollar efficiency. As the clinical results, at least to date, suggest that NHHD is superior to the other conventional methods of haemodialysis, NHHD seems to be a win-win option for both optimal patient outcomes and the national purse.

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