Chapter 7

Home Haemodialysis and Haemodiafiltration

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Additional information is available at the end of the chapter

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Abstract

There has been a resurgence in home haemodialysis over the last decade and interest in online haemodiafiltration in gaining momentum with advances in technology and the results of recent clinical trials. Both increasing haemodialysis frequency and treatment time have a number of potential benefits in improving dialysis efficiency and are ideally placed in the home setting. This chapter describes the rationale behind dialysis treatments, which go beyond conventional haemodialysis (CHD) and future avenues for home dialysis, which may involve combining convective therapy with more frequent treatment.

Keywords: haemodialysis, haemodiafiltration, extended haemodialysis, home haemodialysis

1. Introduction

Haemodialysis treatment has changed the lives of millions of patients around the world who have advanced kidney disease. The treatment has advanced considerably since the first treatment on a human, lasting just 15 minutes and performed by George Haas in Giessen, Germany, in October 1924 [1]. It was not until the 1960s when maintenance haemodialysis really started and at present, over 90 years since Haas, there are over 400,000 prevalent users in the USA alone [2]. Dialysis provides a bridge to transplantation for some, and for others, it allows survival when residual kidney function is no longer sufficient to sustain life. While the survival of patients has improved since the early days of its inception, the survival of haemodialysis patients remains unacceptably poor. In the United Kingdom, 18% of those aged 65–74 starting haemodialysis will not survive 1 year [3]. Five-year survival data has often been compared to those of patients with cancer to make the figures more tangible. With recent

figures showing 50% survival at 5.8 years in the 55–64 years group [4], it is not hard to see why this comparison is made. Clearly, one of the key challenges for the nephrology community is to change this unacceptably high mortality rate. In addition to this, there are many other factors that make a large difference to the patient in front of us, and arguably, these are as important to address and considerably improve.

2. Background

The aim of haemodialysis is to replicate normal physiology as much as possible. Although this may sound straightforward initially, there are a vast array of factors to consider. The ideal treatment should give good survival rates, prevent cardiovascular events and hospitalizations, effectively manage fluid and salt balance and address the anaemia and mineral-bone disorder associated with chronic kidney disease (CKD). Patient well-being, cognition, sleep, the ability to work and nutritional status are also hugely important factors which need addressing and the list could continue. For a treatment, which for the majority of patients is performed for 12 hours of the week (just 7% of the week in terms of time), this is an incredibly tall order and it is not entirely surprising that outcomes remain poor.

Conventional haemodialysis (CHD) is the most common treatment schedule and lasts for 3–4 hours thrice weekly. This treatment mainly takes place in a hospital or in a dedicated dialysis unit. Other treatment regimes include short daily haemodialysis (SDHD), which is performed for 1.5–3 hours 5–7 times per week, long nocturnal daily haemodialysis (LNDHD) which is performed for 6–8 hours 5–7 times per week and long conventional haemodialysis (LHD), which is typically 8 hours 3 times per week.

Although CHD is the most common treatment regime now, LHD was the most common treatment initially in the 1960s [5]. This treatment came about purely by convention. Home haemodialysis in the United Kingdom was started in London in 1964 by Shaldon and his team [6] and expanded following this. Home haemodialysis was necessary as hospital facilities were sparse, treatment times were lengthy and home dialysis offered both financial and logistical benefit. Prevalence in the United Kingdom peaked in 1982 when 62% of HD patients were at home [3]. As dialysis treatment time shortened and patient numbers increased, haemodialysis practice changed from a predominantly home-based therapy to a predominantly hospital-based therapy.

The National Cooperative Dialysis Study (NCDS) ($n = 151$) [7] was published in 1981. It showed no difference between the shorter and longer duration dialysis groups (2.5–3.5 hours three times per week vs. 4.5–5 hours three times per week). This further paved the way to the adoption of CHD. Data from this study were later used to develop a method for calculating haemodialysis adequacy [8] K_t/V_{urea} (K_t/V) which is now used worldwide. K_t/V exclusively looks at small molecule clearance as a marker of dialysis adequacy. There is an association between dialysis dose and mortality [9]; however, the benefit (from the NCDS data) was seen up until a K_t/V of 1.2 with no survival advantage with doses above this. This was later echoed in the much larger HEMO study (involving 1846 patients) and again showed no advantage in

increasing the dialysis dose above a K_t/V of 1.3. Dialysis treatment time was not investigated in this study.

It would seem therefore that with K_t/V we have reached a ceiling where improvements can no longer be made within the restrictions of a thrice weekly schedule, and we must start looking at other ways to improve outcomes in haemodialysis. The most significant causes of death in haemodialysis patients are cardiovascular in nature and this has been well known for some time. UK registry data show that almost a third of deaths in dialysis patients are cardiovascular in nature [4]. It is also clear that the two-day gap in CHD is harmful with all-cause and cardiovascular mortality being higher on the day after the long interval [10]. Further data show the highest rate of cardiovascular events in the first month after starting haemodialysis and a high-risk period extending to 4 months [11].

Based on all of this, a strong argument can be made to further explore more frequent and extended haemodialysis treatments.

3. Extracorporeal dialysis therapy

The basic principle behind dialysis is the removal of solutes across a semipermeable membrane. Haemodialysis relies on the process of diffusion where solutes move from an area of high concentration to an area of low concentration. Solutes pass from the patients' blood to the dialysis fluid across the dialysis membrane in this manner. The concentration gradient is maintained by the countercurrent flow of dialysate and blood and the maintenance of adequate blood and dialysate flow.

Haemofiltration allows the clearance of larger molecules through the process of convection. A hydrostatic pressure gradient is used to pass the patient's blood across a membrane with a large pore size. Solutes follow water through a process called "solvent drag" [12]. Large volumes of fluid are typically filtered and a replacement fluid is required, which enters the dialysis circuit and is mixed with the patient's blood before it is returned.

Haemodiafiltration (HDF) combines the techniques of both haemodialysis and haemofiltration. Solutes are cleared by both diffusion and convection, thus allowing more efficient clearance of both small and middle molecules. The replacement fluid can either be obtained from pre-prepared bags or prepared "online" by the machine (OL-HDF), which is able to produce ultrapure fluid. This dialysis therapy has a number of potential advantages, which are discussed in more detail later in this chapter.

3.1. Clearance in extracorporeal dialysis

K_t/V is widely used to give us information on dialysis adequacy; however, it is solely dependent on the clearance of urea. Urea has the advantage of being easy to measure; however, it may not be directly toxic and many of the identified uraemic toxins are larger in size and are not cleared efficiently by conventional haemodialysis [13]. In general, molecules are classified as small molecular weight (MW) molecules (<500 Da), middle MW molecules (>500 Da) and

protein-bound molecules. β2-microglobulin (B2M), which is commonly used as a marker of middle molecules, has a molecular weight of around 11,800 Da. It has been demonstrated that outcomes are improved when middle molecular clearance (1000–50,000 Da in the study) are enhanced [14]. There has been much interest in increasing middle MW molecule clearance, and it is clear that accumulation of middle MW molecules can be harmful such as in the case of B2M which can lead to dialysis-related amyloidosis [15].

β-Trace protein, cystatin-C and B2M are all middle MW molecules that are freely filtered, resorbed and catabolized in the tubular cells. A study by Lindström et al. [16] has shown clear differences in the clearance of these molecules by different dialysis modalities—CHD did not change the concentrations of any of these proteins while in HDF both cystatin C and B2M were reduced and β-trace protein was only reduced in HDF. This demonstrates a clear difference between dialysis modalities in terms of clearance and a clear biomarker that could be measured. Moreover, β-trace protein had been found to be an independent predictor of both death and cardiovascular mortality in haemodialysis patients [17]. The use of such molecules could be part of the way that we assess haemodialysis adequacy in the future and tailor treatment to the patient.

3.2. Biocompatibilty in dialysis

The specifications of dialysis membranes have improved considerably. The use of cellulose-based membranes were common initially; however, they were associated with complement and leucocyte activation [18] resulting in dialyser reactions. The majority of dialysis membranes in use now are synthetic and are more biocompatible—reactions can still occur however and anaphylactoid reactions have been reported, particularly in patients on ACE inhibitors [19]. More recently, dialysis membranes have been manufactured with larger pore sizes to allow a higher ultrafiltration rate and allow clearance of larger molecules. Membranes can be classified as high flux or low flux and for the purposes of the HEMO study [20] were defined as B2M clearances of <10 ml/min for low flux and >20 ml/min for high flux. High-flux membranes have been found to lower pre-dialysis B2M concentrations [21] and may prevent dialysis-related amyloidosis [22]. Several observational studies have identified a survival benefit with high-flux dialysers [23, 24]. Although the HEMO study showed no benefit from high-flux membranes, the study may not have been sufficiently powered to detect a significant benefit [25]. The subsequent European study, the MPO Study [26], showed survival benefit to those patients with a serum albumin of <40 g/l. Several guidelines now recommend high-flux dialysers including the European Renal Association [27] and practice has also changed considerably.

The production of a high-quality infusion fluid is of paramount importance in HDF. More than 20 litres of infusion fluid can be administered to the patient during a typical HDF session and thus ultrapure water and dialysis fluid are required. Ultrapure water is defined by the standard for replacement fluid requiring <0.1 colony-forming units (CFU)/ml and an endotoxin concentration <0.03 endotoxin unit (EU)/ml [28]. The use of ultrapure dialysis fluid is associated with a reduction in inflammatory markers and an improvement in serum albumin, haemoglobin and ferritin [29].

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4. Increasing haemodialysis frequency and length with home haemodialysis

The seminal paper in 1992 by Bernard Charra and his group in Tassin, France, showed hugely impressive survival rates of their haemodialysis patients of 87% at 5 years and 43% at 20 years, which far surpassed matched patients on both European and US registries. All patients received 8 hours of haemodialysis three times per week (LHD). It is likely that the survival association is related to achieving good blood pressure control (antihypertensives were seldom required in the group) through optimized ultrafiltration and the enhanced clearance of uraemic toxins provided by the longer treatment. Their publication sparked interest once again in extended haemodialysis. With the continued increasing demand for renal replacement therapy and limited resources in hospitals, novel ways of providing haemodialysis were required. Home haemodialysis seemed an attractive option and could also accommodate more frequent and extended schedules. The first daily nocturnal haemodialysis programme was set up in Toronto in 1994 [30].

The prescription of home haemodialysis in the United Kingdom remains very variable; however, the most common prescription in 2009 was still 4 hours thrice weekly (51.9% of home HD patients), followed by alternate day dialysis (20.5%), short daily (17.4%) and nocturnal (2.9%) [31]. This is a surprising finding given the benefits of more frequent and extended haemodialysis (which we will now expand on). This does however reflect patient choice and the comfort of both patients and clinicians with a CHD schedule.

4.1. The benefits of extended and more frequent haemodialysis

Several benefits have come to light from more frequent and extended haemodialysis and these will be outlined in this section.

4.1.1. Survival, cardiovascular outcomes and hospitalizations

Observational studies show a significant mortality benefit associated with home haemodialysis, even when adjustments are made for age and comorbidity [32]. These findings are also apparent in studies in Australia and New Zealand [33], which have a higher uptake of home haemodialysis. Figures of 90% survival at 5 years and 45% at 20 years have been quoted [34]. **Figure 1** shows a clear survival advantage to home haemodialysis over both peritoneal dialysis and facility-based HD. These data have to be interpreted with care given the high number of confounders. Patients selected for home haemodialysis are generally younger with a low comorbidity burden. They are usually highly motivated and take an interest in their healthcare.

The frequent haemodialysis network (FHN) trials were setup to give a more definitive answer to the benefits of more frequent and extended haemodialysis [35, 36]. The SDHD arm of the trial randomized 245 patients to either frequent (6 times per week) or conventional haemodialysis and the nocturnal arm randomized 87 patients to either CHD or LDNHD. Two coprimary composite endpoints were used—death or change in LV mass or death or change in physical-health composite score. There was a favourable outcome with regard to both

coprimary endpoints for the SDHD trial but not with the LNDHD trial. Looking purely at survival, there was no significant benefit from either trial. With a 12-month follow-up period and the numbers involved with the trials, they were not powered to detect an effect on mortality. The question therefore still remains unanswered as to whether more frequent and extended haemodialysis does have a favourable effect on survival.

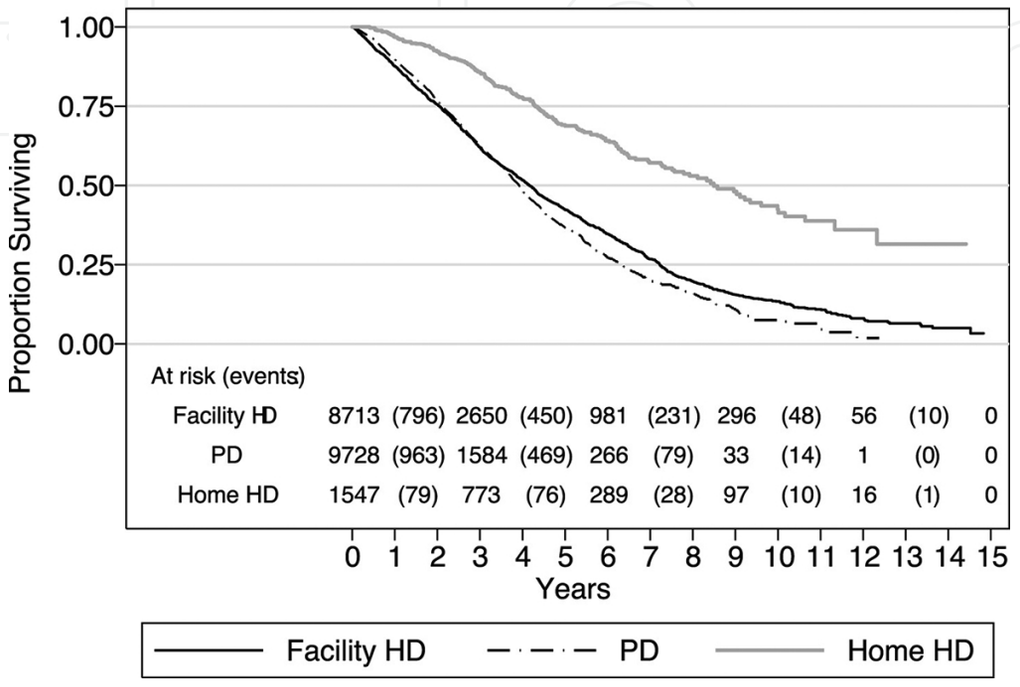

Figure 1. The survival of home HD patients in New Zealand compared with facility HD and peritoneal dialysis (PD). Image adapted from Marshall et al. [35].

There is an associated reduction in cardiovascular-related admissions in converting patients from CHD to LDNHD [37]. There are also fewer cardiovascular-associated hospital admissions associated with SDHD compared with matched CHD; however, all-cause hospitalizations remain unchanged [38]. The FHN studies once again showed no change in the rate of hospitalizations.

4.1.2. Ultrafiltration and blood pressure control

There is a strong association between a high ultrafiltration rate (>10 ml/kg/hour) and mortality [39, 40]. Chronic fluid overload contributes to an increased LV mass and congestive cardiac failure [41] and this is likely to be highly significant in terms of cardiovascular morbidity and mortality. Increasing haemodialysis treatment time improves the tolerance of ultrafiltration [42, 43]. There are also many reports of improved blood pressure control both in LNHD and in SDH [44–46] and a regression of left ventricular hypertrophy [47]. It has also been shown that ejection fraction, in those with heart failure, can be improved through more frequent haemodialysis and ultrafiltration [48]. With CHD, it often the case that dry weight is not achieved. Patients that experience hypotension during haemodialysis often have their

ultrafiltration stopped, receive saline infusions and thus never achieve their dry weight and in fact can exacerbate the situation further. Extended dialysis allows much lower ultrafiltration rates and thus less haemodynamic disturbance. It is likely the effect that extended dialysis has on blood pressure goes beyond the optimization of volume status. When compared to patients on CHD, some patients with a high extracellular volume (measured by bioimpedance) but on extended haemodialysis achieve normotension [49]. A theory put forward for this phenomenon is that extended haemodialysis may lead to efficient removal of vasoactive factors that contribute to hypertension.

4.1.3. Small molecule clearance

Increasing haemodialysis frequency provides more efficient clearance of small MW molecules. It provides a lower peak urea, lower mean urea and less fluctuation [50]. This provides a lower time-averaged concentration (TAC). Looking purely at K_t/V would, however, be misleading as this would remain the same despite the enhanced clearance.

4.1.4. Phosphate balance

There is a clear association between raised serum phosphate and adverse cardiovascular outcomes in patients with CKD [51, 52]. Conventional haemodialysis does provide sufficient phosphate removal for western diets, and as a result, there is a net phosphate gain [53]. As a result of this, multiple phosphate binder tablets are often required to reduce the absorption of phosphate from the gut. On average, haemodialysis patients have an average pill burden of 19 pills per day and many of these are phosphate binders [54]. A higher pill burden in this setting is associated with lower quality of life scores [54].

Phosphate removal on haemodialysis has been found to be time dependent [55] and thus is significantly enhanced in NHD. Phosphate removal is also increased by SDHD but not to the same extent as NHD [56]. In LNDHD, many patients will discontinue their phosphate binders [57] and some require supplementation that can be added to the dialysate [58].

4.1.5. Anaemia

Reports are mixed when it comes to more frequent haemodialysis and anaemia management. Reduced erythropoietin doses have been reported when patients switch to SDHD from CHD [59] and in NHD [60]. One of the theories put forward for this change is the control of inflammation and reduction in IL-6 levels which improve erythropoietin responsiveness [61]. The exact effect that more frequent or extended dialysis has on anaemia, however, is still unclear. Again both FHN studies showed no effect on erythropoietin dose.

4.1.6. Quality-of-life measures and carer burden

Home haemodialysis allows patients the independence to fit their dialysis treatment around their lifestyles. One may expect this to bring significantly improvements to quality of life; however, this may be offset by the burden of having to perform the treatment so frequently, which can lead to burnout or the increased burden on carers. While there are many reports of

improvements in quality-of-life measures from switching to NHD [62] or SDHD [63], some show only small improvements in kidney-specific measure of quality of life [64], while others show no difference. Larger studies have shown a reduction in depressive symptoms related to increased dialysis frequency [65].

Data from the recent FHN daily trial showed a significant increase in quality-of-life score in the SDHD group [35] with no specific benefit from NHD over CHD at home. In the FHN NHD arm, however, both groups had an increase in their quality-of-life score showing the positive effect that the setting of the haemodialysis treatment has on this outcome [36] regardless of prescription. Perceived burden on unpaid carers is high among HD patients [66]; however, the FHN trials did not show a higher perceived burden with either SDHD or LDNHD [67].

The patient-reported experience on both LDNHD and SDHD has been positive in terms of physical, psychological and lifestyle aspects [68]. There is also an associated faster recovery time with home haemodialysis [69]. Once again, it is fair to say once again that the jury is still with regard to whether these treatments truly impact on quality of life. In general, the effect seems to be positive with a paucity of data suggesting a negative impact.

4.1.7. Pregnancy

Intensive dialysis has been used very successfully in pregnancy. A case series from Canada [70] shows a markedly improved live birth rate and duration of pregnancy with a dose response between dialysis and pregnancy outcomes. Women who had >36 hours of dialysis per week had significantly improved live birth rates (85 vs. 45% in those who had <20 hours of dialysis per week), which again demonstrates and gives strength to high-dose dialysis.

4.2. Disadvantages of more frequent and home haemodialysis

While there are many advantages of home haemodialysis, the treatment is not suitable for all patients and it is not a treatment without disadvantages. Although exceedingly rare, there is always the possibility that human error can occur resulting in significant blood loss through a variety of mechanisms. There are reports of patient deaths from exsanguination while on home haemodialysis [71]. The sophistication of safety mechanisms is continually improving to make this event less likely with blood leak detectors, pressure monitoring and line disconnect detectors featuring on newer machines.

A clear finding from the FHN trial was an increase in interventions needed for vascular access with 47% of the frequent dialysis group requiring intervention compared with 29% in the CHD group. Interventions to fistulas were required much more often than in catheters. This was not an entirely surprising finding given the considerably increased use of vascular access form more frequent haemodialysis. A solution to this could be the use of a buttonhole technique for fistula cannulation or using single-needle haemodialysis to reduce the number of needling events. The evidence, however, is not there to support this practice and a systematic review of buttonhole cannulation in home haemodialysis patients found an increase in infectious events, an increase in staff support required and no reduction in surgical interventions compared with

the "rope ladder" technique [72]. The FHN nocturnal trial used single-needle haemodialysis, and despite this, there was still a trend towards increased vascular interventions in this group.

Finally, globally, the uptake of extended higher frequency haemodialysis remains low, despite a range of benefits and favourable health economics. There can be major patient and clinical factors driving modality uptake. A key determinant, however, is patient motivation and choice. Extended time or frequency on home HD may add to patient and carer burden and is therefore often perceived as a barrier limiting its uptake.

5. Haemodiafiltration

Haemofiltration allows clearance of solutes of up to 20 kDa through the process of convection as previously described. Large volumes of replacement fluid are required for the treatment, and this can be administered either before the filter (pre-dilution) or after the filter (post-dilution). Newer technology also allows a mix of pre- and post-dilution or mid-dilution in an attempt to gain the advantages of both pre- and post-dilution (largely the anticoagulant requirement) [73].

Conventional HDF provides enhanced B2M clearance compared with HD [74]. It is associated with a reduction in pro-inflammatory cytokines such as IL-6 and TNF-α [75] and reduced episodes of hypotension during treatment [76]. There does not appear to be a benefit in terms of left ventricular mass, pulse wave velocity or ejection fraction [77]. This could be due to achieving low substitution volumes or large interdialytic fluid shifts induced by conventional thrice-weekly schedule.

There have been three recent large prospective clinical trials, which have compared HDF with high-flux HD with contrasting results. The ESHOL study [78], a Spanish study, showed promising results with a 30% lower all-cause mortality, a 33% lower cardiovascular mortality and 55% lower infection-related mortality compared with haemodialysis. A Dutch study [79] showed no difference in outcome between HDF and HD and a Turkish [80] study drew the same conclusion. Looking back at these studies, the ESHOL study achieved the highest convective volumes (22.9–23.9 l per session) and *post hoc* analyses of the Turkish and Dutch study also show an association between high convection volume and a survival benefit.

In order to provide HDF with high convection volumes, large volumes of sterile replacement fluid are required (>15 l), which would not be practical with pre-packaged solutions. Instead of online preparation of fluid, which is the most practical solution, HDF uses an additional 50–80 l of water per session [81] (with a typical haemodialysis session using around 500 l of mains water to generate dialysate [82]). Ultrapure dialysate must be generated by the machine to the standards previously described.

5.1. Adding HDF in the home setting

There appears to be a benefit from high convective volume haemodiafiltration. The biggest determinants to achieving a high convective volume are treatment time and blood flow [83].

A blood flow between 360 and 500 ml/min is required to achieve the necessary transmembrane pressure [84]. A well-functioning vascular access would therefore also be required. Although there are reports of achieving a convective volume of >20 l with a haemodialysis catheter, a well-functioning AV fistula would allow higher blood flows [84].

Given that treatment time is clearly an important factor in achieving the dose of HDF associated with improved outcomes, the home setting is an ideal place to deliver the treatment. Vascular access would not be a barrier and combining frequent haemodialysis with a convective treatment should maximize middle molecule clearance. Switching patients from a conventional HDF schedule to a short daily schedule has been reported to result in a higher removal of middle and large molecules, a reduction in phosphate binders, the disappearance of post-dialysis fatigue, an improvement in nutritional status as well as a 30% reduction in left ventricular mass [85]. The improvements in switching to more frequent OL-HDF are outlined in **Table 1**.

	Baseline	**Month 3**	**Month 6**
spK_t/V	2.30 ± 0.20	1.13 ± 0.15[b]	1.11 ± 0.11[b]
eK_t/V	1.96 ± 0.17	0.90 ± 0.12[b]	0.88 ± 0.08[b]
URR %	84.3 ± 2.5	64.2 ± 5.3[b]	63.3 ± 4.2[b]
Weekly spK_t/V	6.90 ± 0.59	6.78 ± 0.91	6.67 ± 0.64
Weekly eK_t/V	5.88 ± 0.52	5.39 ± 0.75[a]	5.30 ± 0.50[a]
EKR *mL/min*	19.2 ± 0.5	24.2 ± 2.6[b]	23.8 ± 1.9[b]
stdK_t/V	2.62 ± 0.1	3.87 ± 0.3[b]	3.86 ± 0.2[b]
Weekly URR %	253 ± 7.5	385 ± 32[b]	380 ± 25[b]

a: $P<0.05$;

b: $P<0.01$ with respect to baseline value.

Adapted from Maduell et al. [85].

Abbreviations: URR, urea reduction ratio; spK_t/V, single-pool K_t/V; eK_t/V, equilibrated K_t/V; stdK_t/V, standard K_t/V; TAC, time average concentration; TAD, time average deviation; ERK, equivalent renal urea clearance.

Table 1. Change from three times a week on-line haemodiafiltration (OL-HDF) to short daily on-line haemodiafiltration (D-OL-HDF): comparison of urea kinetics during the two study periods.

While the technology to provide HDF in the home setting exists, it is not widely used at present and there is very little published literature about HDF as a home therapy. Until recently, there have not been haemodialysis machines specifically manufactured for the home market. As a result, patients have been trained on the machines used in the main dialysis unit. Using the same technology both in the home and in the main dialysis unit makes the logistics of maintenance much easier. The health care team, including the technicians, are often more comfortable and experienced using and providing support for a single machine. As technology has developed and haemodialysis machines have become more advanced, it is important that

more user-friendly technology, specifically for the home market, is developed. This will allow further uptake and expansion of home dialysis programmes.

The ideal home HD machine has been described [86] as one which is fast and easy to setup, allows a range of prescriptions (such as short daily and nocturnal), teaches and interacts with the patient and allows the patient to deliver intravenous fluid at the push of a button. The description suggests the ability of the machine to re-use blood sets and dialysers, prepare all fluids to a standard beyond ultrapure and have the ability to provide HDF. There are many machines in development and it is likely that this "ideal machine" will be in existence in the near future. There is the potential for HDF machines to be complex given the choice in pre-dilution, post-dilution and mixed dilution and the blood and dialysate flow. Technology should strike a balance, remaining simple for safe use with minimal margin for error and fast training times but also allow some flexibility to tailor treatment.

As previously described, providing a high water quality is of great importance given the high volume that is infused into the patient. The body of evidence to support the use of ultrapure water really lies in convective treatments, and thus, an essential requirement for any home HDF programme will be the production of ultrapure dialysate. Water may contain both chemical and microbiological contaminants, and in the home setting, this is likely to vary considerably depending on the local feed water. A variety of contaminants can have clinical consequences, such as chloramines, leading to haemolytic anaemia [87], calcium and magnesium contributing to a "hard water syndrome" [88] and nitrates [89], zinc [90] and fluorides [91] have all been documented to have potential clinical effects. After initial assessment of the feed water and the subsequent installation of the filters and water softeners, a surveillance programme for chemical contaminants, endotoxins and bacteria is important. This logistics of such a programme needs to be considered as the sampling protocol, laboratory protocols and the transport and storage of samples must all be carefully planned.

Microbiological contamination can still theoretically occur. Reverse osmosis units filter out substances with a molecular weight > 200 kDa and thus bacterial fragments and small endotoxins can still pass through [92]. Vigilance must be employed for unexplained febrile episodes or signs of chronic inflammation. This would apply to both home haemodialysis and haemodiafiltration.

Portability is an important factor for dialysis patients. Peritoneal dialysis has provided a treatment that can be carried out virtually anywhere making the treatment appealing for patients who work or need to travel. To date, the quantity of water and the size of the water treatment devices has limited the portability of haemodialysis. Increasingly, there are haemodialysis machines that allow portability by utilizing sorbent technology to purify water and thus reduce water requirements [93]. With the high convective volumes required for adequate HDF, water requirements remain high and thus limit portability. Developments in this area are needed allow to make HDF a more appealing home treatment for patients. Water use must be minimized and where possible, water should be recycled. Water rejected from reverse osmosis units can be recycled and used elsewhere in the home or dialysis unit and this is being increasingly utilized [82].

Anticoagulation must be a major consideration for any extracorporeal dialysis therapy. Many patients on home haemodialysis manage well with the administration anticoagulation, and unfractionated heparin and low molecular weight heparin are in common use. These strategies can also be used in HDF and should not pose a barrier to home HDF use. HDF may allow dialysis without anticoagulation through the use of pre-dilution HDF. This may be particularly helpful in patients with prolonged bleeding or intolerances to anticoagulation.

Today's dialysis technology enables HDF to be delivered in the home setting safely with the production of ultra-pure dialysate and detection of venous dislodgement. There is a growing experience of centres using this technology [94] with a positive experience. Further details on optimal heparinization regimes, water quality variability and its surveillance in home HDF are necessary to define best clinical practice. It is likely that new technology coupled with increasing HDF uptake in dialysis centres will lead on to increasing use of HDF at home.

5.2. Economic impact of HD and HDF

Haemodialysis treatment in general is very costly, and in the United Kingdom, 1–2% of the National Health Service budget is spent on renal care with only 0.05% with ESRF [95]. After consumables, a large proportion of the cost is made up of direct nursing care and transportation [96] (both of which are considerably less in home haemodialysis). Home haemodialysis has been estimated to cost over a third less than hospital-based haemodialysis in the United Kingdom [96] and frequent home haemodialysis has been shown to offer a cost saving in both Canada and Australia too [97].

In addition to the reduced transport and nursing costs, savings are also offered from a reduction in hospital admissions [37] and a reduction in medication costs (particularly phosphate binders) [98].

The initial setup costs of home haemodialysis are high due to the cost of training, the equipment and installation. These initial costs are usually paid back by 14 months after which savings occur [99], making home haemodialysis an attractive option not only from the clinical benefits but also from the cost-saving aspect.

Costs of high-flux dialysers have also reduced considerably over time and high-flux haemodialysis is now the common standard care. A UK Study looked at the costs of 34 patients switching to OL-HDF and 44 who remained on high-flux HD. The cost of the treatment was either more expensive or cheaper depending on the choice of blood lines. There was a cost saving in the OL-HDF group in terms of phosphate binders. Lebourg et al. [81] looked at >28,000 dialysis treatments in a single centre and once again HDF was found to be either cheaper or more costly (-€1.29 to +€4.58 per session) depending on treatment variables selected. It is clear that from a cost perspective, there is little difference between HDF and high-flux HD.

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6. Conclusion

Home haemodialysis provides a convenient and clinically effective way of providing both frequent and extended haemodialysis treatment. Although the hard outcome data for survival from prospective randomized trials are lacking, it is unlikely that a larger, adequately powered trial with sufficient follow-up time will be feasible and the answer may need to come from registry data. It is also time to look beyond urea clearance and towards markers, such as convective volume and β-trace protein, as this may pave the way to further improve haemodialysis care in the future.

However, it is clear that there are a number of clinical benefits from more frequent and extended haemodialysis and aside from this, home haemodialysis is a treatment preferred by many patients if choices are given [100] and a treatment that is associated with an increased satisfaction [101].

HDF is also a feasible treatment in the home setting and is already in use. There is growing evidence from randomized trials that dialysis patient outcomes may be improved by high-frequency HD and by using HDF with high convective volumes. Combining increased frequency HD with convective treatment would give patients the benefits of both small and middle MW clearance without additional patient burden or cost implications. This may pave the way to further improved patient outcomes; however, further randomized clinical studies will be needed for a more definitive answer.

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