

Original Paper

Thrice-Weekly Nocturnal In-Centre Haemodiafiltration: A 2-Year Experience

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Key Words

Dialysis adequacy · Haemodialysis · Phosphate

Abstract

Background: Adequate control of plasma phosphate without phosphate binders is difficult to achieve on a thrice-weekly haemodialysis schedule. The use of quotidian nocturnal dialysis is effective but not practical in the in-centre setting. This quality improvement project was set up as an exercise allowing the evaluation of small-solute clearance by combining convection with extended-hour dialysis in a thrice-weekly hospital setting. **Methods:** A single-centred, prospective analysis of patients' electronic records was performed from August 2012 to July 2014. The duration of haemodiafiltration was increased from a median of 4.5 to 8 h. Dialysis adequacy, biochemical parameters and medications were reviewed on a monthly basis. A reduction in plasma phosphate was anticipated, so all phosphate binders were stopped. **Results:** Since inception, 14 patients have participated with over 2,000 sessions of dialysis. The pre-dialysis phosphate level fell from a mean of 1.52 ± 0.4 to 1.06 ± 0.1 mmol/l ($p < 0.05$). The average binder intake of 3.26 ± 2.6 tablets was eliminated. A normal plasma phosphate range has been maintained with increased dietary phosphate intake and no requirement for intradialytic phosphate supplementation. **Conclusion:** Phosphate control can be achieved without the need for binders or supplementation on a thrice-weekly in-centre haemodiafiltration program.

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Introduction

Patients undergoing conventional dialysis 3 times at 4-hour sessions per week exhibit an excess mortality rate 4 times higher than that of the general population for patients under 30 years, and 6 times that of the general population for patients above 65 years [1]. This increased

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mortality has been attributed to a low dialysis dose [2], but two large randomised controlled trials have failed to show any survival benefit for patients receiving a larger dialysis dose [3, 4].

In an effort to improve outcomes, multiple treatment schedules have been utilised. On-line haemodiafiltration (OL-HDF), which combines diffusion and convection, has grown in popularity over the last 20 years. This provides enhanced clearance of toxins [5, 6], increased haemodynamic stability [7] and better quality of life [8]. The use of more frequent dialysis has also been shown to be beneficial [9, 10]. The advantages in bone mineral profile [11, 12], blood pressure (BP) control [13], patient experience and improved mortality [14] in programs with extended-hour dialysis have been well demonstrated. This is often not an acceptable alternative for patients, and few of the studies of extended-hour dialysis are based in a centre, as the majority of patients in these studies undertake nocturnal dialysis at home. The use of convective therapy in combination with extended-hour dialysis has been shown to be beneficial [15] but is not frequently described.

We have established a program of thrice-weekly 7- to 8-hour nocturnal OL-HDF in our centre in the belief that this will improve quality of dialysis by combining convection with extended-hour treatment. This seemed an excellent compromise for patients who could not have home dialysis but wanted to benefit from having extended hours. The frequency was kept at thrice weekly due to patient preference. The program initially started with 10 patients, and over a 2-year period our patients have had over 2,000 sessions of OL-HDF.

Methods

Data were collected prospectively from patients' electronic records over a 2-year period. Patients were self-selected with no stipulated exclusion criteria apart from patients needing to have their own transport due to the timing of commencement and cessation of treatment. Only 10 patients initially came forward.

Patient Characteristics

During the study period, 14 patients (13 male and 1 female) started nocturnal OL-HDF. The mean age was 45.2 ± 13.1 years (range 23.8–66.2), and renal replacement treatment vintage was 42.34 ± 40.62 months (range 6.61–116.94). All patients were on regular OL-HDF for at least 6 months [mean 30.93 ± 27.68 (range 6.67–93.44)] prior to conversion to the nocturnal regime.

The cause of end-stage renal disease was pyelonephritis/interstitial nephritis, Alport's disease, haemolytic uremic syndrome, reflux nephropathy, membranous nephropathy and renovascular disease (1 patient each); adult polycystic kidney disease, IgA nephropathy, rapid progressive glomerulonephritis and unknown causes (2 patients each). All patients except one had a native arteriovenous fistula. Drop-out reasons prior to 12 months were planned change in modality (1 patient), transplantation (3 patients) or lifestyle choice (1 patient).

Ethical approval was not sought, as this study was a part of quality improvements to services.

Nocturnal Treatment Regime

Patients on standard 4- to 5-hour thrice-weekly OL-HDF were switched to 7- to 8-hour thrice-weekly nocturnal OL-HDF. Patients were dialysed using a Fresenius 5008 machine and a Gambro Polyflux dialyser, without reuse. The blood flow (Q_b) was reduced to 200 ml/min, and dialysate flow (Q_d) was reduced to 300 ml/min. All patients continued on post-dilution

OL-HDF with a dialysate calcium concentration of 1.75 mmol/l and potassium adjusted according to pre-dialysis levels. The dialysate bicarbonate concentration was reduced to prevent the development of alkalosis, and anticoagulation was increased by 50%.

Review of Biochemical and Clinical Parameters

A monthly review of dialysis adequacy, electrolytes and haemoglobin (Hb) measurements was carried out. The baseline biochemical parameters were calculated from the averages of the last 3 months during standard thrice-weekly 4- to 5-hour OL-HDF. Routine samples (before and after dialysis) were collected on the first weekday of the short intradialytic gap of the month. Small-solute clearance was assessed using a standard Kt/V equation (Std Kt/V) [16] with mineral bone disease monitored by plasma phosphate and calcium levels. A reduction in plasma phosphate was expected, so all phosphate binders were stopped. All patients were assessed by a qualified renal dietician and advised to relax their phosphate restriction.

Samples for ferritin and vitamin B₁₂ were analysed every 3 months and for parathyroid hormone (PTH) and β-2 microglobulin every 6 months. Doses of intravenous iron, erythropoietin (darbepoetin-α) and BP medication use were recorded. Changes in medication were at the discretion of the responsible physician.

Average readings of clinical parameters, i.e. BP, weight and hydration, were assessed using a multi-channel bioimpedance Fresenius® body mass composition monitor and analysed with Fluid Management Tool software version 3.3.0.1637 on a quarterly basis.

Statistical Analysis

Data were recorded prospectively for a period of 24 months and included in the analysis where 12 months or more of data were available. These data were analysed using SPSS software package version 17. A repeated measure of analysis of variance was performed with respect to baseline. Each patient served as his/her own control. As the sample size was small, non-parametric statistics were used to compare readings at 24 months with baseline using the Wilcoxon signed-rank test. A value of $p < 0.05$ was considered statistically significant.

Results

Bone Profile

The pre-dialysis phosphate level fell from a mean of 1.52 ± 0.41 to 1.21 ± 0.2 , 1.26 ± 0.45 , 1.28 ± 0.32 and 1.06 ± 0.13 mmol/l at 3, 6, 9 and 24 months, respectively ($p < 0.05$ at 24 months; table 1; fig. 1). The use of binders dropped from an average of 3.26 ± 2.63 tablets to zero ($p < 0.05$; table 1; fig. 1). None of the patients have required recommencement of a phosphate binder or supplementation during dialysis due to low phosphate levels.

Calcium levels were non-significantly raised at 24 months, which theoretically could lead to a positive calcium balance. PTH, however, fell from 39.24 ± 31.4 pmol/l at baseline to 23.97 ± 27.1 and 26.13 ± 12.6 pmol/l at 12 and 24 months, respectively ($p < 0.05$; data not shown). This failed to reach significance when the patient on cinacalcet was excluded ($p = 0.08$ at 6 months and $p = 0.07$ at 12 and 24 months; table 2). None of the patients has required a parathyroidectomy.

Small-Solute Clearance

Std Kt/V increased from 2.37 ± 0.21 (range 1.93–2.65) to 2.68 ± 0.16 (range 2.52–2.92) at 24 months, with $p < 0.05$ at 3, 6, 9 and 24 months compared to baseline (table 1; fig. 2).

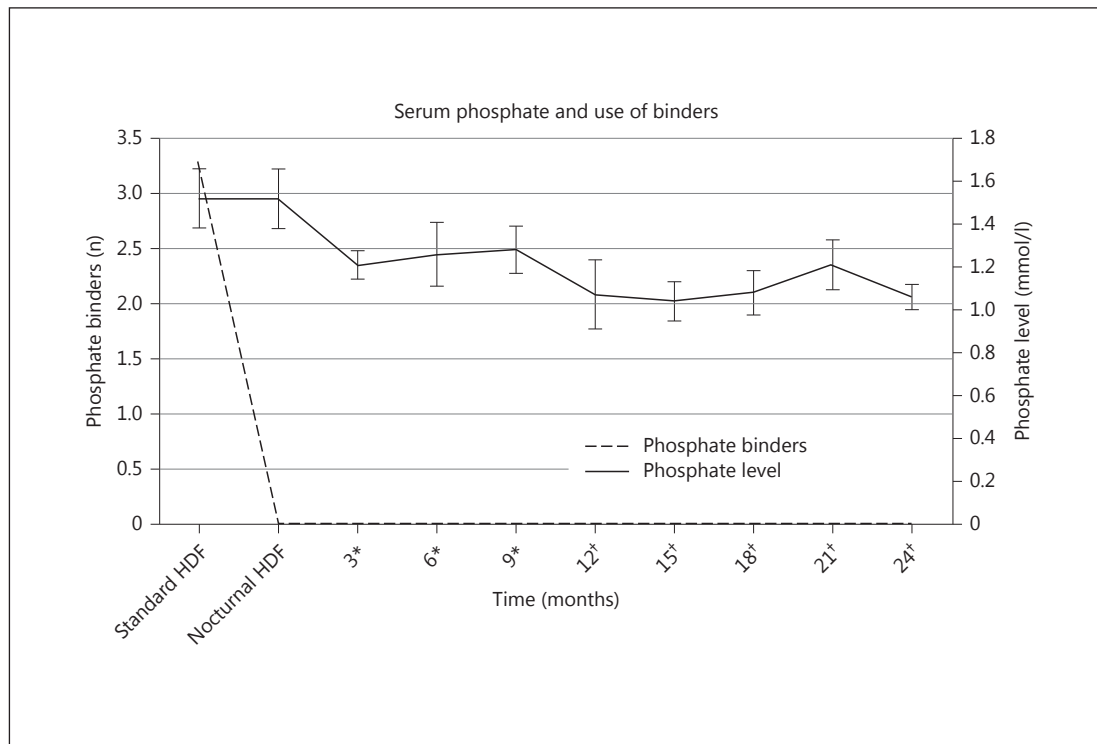


Fig. 1. Significant reduction in the use of phosphate binders ($p < 0.05$ at 3, 6, 9 and 24 months) and phosphate levels ($p < 0.05$ at 24 months) on conversion from standard 4-hour HDF to nocturnal 8-hour HDF. Means \pm standard deviations are given. * $n = 9$, $^{\dagger} n = 5$, where n is the number of patients.

Table 1. Change from thrice-weekly OL-HDF (4–5 h) to thrice-weekly nocturnal HDF (7–8 h)

	Baseline	3 months ($n = 9$)	6 months ($n = 9$)	9 months ($n = 9$)	24 months ($n = 5$)
Time, min	277.22 \pm 25.80	474.26 \pm 9.58 ^a	472.52 \pm 7.92 ^a	476.85 \pm 5.99 ^a	466.60 \pm 13.68 ^c
Volume, l	22.54 \pm 3.91	27.53 \pm 3.19 ^b	27.25 \pm 3.34 ^b	28.26 \pm 3.79 ^a	28.85 \pm 2.22 ^c
URR	0.76 \pm 0.08	0.84 \pm 0.05 ^a	0.83 \pm 0.06 ^a	0.83 \pm 0.05 ^b	0.85 \pm 0.04 ^c
Std Kt/V	2.37 \pm 0.21	2.68 \pm 0.18 ^a	2.62 \pm 0.25 ^b	2.61 \pm 0.19 ^b	2.68 \pm 0.16 ^c
Corr. Ca, mmol/l	2.34 \pm 0.22	2.37 \pm 0.17	2.41 \pm 0.15	2.39 \pm 0.14	2.48 \pm 0.19
PO ₄ , mmol/l	1.52 \pm 0.41	1.21 \pm 0.20	1.26 \pm 0.45	1.28 \pm 0.32	1.06 \pm 0.13 ^c
PO ₄ binders	3.26 \pm 2.63	0.00 \pm 0.00 ^a	0.00 \pm 0.00 ^a	0.00 \pm 0.00 ^a	0.00 \pm 0.00 ^c
Hb, g/dl	11.58 \pm 1.35	11.55 \pm 0.97	11.19 \pm 1.58	12.10 \pm 0.72	11.96 \pm 0.47
Ferritin, μ g/l	492.85 \pm 295.04	463.17 \pm 305.99	423.00 \pm 247.00	342.33 \pm 152.44	321.40 \pm 117.27
EPO, weekly dose	21.85 \pm 21.61	12.96 \pm 16.11	18.52 \pm 16.92	15.74 \pm 13.67	15.00 \pm 8.66
Iron dose, mg/week	50.93 \pm 28.40	29.63 \pm 32.30 ^b	26.85 \pm 23.12 ^b	22.22 \pm 23.20 ^b	45.00 \pm 32.60
Vitamin B ₁₂ , ng/l	440.07 \pm 108.51	480.56 \pm 138.48	520 \pm 141.55	429.67 \pm 128.71	331.80 \pm 37.35
Overhydration, l	1.53 \pm 2.96	1.31 \pm 1.48	1.48 \pm 1.21	1.08 \pm 1.21	1.81 \pm 2.44
Systolic BP, mm Hg	146.63 \pm 21.77	139.52 \pm 26.68	137.26 \pm 25.18	140.30 \pm 30.22	137.47 \pm 17.30
Diastolic BP, mm Hg	75.04 \pm 12.84	70.20 \pm 15.03	67.07 \pm 20.09	70.94 \pm 17.16	69.40 \pm 13.84
BP medications	1.31 \pm 1.04	0.70 \pm 1.31 ^b	0.56 \pm 1.33 ^b	0.67 \pm 1.32 ^b	0.60 \pm 0.89 ^c

Values are means \pm standard deviations. Corr. Ca = Corrected calcium; EPO = erythropoietin; PO₄ = phosphate; URR = urea reduction ratio.

^a $p < 0.01$, with respect to baseline; repeated-measures analysis of variance (ANOVA). ^b $p < 0.05$, with respect to baseline; ANOVA. ^c $p < 0.05$, Wilcoxon signed-rank test.

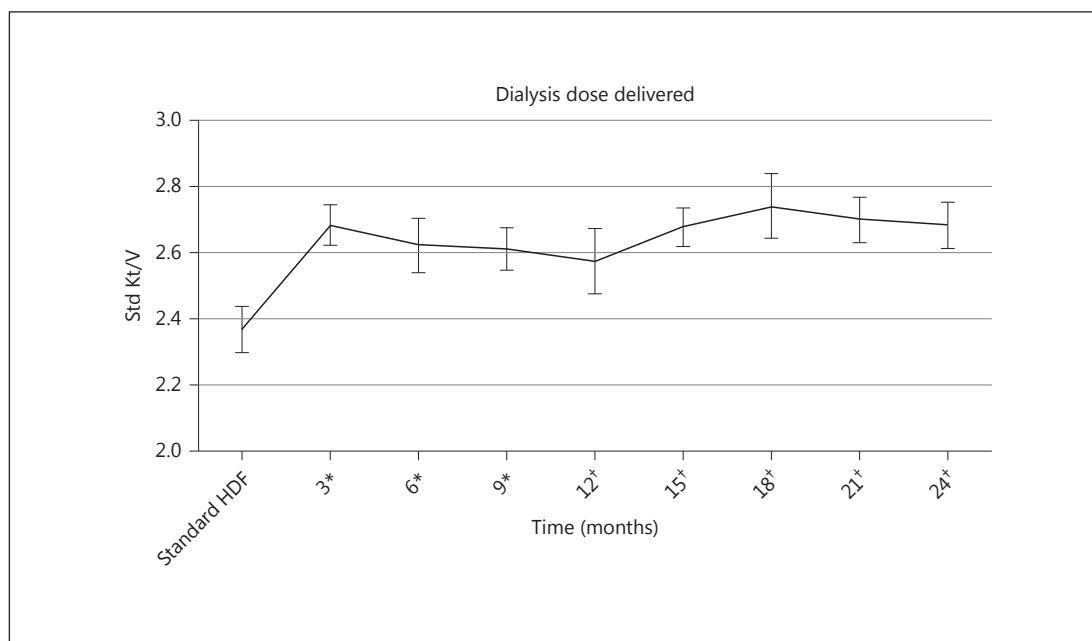


Fig. 2. Significant improvement in the dialysis dose delivered (Std Kt/V) on conversion from standard 4-hour HDF to nocturnal 8-hour HDF at 3, 6, 9, 12 and 24 months. Means ± standard deviations are given. * n = 9, † n = 5, where n is the number of patients.

Table 2. Changes in β -2 microglobulin and PTH levels on changing from thrice-weekly OL-HDF (4–5 h) to thrice-weekly nocturnal OL-HDF (7–8 h)

	Baseline	6 months	12 months	24 months
β 2m, mg/dl	23.34 ± 9.19	20.88 ± 5.99 (n = 9)	20.99 ± 5.21 (n = 9)	24.09 ± 3.13 (n = 5)
PTH, pmol/l	30.52 ± 14.55	21.93 ± 22.53 (n = 7)	15.45 ± 11.84 (n = 7)	20.84 ± 4.82 (n = 4)

Values are means ± standard deviations. PTH data of the patient on cinacalcet were omitted. No significant reduction was observed over time, although changes are almost significant (p = 0.08 at 6 months, p = 0.07 at 12 and 24 months). There was no significant change for β -2 microglobulin.

β 2m = β -2 microglobulin.

Middle-Molecule Clearance

β -2 microglobulin levels showed no significant change. Baseline levels were 23.34 ± 9.19 mg/l and levels at 6, 12 and 24 months were 20.88 ± 5.99, 20.99 ± 5.21 and 24.09 ± 3.13 mg/l, respectively (table 2).

Filtration Volume

The OL-HDF substitution volume increased from 22.53 ± 3.91 litres per session to 27.53 ± 3.19 litres at 3 months and 27.25 ± 3.34, 28.26 ± 3.79 and 28.85 ± 2.22 litres at 6, 9 and 24 months, respectively (p < 0.05 at 3, 6, 9 and 24 months).

BP, Fluid Status and Antihypertensive Medications

BP reduction and changes in overhydration status did not reach statistical significance, but the use of antihypertensive medications decreased from 1.31 ± 1.04 to 0.6 ± 0.89 tablets at 24 months ($p < 0.05$).

Haematological Parameters and Erythropoietin Dose

Intravenous iron use showed a significant decrease from baseline 50.93 ± 28.4 to 29.63 ± 32.3 , 26.85 ± 23.12 and 22.22 ± 23.2 mg/week at 3, 6 and 9 months, respectively, but not at 24 months (45 ± 32.6 mg/week). Erythropoietin use decreased but did not reach statistical significance. Hb levels did not change significantly.

Discussion

Thrice-weekly extended-hour nocturnal OL-HDF seems to be an excellent alternative to current modalities of dialysis. It achieves targets for small-solute clearance and mineral bone disease with elimination of phosphate binders and no dietary phosphate restrictions. It has been accepted and well tolerated by patients.

The unique finding of this study is the complete elimination of phosphate binders without the requirement for intradialytic phosphate supplementation. Phosphate control with dialysis alone was first described in 1998 where patients were converted from conventional thrice-weekly dialysis to dialysis 6 nights weekly. Normal phosphate levels were achieved at 5 months despite a 50% increase in phosphate intake in diet. The blood flow rate was 300–350 ml/min and the dialysate flow rate 500 ml/min [11]. A recent paper by Maduell et al. [15] to evaluate the beneficial effects of alternate-day nocturnal OL-HDF reported a reduction in serum phosphorus from 4.93 ± 1.5 mg/dl (1.59 ± 0.48 mmol/l) to 3.74 ± 1 mg/dl (1.20 ± 0.32 mmol/l) at 12 months. Phosphate binders were reduced, but not eliminated, and intradialytic supplementation was needed in 55% patients. Blood flows were 400 ml/min and dialysate flows were 500 ml/min. The Australian experience of converting patients from a conventional regime to home nocturnal 6- to 9-hour sessions 3.5–4 times weekly resulted in a significant reduction in phosphate levels, again with a reduction in phosphate binder consumption but with 22.7% patients needing supplementation. Blood flow was 200–250 ml/min with a dialysate flow of 500 ml/min [17]. A recent study by a Dutch group comparing conventional [4-hour haemodialysis (HD) and HDF] and extended (8-hour HD and HDF) dialysis reported ‘treatment time’ as a major determinant of small-molecule clearance and haemodynamic stability. The total solute removal (urea, uric acid, creatinine and phosphate) was higher in the longer-duration treatments, with no difference noted in the treatment modalities (HD vs. HDF). Acute effects were only studied in this randomised cross-over trial. Blood flow was 300 ml/min and dialysate flow 600 ml/min in all study sessions [18]. The improvement in small-solute clearance is consistent with other published reports [15, 19]. The normal serum phosphate without the need for supplementation, previously not reported, could either be due to the lower dialysate and blood flows employed or to the reduced frequency of HDF 3 times per week. We, however, could not demonstrate a reduction in middle-molecule levels (β -2 microglobulin). This may be due to the high substitution volumes utilised at baseline in these patients, but it suggests that dialysis duration per se is a less important factor in achieving higher β -2 microglobulin clearance.

Other biochemical parameters such as Hb did not change, though there was a trend towards a reduction in iron and erythropoietin doses. This lowering in erythropoietin doses might have been achieved if iron doses had not been decreased.

Charra et al. [13] in France have reported one of the lowest mortality and morbidity statistics in dialysis patients. Absence of cardiovascular complications and good BP was achieved with maintenance of dry weight, a low-salt diet and no antihypertensive drugs. Despite following a similar regime, our BP lowering did not reach statistical significance. There was a reduction in antihypertensive medications during the study without change in BP, which may suggest overall better BP control. Overhydration (table 1) from a high salt intake contributing to extracellular volume expansion may explain why a significant reduction in BP was not demonstrated.

We noted a significantly higher substitution volume following transfer to the nocturnal program. Theoretically, this may confer a survival advantage in the longer term, as implied by a post hoc sub-analysis of data from two recent randomised controlled trials which showed a lower mortality rate with higher substitution volumes of >17.4 and >21.95 litres per session [3, 4].

Limitations

Our study has limitations due to the small patient numbers and being observational in nature. All patients were self-selected, thus, undoubtedly, more motivated and may have less co-morbidities than conventional dialysis patients. Post-dialysis phosphate monitoring was not conducted. No food charts or 24-hour urine collections were formally recorded to assess increased dietary intake of phosphate, but it is difficult to imagine that patients advised to follow a relaxed diet would continue to adhere to phosphate restriction. Residual renal function was not measured, but as each patient acted as their own control, it is unlikely that this would contribute to the benefits seen. Finally, we do not have a parallel comparator group comparing HD and HDF.

Conclusion

Nocturnal thrice-weekly in-centre OL-HDF is a practical alternative and is superior to conventional OL-HDF in terms of small-solute clearance and control of phosphate and allows a reduction in medication. It has the potential to improve outcomes, but this as yet remains unproven. It has been well tolerated by this patient group and should be considered as a treatment alternative for patients receiving hospital-based HD therapy.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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