THE USE OF NOCTURNAL HOME HEMODIALYSIS AS SALVAGE THERAPY FOR PATIENTS EXPERIENCING PERITONEAL DIALYSIS FAILURE

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Background: Failure of peritoneal dialysis (PD) results in poor quality of life and worsening morbidity in patients with end-stage renal disease (ESRD). Traditionally, hospital-based conventional hemodialysis has been the only option for this patient population. We hypothesized that nocturnal home hemodialysis (NHD), 3–6 sessions per week, 6–8 hours per session, is a suitable alternative salvage therapy for this vulnerable patient group.

Methods: This is a descriptive cohort study of all consecutive ESRD patients failing PD that were converted to NHD at the University Health Network and Humber River Regional Hospital from 2003 to 2005. Our primary objective was to describe the changes in clinical and biochemical indices before and after conversion from PD to NHD.

Results: 69 patients required transfer from PD to another form of renal replacement therapy during the period of interest. Our pilot cohort included 8 ESRD patients (5 males, 3 females; age 53 ± 7 years). Mean duration on PD was 4.8 ± 4.6 years. NHD delivered a higher dose of dialysis, as reflected by lower plasma creatinine concentration 1 year after beginning NHD (from 1107 ± 312 mmol/L with PD to 649 ± 309 mmol/L, p = 0.01) and a rise in standardized Kt/V (from 2.21 ± 0.73 with PD to 4.49 ± 1.92 after 6 months of NHD, to 4.51 ± 1.77 after 1 year of NHD; p < 0.001). There was a progressive and sustained rise in plasma albumin after conversion to NHD (from 31 ± 4 g/L with PD to 39 ± 2 g/L after 1 year of NHD; p = 0.001). Hemoglobin concentrations increased (from 102 ± 13 to 125 ± 7 g/L, p = 0.03), while erythropoietin requirement tended to fall (from 17500 ± 8669 to 9197 ± 7573 U/week). Plasma phosphate fell (from 2.1 ± 0.6 to 1.1 ± 0.3 mmol/L, p = 0.01) despite a decrease in phosphate binder requirement. Blood pressure profile also tended to improve after conversion to NHD.

Conclusion: Nocturnal HD represents a promising, viable, alternative renal replacement therapy for patients experiencing PD failure. The clinical impact of transferring ESRD patients failing PD to NHD deserves further investigation.

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KEY WORDS: Failure on peritoneal dialysis; nocturnal home hemodialysis; home dialysis.

Peritoneal dialysis (PD) is a widely accepted ambulatory form of renal replacement therapy that also offers improved quality of life compared to hospital-based conventional hemodialysis (CHD; 4 hours per session; 3 sessions per week) (1). Unfortunately, peritoneal membrane failure or inadequate clearance is encountered by a subgroup of PD patients, necessitating a switch to CHD. Although various reports have affirmed that conversion from PD to CHD is not associated with an increased mortality, most patients are faced with a more intrusive form of dialysis, resulting in a worsening morbidity profile (2). Moreover, the annual mortality rate of CHD patients in North America remains high, at 15%–20% (3).

Nocturnal hemodialysis (NHD), which provides 8–10 hours of renal replacement therapy during sleep, 5–7 nights per week, is a more intense mode of dialysis (4). To date, NHD has been demonstrated to reverse several important risk factors for adverse cardiovascular events in end-stage renal disease (ESRD) patients, such as hypertension (5), left ventricular hypertrophy (6), systolic dysfunction (7), conduit artery stiffness (8), attenuated baroreflex regulation of heart rate (8), disturbed heart rate variability (9), sleep apnea (10), and endothelium-dependent vasodilation (5). In addition, based on NHD experience, the Toronto group has reported an emerging body of evidence demonstrating the benefits of NHD in anemia management (11), inflammation (12), and endothelial progenitor cell biology (13).

Given that NHD is a home-based therapy that offers an augmented dose of uremia clearance while...
maintaining the patients’ independence, we hypothesized that NHD is a suitable salvage therapy for patients experiencing PD failure. Our primary objective in the present study was to describe the clinical and biochemical course of conversion from PD to NHD in a pilot cohort of ESRD patients failing PD in Toronto.

METHODS

This was a retrospective study using prospectively collected data. Institutional research ethics board approvals were obtained.

Subjects included consecutive ESRD patients failing PD who were converted to NHD at the University Health Network or Humber River Regional Hospital between 2003 and 2005. During this period, NHD was offered widely to all patients failing PD. We did not exclude on the basis of age or comorbidities. Prior to initiating NHD training, a nurse educator conducted an interview to ascertain the patient’s willingness to learn and to adhere to the prescribed therapy.

Patient demographic information such as age, sex, ethnicity, etiology of ESRD, and comorbid conditions was prospectively collected into a computerized clinical database. Clinical information from both PD and NHD data sources were obtained from hospital computer records. All clinical information obtained was cross-referenced and validated with electronic and paper charts as well as with direct patient interview when necessary. For each patient, biochemical and hematological parameters (complete blood count, urea, creatinine, albumin, alkaline phosphatase, calcium, phosphate, and parathyroid hormone) were obtained from the hospital computer records. In total, 69 ESRD patients failed PD during 2003 – 2005 at our centers. Sixty-one patients (24 men, mean age 59 ± 6 years) were transferred to in-center HD. The primary etiologies of renal failure included primary amyloidosis (1), IgA nephropathy (1), lupus nephritis (1), polycystic kidney disease (1), diabetes mellitus (1), congenital horseshoe kidney complicated with hypertension (1), and hypertensive nephrosclerosis (2). While undergoing PD, 5 patients were on continuous cycling PD and the rest were on continuous ambulatory PD. Various mechanical factors and/or inadequate dialysis delivery were responsible for the conversion to NHD, as listed in Table 1. All patients remained on NHD throughout the duration of

HEMODIALYSIS PRESCRIPTION

Each patient received CHD for 4 hours, 3 times per week during CHD treatments and NHD training. Blood flow rate was prescribed at 400 mL per minute and maximized at the nurse’s discretion; dialysate flow rate was 500 – 750 mL per minute. Nocturnal HD treatments consisted of HD at home for 8 – 10 hours, 3 – 6 nights per week (according to treating physician’s prescription). Blood flow rates of 200 – 300 mL per minute and F80 polysulfone dialyzers (Fresenius Medical Care, Lexington, Massachusetts, USA) or Polyflux (polyamide) dialyzers (Gambro, Hechingen, Germany) were used. A dialysate flow rate of 350 mL/minute was used during NHD. The same dialyzers were used for NHD and CHD treatments.

Dialysis dose per treatment was estimated by equilibrated \( Kt/V \) (\( eKt/V \)) as described by Daugirdas and colleagues: \( eKt/V = spKt/V - 0.6(spKt/V)/t + 0.03, \) where \( spKt/V = \) single pool \( Kt/V, K = \) delivered clearance, \( t = \) dialysis time, and \( V = \) urea distribution volume (14). Single pool \( Kt/V \) was determined using the blood urea reduction ratio (15); standardized \( Kt/V \) was derived using the Gotch formula (16). Normalized protein equivalent of nitrogen appearance (nPNA) was calculated by means of urea kinetic modeling using the following formula: \( \text{nPNA} = 9.35U_{\text{Gen}} + 0.294V, \) where \( \text{nPNA} \) is protein equivalent of nitrogen appearance, \( U_{\text{Gen}} \) is urea generation rate, and \( V \) is urea distribution volume.

OUTCOMES AND STATISTICAL ANALYSIS

The primary objective of the study was to determine changes in clinical and biochemical indices before and after conversion from PD to NHD.

Demographic and laboratory data are reported as mean ± SD. Paired Student’s t-test or Wilcoxon rank test was used for comparison of continuous variables before and after conversion to NHD. Repeated measure of analysis of variance was used to ascertain changes in a parameter over time. A two-tailed \( p \) value less than 0.05 (SPSS-14; SPSS Inc., Chicago, Illinois, USA) was required for significance.

RESULTS

In total, 69 ESRD patients failed PD during 2003 – 2005 at our centers. Sixty-one patients (24 men, mean age 59 ± 6 years) were transferred to in-center HD. The main causes of failure on PD were recurrent peritonitis with or without ultrafiltration failure (59%) and mechanical problems (17%). The remainder of the causes for PD failure included failure to cope (13%), patient’s choice (7%), and ultrafiltration failure (4%).

Eight ESRD patients (5 men; mean age 53 ± 7 years) were included in this cohort study. Their baseline characteristics are shown in Table 1. Mean duration of PD was 4.8 ± 4.6 years. The primary etiologies of renal failure were diverse, including primary amyloidosis (1), IgA nephropathy (1), lupus nephritis (1), polycystic kidney disease (1), diabetes mellitus (1), congenital horseshoe kidney complicated with hypertension (1), and hypertensive nephrosclerosis (2). While undergoing PD, 5 patients were on continuous cycling PD and the rest were on continuous ambulatory PD. Various mechanical factors and/or inadequate dialysis delivery were responsible for the conversion to NHD, as listed in Table 1. All patients remained on NHD throughout the duration of
Mean duration of PD 4.8±4.6 years received the more intensive HD prescription. Pressure and phosphate control in those patients that the Tassin regimen. There was a trend for improved blood of the patients received every-other-night dialysis per HD per week (Toronto General Hospital); the remainder (Tables 2 and 3).

Increasing trend in target weight after 1 year of NHD initially during the first 6 months of NHD. There was an medicaments. Dialysis target weight tended to fall initially to NHD, despite withdrawal of antihypertensive conversion to NHD, which suggests that additional mechanisms are needed to explain our present results. Previous reports from the Toronto NHD experience substantiate improvement in nutritional status and a change in amino acid profile (27, 28). More recently, in a cross-sectional study our group also demonstrated a reduction in circulating inflammatory markers associated with the use of NHD when compared with CHD (12). Taken together, it is reasonable to assume that increased nutritional intake and attenuation of uremia-associated inflammation may be responsible for the present observation, which requires further investigation.

Augmentation of uremia clearance by NHD has been shown to normalize phosphate control (29) and enhance erythropoietin responsiveness (11). Hyperphosphatemia is prevalent in ESRD patients secondary to the insufficient phosphate removal offered by conventional renal

### DISCUSSION

Traditionally, CHD has been the only practical option for patients failing PD. Unfortunately, the transfer from PD to CHD is usually associated with increased illness intrusiveness and morbidity (17–19). Nocturnal HD is an emerging mode of intensive HD and has been shown to offer multiple clinical advantages compared to CHD (20). Our present study adds to the growing body of evidence in support of NHD, demonstrating its utility as an alternative mode of renal replacement therapy in patients failing PD. Of specific interest, we observed improvements in albumin levels, anemia management, and phosphate control after conversion to NHD in our pilot cohort.

Malnutrition is prevalent in patients receiving conventional renal replacement therapies (21–23) and has consistently been identified as a potent predictor of death in our patient population (24). Multiple factors contribute to severe malnutrition in ESRD patients and include insufficient dialysis and sustained inflammation. Of the different markers of nutrition and inflammation, hypoalbuminemia is perhaps one of the most potent predictors of increased mortality in the ESRD population (24, 25). Routinely, patients failing PD are demonstrated to have elevated circulatory inflammatory markers. Additionally, the inflamed peritoneal membrane may allow increased protein loss coupled with insufficient uremia clearance (26). In the present study, we documented a progressive and sustained rise in serum albumin level after conversion to NHD. Why would conversion to NHD increase serum albumin? From a hemodynamic standpoint, a fall in extracellular fluid volume may increase the albumin concentration. Interestingly, we noted a fall in dialysis target weight only in the initial 6 months after beginning NHD, which suggests that additional mechanisms are needed to explain our present results. Previous reports from the Toronto NHD experience substantiate improvement in nutritional status and a change in amino acid profile (27, 28). More recently, in a cross-sectional study our group also demonstrated a reduction in circulating inflammatory markers associated with the use of NHD when compared with CHD (12). Taken together, it is reasonable to assume that increased nutritional intake and attenuation of uremia-associated inflammation may be responsible for the present observation, which requires further investigation.

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### TABLE 1

Patient Characteristics (n = 8)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>53±7 years</td>
</tr>
<tr>
<td>Gender distribution (M/F)</td>
<td>5/3</td>
</tr>
<tr>
<td>Mean duration of PD</td>
<td>4.8±4.6 years</td>
</tr>
<tr>
<td>Causes of PD failure (n)</td>
<td>Ultrafiltration failure 2, Repeated peritonitis and ultrafiltration failure 2, Uremic symptoms 2, Uremic symptoms and peripheral neuropathy 1, Nephrectomy 1</td>
</tr>
</tbody>
</table>

PD = peritoneal dialysis.
replacement therapies. Excess accumulation of phosphate is instrumental in inducing secondary hyperparathyroidism. Moreover, emerging evidence demonstrates the cardiovascular toxicity of hyperphosphatemia resulting in soft tissue and vascular calcification (30,31).

Similarly, anemia is a common complication of ESRD that contributes to the high morbidity and mortality in our patient population (32,33). In addition, hospitalization risks and associated costs are significantly less in patients that achieve hematocrit between 36% and 39% (34). Optimal renal replacement therapy can play a role in the correction of anemia and phosphate by removing small and possibly middle/large molecules that inhibit erythropoiesis (35) and delivering appropriate phosphate clearance. Although the long-term clinical impact of transferring failing PD patients with inadequate uremia clearance to NHD remains to be elucidated, the present study affirms the importance of intensive HD in correcting uremia-associated metabolic abnormalities.

Patients failing PD are often transferred to CHD despite the higher cost and increased illness intrusiveness with in-center HD. The use of home-based renal replacement therapies in North America has continued to decrease even though contemporary data support the clinical superiority of PD and NHD over CHD (4,36). The notion of an integrated home dialysis continuum has been hotly debated (37,38). Moreover, home-based dialysis has consistently been demonstrated to provide improved quality of life for ESRD patients (19). It is reasonable to suggest that nocturnal home HD is an intuitive option for patients failing PD. The relative lack of consideration of NHD in the failing PD population signals the need for continual education and research in optimizing dialysis modality case mix and delivering appropriate home-based dialysis regimens. The present study substantiates the feasibility of NHD as a salvage dialysis therapy that provides superior uremia clearance and addresses patient independence.

Our study is limited by its observational nature and its small sample size. We did not compare our NHD cohort with a control conventional dialysis group as this pilot project, given the lack of published data in the transfer of failing PD patients to NHD, was designed as a first step in characterizing the natural clinical course. Despite the limitations of this small observational co-

### TABLE 2
Changes in Biochemical Indices After Conversion to Nocturnal Hemodialysis

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>Training</th>
<th>1st month</th>
<th>6th month</th>
<th>9th month</th>
<th>12th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardized Kt/V</td>
<td>2.21±0.73</td>
<td>2.27±0.37</td>
<td>4.52±1.97a</td>
<td>4.49±1.92a</td>
<td>4.51±1.70a</td>
<td>4.51±1.77a</td>
</tr>
<tr>
<td>Target weight (kg)</td>
<td>66.9±7.5</td>
<td>65.0±8.3</td>
<td>63.9±8.5</td>
<td>63.6±8.2</td>
<td>65.5±10.6</td>
<td>68.7±10.5</td>
</tr>
<tr>
<td>Predialysis creatinine (μmol/L)</td>
<td>1107±312</td>
<td>805±246a</td>
<td>581±197a</td>
<td>549±238a</td>
<td>582±277a</td>
<td>649±309a</td>
</tr>
<tr>
<td>Predialysis urea (mmol/L)</td>
<td>23±8</td>
<td>16±4a</td>
<td>13±5a</td>
<td>13±5a</td>
<td>15±6a</td>
<td>15±7a</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>31±4</td>
<td>34±2a</td>
<td>36±4a</td>
<td>36±2a</td>
<td>39±2a</td>
<td>39±2a</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.25±0.15</td>
<td>2.42±0.23</td>
<td>2.44±0.27</td>
<td>2.40±0.21</td>
<td>2.43±0.17</td>
<td>2.34±0.18</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>2.1±0.6</td>
<td>1.74±0.5</td>
<td>1.46±0.4a</td>
<td>1.47±0.5a</td>
<td>1.30±0.3a</td>
<td>1.13±0.3a</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>88.6±86.2</td>
<td>35.6±19.6</td>
<td>60.7±59.9</td>
<td>65.1±101.8</td>
<td>71.6±117.5</td>
<td>53.1±70.4</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>102±13</td>
<td>107±10</td>
<td>111±14</td>
<td>126±13a</td>
<td>126±10a</td>
<td>125±7a</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>137±18</td>
<td>138±26</td>
<td>141±15</td>
<td>132±21</td>
<td>133±18</td>
<td>123±10</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>87±10</td>
<td>85±18</td>
<td>85±11</td>
<td>82±12</td>
<td>84±15</td>
<td>73±11a</td>
</tr>
</tbody>
</table>

PTH = parathyroid hormone; BP = blood pressure; PD = peritoneal dialysis.

* Denotes $p < 0.05$ compared with PD.

### TABLE 3
Changes in Medication Profile After Conversion to Nocturnal Hemodialysis

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>Training</th>
<th>1st month</th>
<th>6th month</th>
<th>9th month</th>
<th>12th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythropoietin requirement (U/week)</td>
<td>17500±8669</td>
<td>15875±6978</td>
<td>16875±6917</td>
<td>19000±18016</td>
<td>9197±7573</td>
<td></td>
</tr>
<tr>
<td>Patients requiring phosphate binders (n)</td>
<td>8</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>2a</td>
<td></td>
</tr>
<tr>
<td>Antihypertensive requirement (drug/person/day)</td>
<td>1.875</td>
<td>1.125</td>
<td>0.875</td>
<td>0.875</td>
<td>0.57a</td>
<td></td>
</tr>
</tbody>
</table>

PD = peritoneal dialysis.

* Denotes $p < 0.05$ compared with baseline.
hort study, our results, when taken in the context of previous data suggesting that intensive renal replacement therapy may offer significant clinical advantages over CHD, provide sufficient evidence to warrant further examination of NHD as an alternative dialysis therapy for patients experiencing PD failure.

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REFERENCES