Polydipsia: a feature of peritoneal dialysis

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Abstract

Background. Some dialysis patients fail to comply with their fluid restriction causing problems due to volume overload. These patients sometimes blame excessive thirst. There has been little work in this area and no work documenting polydipsia among peritoneal dialysis (PD) patients.

Methods. We measured motivation to drink and fluid consumption in 46 haemodialysis patients (HD), 39 PD patients and 42 healthy controls (HC) using a modified palmtop computer to collect visual analogue scores at hourly intervals.

Results. Mean thirst scores were markedly depressed on the dialysis day (day 1) for HD ($P<0.0001$). The profile for day 2 was similar to that of HC. PD generated consistently higher scores than HD day 1 and HC ($P = 0.01$ vs HC and $P < 0.0001$ vs HD day 1). Reported mean daily water consumption was similar for HD and PD with both significantly less than HC ($P < 0.0001$ for both). However, measured fluid losses were similar for PD and HC whilst HD were lower ($P < 0.0001$ for both) suggesting that the PD group may have underestimated their fluid intake.

Conclusion. Our results indicate that HD causes a protracted period of reduced thirst but that the population’s thirst perception is similar to HC on the interdialytic day despite a reduced fluid intake. In contrast, the PD group recorded high thirst scores throughout the day and were apparently less compliant with their fluid restriction. This is potentially important because the volume status of PD patients influences their survival.

Keywords: compliance; haemodialysis; peritoneal dialysis; polydipsia; thirst

Introduction

Some dialysis patients have difficulty adhering to their prescribed fluid restriction. Consequently, they are susceptible to chronic volume overload, which may contribute to hypertension, left ventricular dilatation or life-threatening pulmonary oedema. Some of them blame an intense, unquenchable thirst for their non-compliance. There has been little work to study this polydipsia partly because thirst is a difficult parameter to quantify.

Fluid intake is regulated by poorly defined systems. It is believed that central osmoreceptors are responsible for generating the perception of thirst as well as stimulating vasopressin release from the posterior pituitary. There is further evidence to suggest that ingested sodium may influence thirst by mechanisms other than increasing serum osmolality. Central volume sensors may also stimulate thirst in states of rapid and extensive volume depletion. Furthermore, there is evidence that the renin–angiotensin axis may also stimulate thirst.

Previous work has suggested that the osmoreceptor system appears to be intact in patients with advanced renal failure [1]. Hyperangiotensinaemia has also been implicated in the polydipsia found in some haemodialysis (HD) patients [2]. More recently, there has been renewed interest in the relationship between sodium balance and thirst in HD patients [3,4]. We are unaware of any data on the prevalence of polydipsia among patients treated with peritoneal dialysis (PD).

We have described previously a novel technique for the measurement of subjective motivation to eat [5–7]. The electronic appetite rating system (EARS) employs a palmtop computer to record serial visual analogue scores (VAS). The recordings can be used to generate profiles showing how subjective parameters such as thirst vary through the day. It is possible to assess the effect of an intervention upon these profiles by making serial recordings and deriving summary statistics for comparative purposes.

This part of our extensive project looking at motivation to eat and nutrient intake was designed to...
determine the thirst profiles for a group of healthy controls (HC) and patients with end-stage renal failure treated with HD and PD. We expected that HD would interfere with thirst perception, but it was unclear whether thirst would fall as osmotically active molecules were removed or increase as a response to the rapid reduction of circulating volume. We expected that PD would have a lesser effect on thirst as patients treated by this modality are in a relatively steady state and tend to be water loaded compared with their HD counterparts.

Subjects and methods

The hospital ethics committee approved the study and informed consent was obtained from all subjects. No individual with a history of surgery to the upper intestine was recruited. Forty-two HC, 46 HD patients and 39 PD patients returned meaningful profiles. All patients were clinically stable and had been established on outpatient treatment for at least 3 months. All dialysis patients were routinely advised to follow a diet with a daily sodium intake of 80–100 mmol. Their recommended fluid restriction varied depending upon their residual urine output. Anuric individuals were typically on a 1000 ml restriction.

The aetiology of renal failure for the HD group was unknown for 11, chronic glomerulonephritides 10, polycystic kidney disease 8, ischaemic nephropathy 7, acute glomerulonephritides 3, atherosclerotic renal artery stenosis 2 and bilateral renal infarction, acute tubular necrosis, reflux nephropathy, cast nephropathy and myeloma 1 each. All HD patients were on thrice weekly bicarbonate-based dialysis employing low-flux ‘biocompatible’ membranes (Asahi AM Bio-wet, Asahi Medical Co. Ltd, Tokyo, Japan or Fresenius F-6 or F-8, Fresenius Medical Care, St Wendel, Germany). Most patients used a dialysate with a sodium concentration of 137 mmol/l.

The aetiology of renal failure for the PD group was unknown for 13, chronic glomerulonephritis 10, ischaemic nephropathy 4, acute glomerulonephritides 2, polycystic kidney disease 2, diabetic nephropathy 2, reflux nephropathy 2, interstitial nephritis 1, myeloma 1, hereditary amyloidosis 1 and atherosclerotic renal artery stenosis 1. Eighteen used continuous ambulatory PD (CAPD) and 21 used automated PD (APD) with a daytime dwell. Fifteen of the APD patients used icodextrin-based fluid for their daytime dwell. Two of the CAPD patients used icodextrin-based fluid for their night-time dwell. All participants attended the dialysis unit in the morning having fasted since the preceding midnight. Fasting blood samples were drawn then participants were instructed how to use the EARS. Three-day dietary records were used to assess water intake. The study participants measured the volume of fluid consumed. The water content of the food eaten was determined by using ‘Microdiet 8.08’ software (University of Salford, Manchester, UK). The controls and PD patients collected their urine for 24 h prior to their visit. The HD group collected their urine for a 48-h period after their initial visit between dialysis sessions. The PD patients also collected their effluent dialysis fluid for 24 h prior to the sampling point. The HD patients all underwent morning dialysis for the purpose of the study. Most completed their treatment at 12:00. All were finished by 13:00. Seven HD and 15 PD patients were taking ACE inhibitors or angiotensin receptor blockers. Standard biochemical and haematological tests were performed in the hospital laboratory. The albumin assay used a bromocresol green method.

Depression scores were collected using the Beck Depression Inventory (BDI) and Cognitive Depression Index (CDI) [8,9]. This represented an attempt to look for links between psychological state and the thirst data.

Thirst recordings

The EARS utilized a palmtop computer (Psion series 3, Psion Computers Ltd, London, UK) programmed with EARS software, which allowed question sets to be entered. The device was programmed to alarm at hourly intervals. Each time the alarm rang the question ‘How thirsty do you feel?’ appeared on the screen. The question was accompanied by a line with ‘extremely’ and ‘not at all’ displayed at either end. Participants used one of two keys to move a cursor left or right along the line thus indicating how thirsty they felt at each time point. Hourly scores were used to produce a profile between 08:00 and 20:00 for the controls and PD. Nineteen controls and 33 PD patients returned results for 2 days. HD entered data between 10:00 and 20:00 on the day of dialysis (day 1) and between 08:00 and 20:00 on the following interdialytic day (day 2). Both days of the HD recording were used for analysis. For a more detailed account of the methodology see Wright et al. [5,6].

Statistical analyses

The EARS stored each VAS as a number between 0 and 100 and the serial recordings were used to generate profiles from the mean of the individuals’ scores at each time point. Summary data derived from the EARS recordings were used to compare the groups. The mean of each individual’s daily scores was used to generate a group mean score. This figure was useful for comparisons but offered little information about the variability of responses so other parameters were created. Each individual’s highest score was reported as the peak and a group mean generated. The standard deviation (SD) of each individual’s thirst scores was calculated and a group mean produced in order to provide some indication of the variability of responses for each group. The reproducibility of the derived scores was assessed using the Bland and Altman technique.

Between group comparisons used ANOVA. Post hoc tests used t-tests with a Bonferroni correction. The HD day 1 and day 2 results were compared directly using paired t-tests. The PD group was subdivided according to modality (CAPD or APD) and compared using t-tests. The populations were divided into quartiles depending upon their mean thirst score and the most and least thirsty individuals compared with t-tests. GraphPad ‘Prism II v 2.01’ and SPSS 9.0 software were used for analyses.

Results

The demographic data from the study groups is shown in Table 1. The dialysis groups had an excess of men compared with the controls. This was not statistically
The HD group was significantly older than the others. None of the subsequent HD data correlated with age. When the PD group was divided according to modality (i.e. APD or CAPD), the APD group were younger (45.4 ± 12.7 vs 55.3 ± 14.7 years, \( P = 0.03 \)) and lighter (64.3 ± 9.5 vs 68.9 ± 12.1 kg, \( P = \text{NS} \)). The weekly \( K_t/V \) and creatinine clearance were higher for those using APD (\( K_t/V \) 2.54 ± 0.42 vs 2.06 ± 0.34, \( P < 0.001 \); creatinine clearance 76.3 ± 28.5 vs 60.7 ± 15.5, \( P = 0.039 \)).

The mean thirst profiles are shown in Figures 1 and 2. The control and HD day 2 profiles were similar in that there was a cyclical pattern with peaks of thirst occurring close to meal times. HD day 1 produced relatively flat traces. The HD day 1 scores were consistently lower than the control group, however, the PD scores were consistently higher.

The derived thirst scores are shown in Table 2. The mean thirst scores demonstrated significant variability between groups with the PD scores higher than control.

### Table 1. Demographic and biochemical features of the study groups

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>HD</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>42</td>
<td>46</td>
<td>39</td>
</tr>
<tr>
<td>Sex</td>
<td>22 M:20 F</td>
<td>31 M:15 F</td>
<td>23 M:16 F</td>
</tr>
<tr>
<td>Age</td>
<td>50 (36–73)</td>
<td>64 (24–77)</td>
<td>53 (23–75)</td>
</tr>
<tr>
<td>Months on dialysis</td>
<td>21 (3–96)</td>
<td>21 (3–140)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.7 ± 4.4</td>
<td>25.3 ± 3.6</td>
<td>23.8 ± 3.9</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>141.0 ± 2.3</td>
<td>139.3 ± 4.2</td>
<td>139.1 ± 3.3</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>5.5 ± 0.56</td>
<td>5.4 ± 1.6</td>
<td>5.6 ± 1.0</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>43.5 ± 2.1</td>
<td>38.2 ± 3.5</td>
<td>36.9 ± 3.1</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>6.8 ± 6.0</td>
<td>13.4 ± 19.4</td>
<td>13 ± 11.9</td>
</tr>
<tr>
<td>Urea (mmol/l)</td>
<td>5.6 ± 1.1</td>
<td>24.8 ± 5.3</td>
<td>17.2 ± 4.7</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>94 ± 12</td>
<td>950 ± 252</td>
<td>876 ± 259</td>
</tr>
<tr>
<td>Total Kt/V</td>
<td>6.6 ± 5.1</td>
<td>11.0 ± 5.2</td>
<td>13.2 ± 7.4</td>
</tr>
<tr>
<td>BDI</td>
<td>6.5 ± 5.0</td>
<td>5.7 ± 4.2</td>
<td>7.9 ± 5.5</td>
</tr>
</tbody>
</table>

Numbers represent mean ± SD except age and months on dialysis (median and range). Blood tests represent predialysis values for HD. \( K_t/V \) figures are per treatment for HD and per week for PD. Mean weekly PD creatinine clearance was 69.34 ± 24.57. \( P < 0.001 \) vs control; \( b P < 0.001 \) vs PD; \( c P < 0.05 \) vs control.
and HD day 1 on post hoc tests. The HD group had a significantly lower mean score on day 1 than day 2 ($P < 0.0001$) when compared by paired t-test. Peak values also demonstrated significant variation with PD significantly higher than HD day 1. The HD day 1 peak was significantly lower than day 2 when compared directly ($P < 0.0001$). The SD scores were not significantly different by ANOVA. Despite this, the HD day 2 SD was significantly greater than day 1 by paired t-test ($P = 0.018$).

The reproducibility of the derived thirst scores are shown in Table 3. Again, there were significant differences between day 1 and day 2 for the HD group. The control and PD groups demonstrated little day-to-day bias. The limits of agreement were appreciable indicating that some people did return different values on the 2 days. The reader will recognize that people do feel more thirsty on some days than others.

The reported water intake was lower for the PD and HD patients than the controls. The dialysis groups reported similar mean daily fluid consumption. When the PD group was divided by modality, water consumption was higher for the APD group (20.6 ± 7.4 vs 16.0 ± 5.1 g/kg/day, $P = 0.041$). When the patients using icodextrin were compared with those that were not, the difference was more pronounced (icodextrin 22.1 ± 7.5 vs glucose only 15.7 ± 4.9 g/kg/day, $P = 0.005$).

It was possible to assess the accuracy of the reported fluid consumption figures by measuring the participants’ fluid losses. If the daily fluid loss derived from volume of urine, interdialytic weight gain (HD) and volume of effluent (PD)] were subtracted from the reported fluid intake, the result should have been approximately +0.5 kg/day (insensible losses). HD vs both $P < 0.01$, PD vs control $P < 0.001$.

The depression scores were higher for the dialysis patients than controls with the BDI but not the CDI. The CDI questionnaire is an abbreviated version of the BDI. The six questions removed cover somatic symptoms. These can be attributable to depression, but they can also reflect chronic disease states such as renal failure. Consequently, it is not surprising that the dialysis patients had high BDI scores. The CDI scores were similar to controls indicating that cognitive function was similar between the three groups.

<table>
<thead>
<tr>
<th>Table 2. Mean derived thirst scores and water intake data</th>
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<tbody>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Mean thirst</td>
</tr>
<tr>
<td>Peak thirst</td>
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<tr>
<td>SD thirst</td>
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<tr>
<td>Water intake g/kg/day</td>
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</table>

Numbers represent mean ± SD. $^a P < 0.001$ vs PD; $^b P < 0.05$ vs control; $^c P < 0.001$ vs control.

<table>
<thead>
<tr>
<th>Table 3. Reproducibility of the derived thirst scores over 2 days (day 1–day 2)</th>
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<tbody>
<tr>
<td>Bias</td>
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<tr>
<td>Control mean</td>
</tr>
<tr>
<td>HD mean</td>
</tr>
<tr>
<td>PD mean</td>
</tr>
<tr>
<td>Control peak</td>
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<tr>
<td>HD peak</td>
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<tr>
<td>PD peak</td>
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<td>Control SD</td>
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<td>HD SD</td>
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<td>PD SD</td>
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$P$ value represents the result of a paired t-test between the day 1 and day 2 values.
was no relationship between the BDI or the CDI and the thirst parameters or fluid intake for any group.

Discussion

We are unaware of any previous data measuring thirst profiles even in healthy populations. The control group indicated that most people felt thirsty around meal times with another peak at mid-afternoon. Both dialysis groups demonstrated notable departures from this 'normal' pattern.

The process of HD caused a protracted suppression of thirst whilst the interdialytic day profiles followed the control group closely. This may indicate that changes in osmoreceptor hydration were more important to thirst regulation than the rapid loss of circulating volume caused by ultrafiltration. Patients with advanced renal failure appear to have normal osmoreceptor function [1] and low sodium HD has been shown to reduce thirst scores and interdialytic weight gain [4] implying that this mechanism is relevant in dialysis patients.

Urea traverses the cell membrane with relative ease; consequently, the rise in urea between HD treatments should not produce an osmotic gradient sufficient to cause osmoreceptor dehydration. However, the rapid removal of solutes from the blood during HD will lead to a transmembrane concentration gradient as urea movement out of the intracellular compartment lags behind. This may cause a transient increase in osmoreceptor cell hydration with a consequent decrease in perceived thirst. The similarity between the HD day 2 and control results indicates that the 'osmostat' resets to a new level over time. Indeed, there is evidence that brain cells eventually achieve osmotic equilibrium with persistently hypertonic plasma in vitro [10].

The PD thirst profiles were different to the controls and HD suggesting that other factors must explain their significantly higher scores. Previous work on polydipsia has concentrated on the HD population. Our results suggest that PD patients are more likely to suffer from persistent thirst than HD patients. This is important because PD patients are often salt and water overloaded [11–13] and this is associated with an adverse outcome [14]. Furthermore, the hypertonic glucose solutions used to remove this excess are detrimental to the long-term function of the peritoneal membrane.

Figure 3 indicated that many of the PD patients appeared to under-report their water consumption, indeed, 80% of the PD patients rated their fluid intake below their measured fluid losses. Clinical assessment did not indicate widespread fluid depletion but the higher serum albumin and creatinine concentrations seen in the thirstiest individuals could represent intravascular volume depletion.

It is important to recognize that thirst perception and fluid intake are governed by a complex interaction between psychological and physiological stimuli. Whilst our crude assessment of psychological state using the depression rating scores did not show any large differences between the HD and PD groups, they clearly do represent different lifestyles. PD patients have a greater degree of autonomy than their HD counterparts. Furthermore, they often have a more liberal fluid allowance because of ongoing ultrafiltration and greater residual renal function. The HD population have their interdialytic weight gain assessed thrice weekly with excessive gains prompting advice from the dialysis unit staff and dieticians. The apparent inaccuracy of the PD dietary records suggest that they were less stringent in monitoring their fluid balance.

The discrepancy in water intake between the APD and CAPD patients was of interest. When short fluid dwell times are used (APD) there is less sodium removal per litre of ultrafiltrate than with long dwells (CAPD). This may lead to sodium loading and increased fluid consumption in APD [15]. We did not detect differences in the APD and CAPD thirst data in this cross-sectional study, possibly because most of the APD group used icodextrin, which removes sodium more effectively than glucose-based fluid [16]. A prospective comparison of thirst data and sodium removal before and after conversion from one modality to the other would be required to test this hypothesis.

There is a theoretical mechanism by which icodextrin itself could lead to increased fluid consumption. The glucose polymer is broken down to smaller osmotically active molecules that accumulate in the circulation. The early icodextrin studies suggested that this hyperosmolar state caused movement of water out of cells [17]. It is conceivable that resulting osmoreceptor dehydration may be reflected by an increased motivation to drink and thus fluid intake. This may indicate that although icodextrin-based fluid is effective at removing water, the metabolic consequences of its use increase fluid intake.

In summary, the data we present here indicate that PD patients feel more thirsty than controls and HD patients. The clinical relevance of this finding requires further investigation, but it may be relevant to the volume overload common in PD patients and is likely to adversely affect their quality of life. We believe that the technique described here has considerable potential to help us understand the mechanisms that drive dialysis patients to drink to excess and to find new strategies to tackle the problem.

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Conflict of interest statement. None declared.

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