A novel technique to demonstrate disturbed appetite profiles in haemodialysis patients

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Abstract

Background. Malnutrition is common among dialysis patients and is associated with an adverse outcome. One cause of this is a persistent reduction in nutrient intake, suggesting an abnormality of appetite regulation.

Methods. We used a novel technique to describe the appetite profile in 46 haemodialysis (HD) patients and 40 healthy controls. The Electronic Appetite Rating System (EARS) employs a palmtop computer to collect hourly ratings of motivation to eat and mood. We collected data on hunger, desire to eat, fullness, and tiredness. HD subjects were monitored on the dialysis day and the interdialytic day. Controls were monitored for 1 or 2 days.

Results. Temporal profiles of motivation to eat for the controls were similar on both days. Temporal profiles of motivation to eat for the HD group were lower on the dialysis day. Mean HD scores were not significantly different from controls. Dietary records indicated that dialysis patients consumed less food than controls.

Conclusions. Our data indicate that the EARS can be used to monitor subjective appetite states continuously in a group of HD patients. A HD session reduces hunger and desire to eat. Patients feel more tired after dialysis. This does not correlate with their hunger score, but does correlate with their fullness rating. Nutrient intake is reduced, suggesting a resetting of appetite control for the HD group. The EARS may be useful for intervention studies.

Keywords: appetite; electronic appetite rating system; haemodialysis; malnutrition; protein intake

Introduction

Malnutrition is present in up to two-thirds of haemodialysis (HD) patients [1,2]. Malnourished dialysis patients are at a greatly increased risk of infection, morbidity, and mortality when compared to their well-nourished counterparts [1,3]. Numerous factors interact to cause depletion of body tissue and nutrients in end-stage renal disease (ESRD). These factors include ongoing inflammation, dialysis-related nutrient losses, and metabolic acidosis. In order to counterbalance these catabolic drives, the dietary requirements for HD patients are greater than for healthy subjects (minimum protein intake of 1.0–1.2 g/kg/day compared with 0.75 g/kg/day for healthy subjects and energy intake of 35–40 kcal/kg/day) [4–6]. Unfortunately, nutrient intake begins to reduce spontaneously long before dialysis is required to replace renal function [7] and progresses such that anorexia is one of the hallmarks of uraemia. The discrepancy of increased nutrient requirements but decreased nutrient intake implies that these patients have a disorder of their appetite regulation system and that this disorder is an important factor in the aetiology of malnutrition in this group.

It is assumed that the low nutrient intake of ESRD patients is related to accumulation of toxins that are normally removed from the body by the kidney. There is evidence to support this in that nutrient intake increases when dialysis commences and is related to the amount of dialysis in some studies [8,9]. Despite this, dietary surveys of HD patients have consistently documented a mean protein intake of less than 1.0 g/kg ideal body weight/day and energy intake 26–29 kcal/kg ideal body weight/day [10]. No single anorectic factor has been identified, although animal studies suggest that ‘middle’ molecules between 1 and 5 kDa are the most potent appetite suppressants [11]. More recently, elevated levels of the hormone leptin have been documented in dialysis patients and related to surrogate measures of appetite [12]. Numerous other factors such as intercurrent inflammatory illness, depression, and medication may contribute to the anorexia of ESRD.
Research in this field has been limited because appetite is a difficult parameter to quantify. Previous studies of dialysis patients have examined surrogate measures such as nPCR or self-reported dietary intake. Both of these techniques have their limitations. The electronic appetite rating system (EARS) uses a modified electronic personal organizer (Psion 3 series, Psion Computers plc, London, UK) to record serial visual analogue scores (VAS). VASs have been extensively used in appetite studies to track subjective states and have been shown to be sensitive to physiological state and nutritional challenges [13]. By periodically asking volunteers to rate their appetite using VASs, a profile of motivation to eat and mood can be achieved. The EARS has previously been validated [14] and used to track subjective states of appetite and mood in healthy volunteers [15,16]. This cross-sectional observation study was designed to assess the utility of the EARS in a group of HD patients. The effect of a HD session on the various profiles was assessed and the results compared with a group of healthy controls. EARS profiles were also compared with self-reported nutrient intake.

Subjects and methods

The study was granted ethics committee approval and informed consent obtained from all subjects. Fifty HD patients were recruited with four returning insufficient records, leaving 46 sets of data for analysis (31 M, 15 F; mean age 60.4, range 24–77 years). All of the patients recruited tolerated the dialysis procedure without overt symptomatic hypotension or other dialysis-related symptoms. Two of those whose recordings were discarded failed to enter data because they were asleep for much of the day following their dialysis session. Forty-one healthy controls were recruited with only one returning an insufficient record (21 M, 19 F; mean age 50.1, range 36–73 years). Controls were recruited from hospital/university staff and the relatives of other staff and patients.

All subjects attended our unit in the morning. HD patients were clinically stable and had been on outpatient HD for a median of 21 months (range 3–96). Aetiology of renal failure was chronic glomerulonephritis, 9; hypertensive nephropathy/renovascular disease, 9; autosomal dominant polycystic kidney disease, 8; rapidly progressive glomerulonephritis, 4; myeloma, 2; cortical infarction, 1; reflux nephropathy, 1; and uncertain, 12. Patients with severe visual impairment, deafness, or a history of surgery to the upper intestine were excluded. No diabetic patients were included in the analysis because few were eligible for recruitment. This reflects our preference for peritoneal dialysis for most of our diabetic patients and poor visual acuity in those who were maintained on HD.

Patients were instructed in the use of the EARS during their routine dialysis session. All patients were on thrice-weekly bicarbonate-based dialysis. The duration of treatment ranged from 210 to 300 min (median 240 min). All treatments used low-flux ‘biocompatible’ membranes, i.e. polyethylene glycol grafted cellulose (Asahi AM Bio-Wet, Asahi Medical Co Ltd, Tokyo, Japan) or polysulphone (F-6 or F-8, Fresenius Medical Care, St Wendel, Germany).

The EARS was programmed to ask: ‘How hungry do you feel?’, ‘How strong is your desire to eat?’, ‘How full do you feel?’ and ‘How tired do you feel?’. Each question was accompanied by a line with ‘extremely’ and ‘not at all’ displayed at either end. The subjects used two keys to move a cursor along the line, thus providing a subjective score for each parameter at each time point. For a further description see King et al. [16]. All questions were repeated hourly between 10:00 and 20:00 on the dialysis day (day 1) and again between 08:00 and 20:00 on the following day (day 2). Controls entered responses between 08:00 and 20:00 for one (n = 27) or two days (n = 12). All subjects were instructed in the use of the EARS by the same investigator.

Body mass index (BMI), mid-arm circumference (MAC) and percentage body fat (derived from four-site skinfold anthropometry) were recorded for each patient. Kt/V and nPCR were calculated from blood samples and residual urine output [17].

Breakfast, mid-morning biscuits, and a light lunch were provided for HD patients during their dialysis. All other meals were ad libitum. Most dialysis sessions were completed by 13:00, the latest being completed at 14:05. Patients returned home after their treatment session.

All subjects were asked to complete a 3-day diet diary in order to assess their protein and energy intake. The HD group began their dietary record on the same day as their EARS recording. Some controls began their dietary record on the same day as the EARS recording, some began on the preceding day. One specialist renal dietician assessed all of the records. Total nutrient intakes were estimated using ‘Microdiet 8.08’ software (University of Salford, Manchester, UK). Forty-three of the HD group (29 M, 14 F) and 36 controls (19 M, 19 F) returned useful dietary records. The others had insufficient information to estimate nutrient intake accurately.

Statistics

All data was normally distributed (confirmed by Kolmogorov–Smirnov normality test). A repeated measure ANOVA was used to assess the temporal pattern of appetite and mood within each group. Mean daily scores were compared between groups using one-way ANOVA. Post hoc comparisons used paired t-tests for HD day 1 and day 2 and unpaired t-tests for HD and control analyses (Bonferroni correction). Correlation used Pearson’s method. The GraphPad Prism II v 2.01 software (GraphPad Software Inc, San Diego, USA) was used for all comparisons.

Results

There was no significant difference in sex distribution between the groups; however, there was a significant age difference (P < 0.0001). None of the subsequent mean EARS scores or dietary intake data correlated with age (e.g. mean hunger vs age, control t = −0.245; HD day 1 r = −0.163; HD day 2 r = −0.014; mean fullness vs age, control r = 0.180; HD day 1 r = 0.117 and HD day 2 r = 0.049). When the HD and control groups were divided according to sex or age (by decade) there was no significant difference for any of the mean EARS scores. There was no significant difference between day 1 and day 2 EARS scores for the control group (e.g. mean hunger day 1 = 36.7 (9.4)
VS day 2 = 35.0 (9.7); P = NS), for this reason, subsequent results report control day 1 data only.

**EARS profiles**

The profiles for controls and HD patients are shown in Figures 1–3. Control profiles of hunger and ‘desire to eat’ (Figure 1) demonstrate the typical meal-induced fluctuations for lunch (12:00–14:00) and dinner (17:00–19:00). Control fullness demonstrated a reciprocal pattern to hunger and desire to eat (Figure 2). Control tiredness showed a progressive increase through the day (Figure 3). Table 1 shows the repeated measures ANOVA results to test for variability of EARS responses with time. The F value represents the ratio of between-group and within-group variance where each group is an hourly time point. Higher F values indicate that responses vary to a greater degree when compared to the daily mean. The results indicate that the fluctuating responses seen in Figures 1–3 represent highly significant changes for all of the control parameters.

Figures 1–3 also show the results for the HD patients. Table 1 confirms that there was a significant effect of time on all parameters except HD day 1 tiredness. The variability with time was greater on day 2 as illustrated by the relatively flat day 1 profiles. Furthermore, when the HD scores on each day were compared (Table 2), the mean daily ratings for hunger and desire to eat were significantly higher on day 2. In contrast, fullness and tiredness ratings were higher on the dialysis day. Mean HD scores were not significantly different from controls on either day.

There was a strong correlation between ‘hunger’ and ‘desire to eat’ (controls r = 0.923; HD day 2 r = 0.972, both P < 0.001 and HD day 1 r = 0.785, P = 0.004). Hunger and fullness inversely correlated for the controls and HD day 2 results (controls r = −0.701, P = 0.008. HD day 2 r = −0.919, P < 0.0001) but not on HD day 1. There was no correlation between hunger and tiredness on either day, but the HD day 1 fullness and tiredness scores were related (r = 0.657, P = 0.028).

**Dietary records**

Neither groups’ dietary records showed any significant day-to-day variation by repeated measures ANOVA. Table 2 indicates that the protein and energy intake was lower for the HD patients than the controls (mean daily protein intake HD vs control P = 0.001; mean daily energy intake HD vs control P = 0.019). Approximately two-thirds (63%) of the HD group reported their protein intake to be less than 1.0 g/kg/day, and 86% reported an energy intake below 35 kcal/kg/day.

The HD day 1 fullness scores were positively related to mean protein intake (r = 0.4, P = 0.008), but the control group demonstrated a weak negative relationship between these parameters (r = −0.315, P = 0.051). There was no correlation between hunger and protein intake.

The mean two-pool Kt/V for the HD population was 1.20 ± 0.27 and the nPCR was 0.96 ± 0.23. The Kt/V was related to energy intake (r = 0.342, P = 0.020) and nPCR correlated with reported protein intake (r = 0.404, P = 0.005). Neither Kt/V nor nPCR was related to any EARS parameter.

**Nutritional markers**

Table 3 indicates that the mean anthropometric measurements of the HD group were similar to the controls with the exception of their lower fat mass (P < 0.05). Haemoglobin and albumin values were also lower for HD (P < 0.001). The mean CRP was nonsignificantly higher for the HD group. Correlation was
Fig. 2. Fullness profiles.

Fig. 3. Tiredness profiles.

Table 1. Repeated measures ANOVA results to test for variability of responses with time

<table>
<thead>
<tr>
<th></th>
<th>HD day 1</th>
<th>HD day 2</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>P</td>
<td>F</td>
<td>P</td>
</tr>
<tr>
<td>Hunger</td>
<td>2.51</td>
<td>&lt;0.0007</td>
<td>6.17</td>
</tr>
<tr>
<td>Desire to eat</td>
<td>2.93</td>
<td>&lt;0.002</td>
<td>5.89</td>
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<tr>
<td>Fullness</td>
<td>2.50</td>
<td>&lt;0.0007</td>
<td>4.86</td>
</tr>
<tr>
<td>Tiredness</td>
<td>1.69</td>
<td>NS</td>
<td>4.78</td>
</tr>
</tbody>
</table>

Table 2. Mean daily EARS scores and nutrient intake

<table>
<thead>
<tr>
<th></th>
<th>HD day 1</th>
<th>HD day 2</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunger</td>
<td>31.4 ± 10.9*</td>
<td>37.6 ± 12.3</td>
<td>34.4 ± 10.4</td>
</tr>
<tr>
<td>Desire to eat</td>
<td>32.1 ± 12.3*</td>
<td>40.6 ± 12.7</td>
<td>34.7 ± 11.2</td>
</tr>
<tr>
<td>Full</td>
<td>54.2 ± 10.4*</td>
<td>51.5 ± 8.2</td>
<td>52.0 ± 9.1</td>
</tr>
<tr>
<td>Tired</td>
<td>48.1 ± 18.0*</td>
<td>41.0 ± 16.1</td>
<td>39.2 ± 19.1</td>
</tr>
</tbody>
</table>

EARS scores represent the mean ± SD of each subject’s daily means. *P < 0.0001 vs HD day 2; †P < 0.05 vs HD day 2; ‖P < 0.01 vs HD day 2 (all using paired t-test). Nutrient intake scores represent the mean daily intakes from 3-day dietary records (protein intake P < 0.01; energy intake P < 0.05).
evident between several measures of nutritional status and EARS scores for the control group. BMI was related to mean fullness \( r = 0.336, P = 0.03 \) as was fat mass \( r = 0.327, P = 0.034 \). Serum albumin demonstrated a negative correlation with mean fullness \( r = -0.315, P = 0.042 \). Haemoglobin was negatively related to mean tiredness \( r = -0.324, P = 0.038 \).

There was no relationship between any of the EARS parameters on either day 1 or day 2 and the nutritional indices for the HD group.

**Discussion**

We have demonstrated that the hunger, desire to eat, and fullness profiles of a group of HD patients are similar to those of controls on days without dialysis, but markedly different on dialysis days. We have also demonstrated that these normal profiles exist in the presence of a low protein and energy intake for the HD group.

Appetite regulation can be regarded as a series of feedback loops governing satiation (the process which stops ingestion at the end of a meal), satiety (the process which provides background inhibition of feeding urges), and feeding (which occurs in the absence of satiety) [18]. A considerable number of circulating molecules and neural pathways have been implicated in the peripheral and central regulation of nutrient intake in addition to various psychosocial factors. The EARS constructs a profile that summarizes the effect of these interacting factors in a convenient way and facilitates data processing. The profiles in this study indicate that subjective states of appetite in most HD patients follow the same predictable cyclical pattern seen in healthy individuals; however, this pattern is markedly abnormal on the dialysis days, with a protracted suppression of hunger. The dietary records suggested that this was not caused by over-eating after dialysis.

The similarity of the control and HD day 2 profiles is striking. This suggests that the mechanisms governing motivation to eat are interacting normally but at a lower level of nutrient intake. Target nutrient requirements for dialysis patients are higher than for controls [19]. Reduced mobility resulting from chronic illness may counteract disease-related catabolism to a degree [20], but our patients were mostly mobile and several of them were in full-time employment. In order to explain the discrepancy between predicted nutrient requirements and appetite scores we have to assume that the appetite regulation systems are malfunctioning (even on interdialytic days) or that the nutritional guidelines overestimate the requirements of most HD patients. One possible mechanism that could explain such a malfunction is premature satiety related to high levels of gastrointestinal peptides [21,22]. Indeed, there was a positive relationship between subjective fullness ratings and protein intake. Alternatively, long-term central suppression of food intake by substances such as leptin may be the dominant factor. Whatever the underlying pathophysiological problem, patients currently need to eat beyond their appetite drive if they are to achieve their target nutrient intake.

The differences between day 1 and day 2 indicate a severe disruption of the usual regulatory mechanisms following dialysis. This may reflect a protracted action of accumulated anorexigen prior to dialysis or the effect of cytokine release following contact between blood and the dialysis membrane. Alternatively it may be related to the rapid changes in body chemistry and circulating blood volume that occur during treatment. The resulting ‘post-dialysis fatigue’ may be relevant because tiredness scores were consistently higher on day 1. Tiredness may reduce physical activity after dialysis, which, in turn, may reduce the overall daily energy expenditure [20]. This is unlikely to be the sole explanation for the markedly abnormal appetite profiles because there was no correlation between tiredness and hunger. It seems more likely that the metabolic changes of dialysis disrupt the complex chemical and social mechanisms regulating feeding and, coincidentally, induce a sense of tiredness.

Our data demonstrated a relationship between mean fullness and nutrient intake for HD day 1. Furthermore, Hylander et al. [23] demonstrated a marked reduction of eating velocity and total food consumed in HD patients when compared to controls. This phenomenon may be related to disturbances of gastric motility and myoelectrical activity that have been documented post-dialysis [24,25]. The aetiology of this disturbance is not clear, but release of gastrointestinal hormones such as CCK may contribute. If disturbed gastric motility were the dominant factor underlying the post-dialysis appetite disturbance, it would explain why some patients anecdotally report a marked increase in hunger after dialysis, yet fail to show a significantly higher nutrient intake or hunger profile on that day. They may consume food soon after dialysis but quickly feel full and this sense of fullness then persists through the rest of the day until gastric motility improves.

It is not surprising that the mean daily scores show little correlation with the mean daily nutrient intake. When recordings are made on an hourly basis, there is opportunity for the participants to eat between recordings. Consequently, an individual who eats several times per day will have a high nutrient intake without...
ever generating high hunger scores. Eating and hunger can become disengaged; therefore hunger cannot be regarded as a predictor of food intake in all situations [26,27]. Appetite ratings have been shown to correlate with nutrient intake in some intervention studies [28], but this effect depends heavily upon the design of the study and the way the data is processed [29]. The purpose of this paper is to report the baseline profiles for a group of HD patients. The EARS could be a useful tool to assess the effect of antagonists for putative appetite suppressants (e.g. leptin) on the appetite profiles of malnourished individuals. Further studies will be needed to assess the relevance of such changes to the long-term effects on nutritional end-points or mortality/morbidity.

In summary, we used the EARS to define appetite patterns in a group of HD patients and compare them with controls. We have demonstrated that the dialysis procedure disrupts appetite regulation but that the profile returns to normal on the interdialytic day. HD patients apparently reset their appetite perception to a lower nutrient intake, and therefore they need to eat beyond their appetite drive if they are to reach their target nutrient intake. Further studies could use this tool to elucidate the pathophysiology underlying these abnormalities.

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References

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