Nutritional status of hemodialysis patients with secondary hyperparathyroidism


Abstract

The repercussions of secondary hyperparathyroidism on the nutritional status of chronic renal failure patients have not been well established. Therefore, the aim of this study was to compare the nutritional indices of hemodialysis patients with and without secondary hyperparathyroidism. Sixteen hemodialysis patients with serum parathyroid hormone (PTH) levels higher than 420 pg/ml (hyperparathyroidism group) were matched for gender, age and length of dialysis treatment to 16 patients with serum PTH between 64 and 290 pg/ml (control group). The following parameters were assessed: anthropometric indices (body mass index, skinfold thickness, midarm muscle circumference and body fat), 4-day food diaries, protein catabolic rate, biochemical indices (blood urea nitrogen, serum creatinine, albumin, ionized calcium, inorganic phosphorus, serum alkaline phosphatase, PTH, pH and HCO₃⁻) and dialysis efficiency. We did not observe differences in the anthropometric indices between the two groups. Only calcium intake was significantly different between groups (307.9 mg/day for the hyperparathyroidism group vs 475.8 mg/day for the control group). Protein catabolic rate tended to be higher in the hyperparathyroidism group compared to the control group (1.3 vs 0.9 g kg⁻¹ day⁻¹; P = 0.08). Except for blood urea nitrogen (86.4 vs 75.7 mg/dl), alkaline phosphatase (175 vs 65 U/l) and PTH (898 vs 155 pg/ml), no other differences were found between groups in the biochemical indices studied. PTH was directly correlated with protein catabolic rate (r = 0.61; P<0.05) and length of dialysis (r = 0.53; P<0.05) only in the hyperparathyroidism group. Considering the indices used, we could not demonstrate the deleterious effect of high PTH levels on the nutritional status of hemodialysis patients. Indirect evidence, however, suggests an action of PTH on protein metabolism.

Introduction

Malnutrition is present to some extent in approximately 40% of chronic renal failure (CRF) patients on maintenance hemodialysis (1,2). Several markers of malnutrition such as low body mass index and low serum albumin have been associated with high morbidity and mortality rates in this group of patients (3,4). Malnutrition in these patients is considered to be due to anorexia with low food intake (5-7), to the loss of nutrients and catabolism during the dialysis procedure (8,9), intercurrent illnesses (10), metabolic...
acidosis (11), glucose intolerance (12), increased cytokine levels (13), and other hormonal derangements (14). Among these last disturbances, high parathyroid hormone (PTH) levels, frequently observed in CRF patients, may be implicated in the nutritional abnormalities found in these patients. In fact, it has been observed that patients with primary hyperparathyroidism may show evidence of weight loss, weakness and muscle atrophy and negative nitrogen balance (15-17). It is not clear, however, to what extent these findings may be caused by either a direct deleterious effect of PTH on protein metabolism (18) or an indirect effect causing fatigue, anorexia, neuropsychiatric disturbances, myopathy or bone disease (15,16).

Few studies have analyzed the effects of high PTH levels on protein metabolism. Experimental work on muscle tissue suggests that PTH induces an increase in protein catabolism (18), although this finding has not been confirmed by other investigators (19). Conversely, the effects of secondary hyperparathyroidism on the nutritional status of chronic hemodialysis patients have not been studied. Thus, the aim of this study was to compare the nutritional status of hemodialysis CRF patients with and without secondary hyperparathyroidism.

**Material and Methods**

**Patients**

The patients studied were selected from 189 patients dialyzed at the outpatient Dialysis Unit, Nephrology Division, Federal University of São Paulo (UNIFESP). Sixteen patients with secondary hyperparathyroidism on chronic hemodialysis were selected for this study. They were included in the study if they had serum PTH concentration higher than 420 pg/ml (hyperparathyroidism group; N = 16). They were matched for gender, age and length on dialysis to a group of patients with serum PTH concentration between 64 and 290 pg/ml (control group; N = 16). According to some studies, normal bone metabolism in chronic renal failure has been associated with PTH levels up to 4 times the upper normal limit (20,21). None of the patients in the control group had ever been treated for secondary hyperparathyroidism. Exclusion criteria for both groups were age lower than 18 years, diabetes mellitus, autoimmune, malignant or infectious diseases, chronic alcoholism, patients submitted to parathyroidectomy or to immobilization, and those with kidney transplantation failure in the last 6 months. All subjects were instructed to eat approximately 30 to 35 kcal kg desirable body weight\(^{-1}\) day\(^{-1}\) and to eat 1.0 to 1.2 g kg desirable body weight\(^{-1}\) day\(^{-1}\) of protein. All patients studied were dialyzed 3 times a week for 4 h with a Cuprophan\(^{\textregistered}\) membrane.

The study was approved by the Ethics Committee of UNIFESP and informed consent was obtained from each subject.

**Study protocol**

After selection, we first interviewed the patients in order to obtain informed consent, to collect blood samples for biochemical analysis and to instruct them to fill out the food diaries. Anthropometric data and the food diaries were obtained one week later and after a regular hemodialysis session.

**Nutritional assessment**

Anthropometric measurements included body weight, height, tricipital skinfold (TSF), biceps, subscapular and suprailliac skinfold thickness, and midarm muscle circumference (MAMC). Body mass index (BMI) was calculated as body weight divided by squared height (22). Skinfold thicknesses were measured using Lange calipers (Cambridge Instrument, Cambridge, MD, USA). These measurements were performed by the same observer on the side of the body opposite to
that of the vascular access for hemodialysis. Percentage of fat was estimated from the sum of four skinfold thicknesses according to the equations of Durnin and Wormersley (23). MAMC was calculated using the formula (24): MAMC = arm circumference - (0.314 x TSF). Percent standard TSF and MAMC were obtained using the National Health and Nutrition Examination Survey (NHANES) percentile distribution tables adapted by Frisancho (24). Dietary intake was evaluated from 4-day food diaries that included 1 dialysis day, 2 days without the treatment and 1 weekend day. Energy and protein intakes were expressed in relation to desirable body weight. Energy and nutrients were calculated using a computer software developed at UNIFESP which contains the US Department of Agriculture tables as the nutrient data base (25). Protein catabolic rate was determined according to the formula of Sargent and Gotch (26).

Biochemical parameters

Blood samples were drawn from the patients under fasting conditions immediately before the dialysis session for determination of ionized calcium, phosphorus, alkaline phosphatase, PTH, pH, bicarbonate, albumin, urea nitrogen, and serum creatinine. Phosphorus, creatinine and urea nitrogen were determined with a standard autoanalyzer. Ionized calcium was determined using a calcium-specific electrode (AVL 9140, Medical Instruments AG, Schaffhausen, Switzerland; normal range = 1.12 to 1.32 mmol/l). Total alkaline phosphatase was determined using a commercial enzyme linked immunosassay kit (ELISA; normal values range from 40 to 190 U/l). PTH was determined using an immunofluorimetric assay which detects the intact PTH molecule with normal values ranging from 10 to 70 pg/ml (27). Bicarbonate and pH were measured using a specific electrode (normal value range = 24 to 28 mEq/l and 7.32 to 7.42, respectively). The colorimetric method was used to determine serum albumin. Hemodialysis efficiency was assessed by calculating Kt/V (28).

Statistical analysis

All data are expressed as median and range. The Mann-Whitney U-test was used to compare patients with and without secondary hyperparathyroidism. The Spearman rank correlation coefficient was calculated to test quantitative associations between two variables. The Fisher test was used to compare the frequency of malnutrition between the two groups. Statistical significance was defined as P<0.05.

Results

The clinical and biochemical characteristics of the patients are shown in Table 1. There was a predominance of males and the patients were relatively young. The median length of dialysis was relatively short. In-

Table 1 - Clinical and biochemical characterization of the patients.

<table>
<thead>
<tr>
<th></th>
<th>Hyperparathyroidism group (N = 16)</th>
<th>Control group (N = 16)</th>
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</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>10/6</td>
<td>10/6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.5 (20-80)</td>
<td>47.0 (20-81)</td>
</tr>
<tr>
<td>Length of dialysis (months)</td>
<td>17.5 (7-289)</td>
<td>21.5 (12-132)</td>
</tr>
<tr>
<td>Etiology</td>
<td>H = 4, CG = 4, PKD = 2</td>
<td>H = 9, CG = 2</td>
</tr>
<tr>
<td></td>
<td>ND = 5, Others = 1</td>
<td>Others = 5</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>86.4 (60.2-110.2)</td>
<td>75.7 (50.4-110.2)*</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>13.5 (6.8-17.0)</td>
<td>13.6 (6.5-16.3)</td>
</tr>
<tr>
<td>Dialysis efficiency (Kt/V)</td>
<td>1.4 (0.4-1.7)</td>
<td>1.2 (0.8-1.6)</td>
</tr>
<tr>
<td>pH</td>
<td>7.20 (7.10-7.30)</td>
<td>7.25 (7.10-7.40)</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/l)</td>
<td>17.1 (11.7-28.7)</td>
<td>17.3 (13.5-26.2)</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>4.2 (3.3-5.3)</td>
<td>4.0 (3.4-4.9)</td>
</tr>
<tr>
<td>Serum ionized calcium (mmol/l)</td>
<td>1.20 (1.0-1.60)</td>
<td>1.20 (1.0-1.30)</td>
</tr>
<tr>
<td>Serum inorganic phosphorus (mg/dl)</td>
<td>5.5 (1.7-9.1)</td>
<td>6.0 (1.7-9.5)</td>
</tr>
<tr>
<td>Serum alkaline phosphatase (U/l)</td>
<td>175.0 (51.0-1095.0)</td>
<td>65.0 (31.0-215.0)*</td>
</tr>
<tr>
<td>Serum PTH (pg/ml)</td>
<td>898.0 (439.0-2120.0)</td>
<td>155.0 (64.0-288.0)*</td>
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</tbody>
</table>
Indeed, 25% of the patients in the hyperparathyroidism group and 19% of the patients in the control group had been on chronic hemodialysis for less than 12 months. Patients with hyperparathyroidism had significantly higher levels of blood urea nitrogen (BUN) as compared with the control group. Both groups had metabolic acidosis. In fact, 9 patients (56%) in the hyperparathyroidism group and 8 (50%) in the control group had venous blood pH below 7.32. The median serum albumin levels were within the normal range in both groups and only one patient in each group had a serum albumin level of less than 3.5 g/dl. The Kt/V values were similar and adequate in both groups of patients. Median ionized calcium value was normal, with only one patient presenting hypercalcemia (iCa$^{2+} = 1.60$ mmol/l). Eleven patients (69%) in each group showed serum phosphorus levels higher than 4.5 mg/dl. As expected, PTH values were significantly higher in the hyperparathyroidism group.

As can be seen in Table 2, we did not find any significant difference in the anthropometric indices between groups. Twelve patients (75%) with secondary hyperparathyroidism and 10 patients (62.5%) in the control group had BMI between 18.5 and 25.0 kg/m$^2$. The median standard percent of TSF was 76.7 and 77.1%, respectively. Only 3 patients (18.8%) with secondary hyperparathyroidism and 1 (6.2%) in the control group showed signs of malnutrition with TSF values below the 5th percentile. These frequencies were not different between groups. The median percent standard values of the MAMC were 92.0% in the hyperparathyroidism group and 89.5% in the control group. However, 5 patients (31.3%) with secondary hyperparathyroidism and 6 patients (37.5%) in the control group showed MAMC values below the 5th percentile. Considering both parameters (TSF and MAMC), only 2 patients in the hyperparathyroidism group and 1 patient in the control group had values below the 5th percentile.

### Table 2 - Anthropometric indices.

Data are reported as median and range (in parentheses). BMI = Body mass index, TSF = tricipital skinfold thickness, MAMC = midarm muscle circumference, LBM = lean body mass.

<table>
<thead>
<tr>
<th></th>
<th>Hyperparathyroidism group (N = 16)</th>
<th>Control group (N = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>61.4 (50.0-81.1)</td>
<td>63.1 (50.0-78.6)</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>24.0 (18.6-30.7)</td>
<td>22.1 (18.9-30.6)</td>
</tr>
<tr>
<td>TSF (standard %)</td>
<td>76.7 (41.7-136.4)</td>
<td>77.1 (37.5-167.0)</td>
</tr>
<tr>
<td>MAMC (standard %)</td>
<td>92.0 (70.0-115.4)</td>
<td>89.5 (68.4-122.0)</td>
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<tr>
<td>Body fat (%)</td>
<td>24.7 (11.2-40.0)</td>
<td>22.0 (9.8-37.7)</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>46.8 (36.4-60.2)</td>
<td>49.9 (34.0-64.0)</td>
</tr>
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</table>

### Table 3 - Dietary intake and protein catabolic rate.

Data are reported as median and range (in parentheses). +N = 12. *P<0.05 vs control group (Mann-Whitney U-test).

<table>
<thead>
<tr>
<th></th>
<th>Hyperparathyroidism group (N = 16)</th>
<th>Control group (N = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal kg$^{-1}$ day$^{-1}$)</td>
<td>25.4 (12.9-59.5)</td>
<td>23.3 (20.0-61.6)</td>
</tr>
<tr>
<td>Protein (g kg$^{-1}$ day$^{-1}$)</td>
<td>0.95 (0.5-2.3)</td>
<td>0.90 (0.6-2.8)</td>
</tr>
<tr>
<td>Calcium (mg/day)</td>
<td>307.9 (109.8-1280.0)</td>
<td>475.8 (226.8-1300.4)*</td>
</tr>
<tr>
<td>Phosphorus (mg/day)</td>
<td>639.7 (387.7-2206.4)</td>
<td>816.4 (426.3-1724.8)</td>
</tr>
<tr>
<td>Protein catabolic rate (g kg$^{-1}$ day$^{-1}$)</td>
<td>1.3 (0.7-1.9)</td>
<td>0.90 (0.5-1.8)</td>
</tr>
</tbody>
</table>

Figure 1 - Protein catabolic rate versus parathyroid hormone (PTH) in the hyperparathyroidism group.
The analysis of the food diaries showed that the median energy and protein intakes were below the recommendations and were similar in both groups, averaging 23 to 25 kcal kg\(^{-1}\) day\(^{-1}\) (Table 3), but calcium intake was significantly lower in the hyperparathyroidism group. There was a trend to a higher phosphorus intake in the patients in the control group; protein catabolic rate was higher in patients in the hyperparathyroidism group but the difference did not reach statistical significance (1.3 vs 0.9 g kg\(^{-1}\) day\(^{-1}\); \(P = 0.08\)). No correlations were found between PTH values and anthropometric indices in the population as a whole or in the hyperparathyroidism group. However, in the latter group PTH was significantly correlated with protein catabolic rate (\(N = 12\); \(r = 0.61\); \(P<0.05\); Figure 1). Furthermore, PTH levels were correlated with length of dialysis (\(N = 16\); \(r = 0.53\); \(P<0.05\)) only in the hyperparathyroidism group.

**Discussion**

In the present study we tested the hypothesis that high PTH levels could have deleterious effects on the nutritional status of patients with secondary hyperparathyroidism. However, when comparing the hyperparathyroidism patients to their respective controls, we did not observe any significant difference in any of the nutritional indices studied. In fact, although they were matched only for age, gender and length of dialysis, both groups of patients showed similar values of BMI, TSF, MAMC, body fat, lean body mass and serum albumin.

The energy intake of our patients, of 23 to 25 kcal kg\(^{-1}\) day\(^{-1}\), was far below the recommended amount for patients on hemodialysis (29), as systematically observed in many studies (1,6,7). Anorexia of chronic renal failure may be implicated in this low energy intake and may be related to the malnutrition of these patients (30). It is worthy of note that, even with low energy consumption, only 2 patients in the hyperparathyroidism group and 1 patient in the control group were considered malnourished. Probably, in both groups the deleterious effects of such a low energy intake on nutritional status was not observed because most of the patients had been on dialysis for a short period of time. In fact, the hemodialysis procedure may cause malnutrition either by inducing losses of nutrients or by promoting inflammatory responses through blood-membrane interactions (8,9). Another possibility is underreporting and/or systematic errors in the estimation of food consumption by the patients as observed by some authors (31).

PTH has long been considered a uremic toxin, with many deleterious cellular and metabolic effects (32). It increases bone turnover (33) and induces neuropathy (34), myopathy (15,16), cardiac hypertrophy (35), hyperlipidemia (36), carbohydrate intolerance (12) and immune dysfunction (37). Although specific studies are lacking, such conditions could influence the nutritional status of uremic patients with secondary hyperparathyroidism. Garber (18) demonstrated in vitro that high PTH levels enhanced muscle proteolysis and increased the release of alanine and glutamine. This effect, however, was observed only in normal rats. On the other hand, Wassner and Li (19) did not observe any change in protein metabolism when muscle of normal rats was perfused with PTH. In humans, it was observed that patients with primary hyperparathyroidism have a negative nitrogen balance that is corrected after parathyroidectomy (17). In the present study, according to the anthropometric indices, we did not observe any interference of secondary hyperparathyroidism with the nutritional status of the patients. However, there was some indirect evidence suggesting that PTH could have exerted its action causing some degree of protein catabolism. In fact, BUN was significantly higher and protein catabolic rate tended to be more elevated in patients with hyperparathyroid-
ism, despite the similar protein intake observed in both groups. Moreover, PTH was directly correlated with protein catabolic rate in the hyperparathyroidism group, suggesting an action of PTH in increasing protein catabolism. On the other hand, we must consider that this indirect evidence of protein catabolism (high BUN and protein catabolic rate values) could also be the result of a higher protein intake in the hyperparathyroidism group which, however, was not detected in the food diaries. If that effect did occur, the anthropometric indices used to estimate the muscle mass of these patients may have not been sensitive enough to detect such interference. Alternatively, it is also possible that the duration of secondary hyperparathyroidism was too short to adversely affect muscle mass as these patients had been on dialysis for a relatively short period of time. Accordingly, PTH was significantly correlated with the length of dialysis treatment in the patients with hyperparathyroidism.

Finally, despite the reasonable strength of this study protocol, the number of patients studied does not permit the characterization of a definite effect of secondary hyperparathyroidism on the nutritional status of hemodialysis patients. Furthermore, as indicated by the relationship between time on dialysis and degree of hyperparathyroidism, a study protocol including the duration of hyperparathyroidism would better analyze its influence on nutritional status. Since there was indirect evidence that PTH could interfere with protein catabolism, other studies are necessary to elucidate this interaction.

References

19. Wassner SJ & Li JB (1987). Lack of an acute effect of parathyroid hormone...
Nutritional status in secondary hyperparathyroidism


