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HORMONAL RESPONSES TO ORAL PHOSPHORUS (P) SUPPLEMENTATION IN PRE-DIALYSIS PATIENTS (PRD) WITH LOW LEVELS OF PTH OR ADYNAMIC BONE DISEASE (ABD). L. Cuppari, A. Carvalho, R. Leblon, R. Ventura, L. Martini, J. G. Vieira, S. A. Draibe.

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Normal to low serum P, low PTH and normal to high levels of calcitriol are frequently seen in our PRD patients with ABD. In order to test the hypothesis that the observed low P intake could contribute to this condition, 18 PRD patients with iPTH levels ≤ 40 pg/ml and serum P ≤ 45 mg/dl (n=7) or with ABD (bone biopsy; n=11) were studied. They were 13M/5F, age=66.5 (35-78) years; creatinine=2.2 (1.0 -3.5) mg/dl; body mass index=26.2 (18-33) kg/m². [median(range)]. Initially, they received 0.5 g/d of oral P (as neutral complex) for one month and then 1 g/d for another month. Serum ionized calcium ([iCa]), iPTH, P, calcitriol (1,25), and urinary P(U) were measured pre and at the end of each period.

<table>
<thead>
<tr>
<th></th>
<th>iPTH (pg/ml)</th>
<th>P (mg/dl)</th>
<th>iCa (mmol/l)</th>
<th>UP (mg/24 h)</th>
<th>1,25 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>58.5</td>
<td>3.25</td>
<td>1.26</td>
<td>406</td>
<td>34.5</td>
</tr>
<tr>
<td>P</td>
<td>(8-466)</td>
<td>(2.4-4.4)</td>
<td>(1.1-1.38)</td>
<td>(254-2131)</td>
<td>(19-74.0)</td>
</tr>
<tr>
<td>0.5 g P</td>
<td>50.5</td>
<td>3.50</td>
<td>1.25</td>
<td>774 *</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>(2.3-164)</td>
<td>(2.7-4.6)</td>
<td>(1.1-1.32)</td>
<td>(399-1241)</td>
<td>-</td>
</tr>
<tr>
<td>1 g P</td>
<td>83.0*</td>
<td>3.55</td>
<td>1.19*</td>
<td>1061*</td>
<td>24.9*</td>
</tr>
<tr>
<td></td>
<td>(27-124)</td>
<td>(2.1-5.7)</td>
<td>(1.1-1.31)</td>
<td>(553-1281)</td>
<td>(16-99.4)</td>
</tr>
</tbody>
</table>

*p<0.05 as compared to pre

Before supplementation, P and protein intakes and protein catabolic rate were 52.2 (37.1-127) mg/1.73 m²/24h, 0.79 (0.57-1.31) g/kg/d, and 1.03 (0.57-1.37) g/kg/d respectively. Only one patient had signs of malnutrition. Pre supplementation iPTH correlated with PCR (r=0.56), calcitriol correlated negatively with iCa (r=0.47) and with P (r=-0.53; p<0.05).

Serum creatinine did not change. Fifteen patients (83%) experienced an increase in iPTH. The percent iPTH changes correlated negatively with basal iPTH (r=-.62; p<0.01). Although 1.25 levels decreased significantly they remained within the normal range. This study shows that oral P supplementation reverses the relative hypocalciuric/panmiin observed in our PRD patients. Thus this treatment could contribute to improve the low bone turnover of ABD patients.


The aim of the study was to investigate the serum magnesium (Mg) level in HD and PD patients and their relationship with the iPTH concentration. We studied 50 patients on HD (30 males, 20 females; mean age 55±15 years) and 13 on PD (10 males, 3 females; mean age 55±18 years). The mean time on dialysis was respectively 2718 y 1519 months.

We found a high incidence of hypermagnesemia (serum Mg > 2.5 mg/dl): 56% in HD and 54% in PD. The iPTH levels were significantly lower in these patients than in those with normal serum Mg, both in HD and PD: 125±65 vs 308±186 (p<0.001) and 127±134 vs 276±268 mg/ml (p<0.01), respectively. Patients on HD were classified into 3 groups according their PTH level: Group A (N=17), low PTH (<20 pg/ml); Group B (N=19), adequate PTH (120-250 pg/ml); and Group C (N=14), high PTH (>250 pg/ml).

The serum Mg levels in HD patients with inadequately low PTH were significantly higher than in patients with adequate and high iPTH (2.7±0.2 vs 2.3±0.1 and 2.3±0.1 respectively, p<0.01). In PD patients the serum Mg was also significantly higher in subjects with low iPTH respect to patients with adequate or high PTH (2.69±0.3 vs 2.34±0.2 mg/dl, p<0.05). Finally, in patients on HD we observed a negative correlation between serum the Mg concentration and the iPTH level (r=-0.47, p<0.001).

Conclusion: Hypermagnesemia is frequent in dialysis patients. The elevated serum Mg concentrations are related to inadequately low iPTH levels. Are necessary more studies to analyze the influence of hypermagnesemia on renal osteodystrophy.

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STROUMIUM-INDUCED OSTEOALACIA. A NEW DISEASE ENTITY IN THE DIALYSIS POPULATION. AN EPIDEMIOLOGICAL SURVEY.

We examined bone biopsies of a cohort of 100 dialysis patients and found bone strontium levels to be increased in subjects with osteomalacia as compared to those presenting the other types of renal osteodystrophy. In this study the incidence of osteomalacia as well as the elevated strontium levels appeared to be country- and/or centre dependent also. To further elucidate the latter issue and to find out whether dialysis patients from particular centres were at a particular risk for strontium accumulation/bone toxicity we started up a worldwide multicentre study. In total 850 patients from 34 dialysis centres in 17 countries were included. In each of the patients a serum sample was taken for the determination of stron-dium as were a tap water and dialysate sample of each centre. Strontium was measured with E. Delmelle by Zee-Man spectroscopy. Our results indicate strontium levels in serum of dialysis patients to differ significantly from country to country ranging from values comparable to those noted in subjects with normal renal function up to 15-fold higher, i.e. mean ± SD: 30.9 ± 11.7 µg/L in the centre with the lowest strontium concentrations as compared to 362.8 ± 113.2 µg/L in the centre with the highest levels. Comparison of serum values of dialysis patients from different centres in one and the same country indicates that stron-dium levels may also differ significantly from one centre to another. Furtheron our data point towards a role of both the strontium content of the dialysis fluid and the diet in the accumulation of the element in dialysis patients. To which extent other factors such as medication, dialysis treatment modalities, ... may contribute also to increased strontium levels is under current investigation. Data of this multicentre study indicate patients of particular dialysis centres to be at an increased risk for strontium accumulation/bone toxicity. They also support the hypothesis of a causal role of the element in the development of osteomalacia and as such might be indicative for the presence of a particular disease entity in the dialysis population.

INCREASED STRONTIUM LEVELS IN BONE OF DIALYSIS PATIENTS WITH OSTEOMALACIA
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The role of aluminum (Al) in the development of dialysis osteomalacia and adynamic bone disease is well known.

In order to look whether besides Al other trace metals might be associated with the presence of a particular type of renal osteodystrophy (RO) a number of trace elements were determined in bone biopsies of 99 dialysis patients coming from dialysis centres in Belgium (N=46), Greece (N=39), Czechia (N=7), Argentina (N=3) and Egypt (N=4). After histological examination 13 of these subjects were classified as having normal bone histology (N), 21 had hyperparathyroidism (HPT), 9 osteomalacia (OM), 35 adynamic bone disease (ABD), 21 mixed lesion (M). Bone trace metal analyses were performed by means of Zeeman atomic absorption spectrometry. Bone density was corrected for by measurement of the bone calcium content.

Results indicated both strontium (Sr) levels and bone Sr/Ca ratios in patients with OM (mean±SD: 91.5±54 µg/g; 92±45×10⁻³) to be significantly (p<0.006) increased as compared to all other types of RO taken together (45±31 µg/g; 45±22×10⁻³). Taking all types of RO separately ANOVA followed by Bonferroni-t-test revealed both Sr and Sr/Ca ratio in the presence of osteomalacia to be significantly (p<0.05) increased as compared to all other types of bone disease; N (30.2±4 µg/g; 33±13×10⁻³), HPT (48±32 µg/g; 54±28×10⁻³), ABD (48±25 µg/g; 44.2±14×10⁻³), M (45±42 µg/g; 47±28×10⁻³). Within the group of patients with osteomalacia Sr bone and Sr/Al levels significantly correlated (r=0.73; p=0.028) with each other.

Our data demonstrate an association between the presence of osteomalacia and Sr. Further experimental animal studies are set-up to investigate whether these increased levels may either have contributed to or are occcurs secondary to the development of this particular type of renal osteodystrophy.

PARATHYROID FUNCTIONAL RESPONSE CURVES IN PATIENTS WITH DIFFERENT FORMS OF RENAL OSTEODYSPLASTIC DISEASE

Twenty one patients (pts) on haemodialysis (HD) were studied. 10 women, 11 men, age 57±13 years, time on HD 60±29 months, with different bone disease forms diagnosed by bone biopsy in the year previous to the study. In all pts, parathyroid stimulation by 4 hours dialysis with Ca⁺⁺ 1 mEq/L in the dialysate were done, as well as an inhibition test in other dialysis with Ca⁺⁺ 4 mEq/L for 48 hours interval. Ca²⁺ and iPTH previous to dialysis and hourly were done to build up Ca²⁺ x iPTH curve for each patient. The analysis of the curve was made using Brown 4.5 PTH model (slopes, set-point and minimal PTH), basal PTH, basal Ca²⁺, minimal and maximal Ca²⁺. Basal PTH were significantly different in the 3 histological groups, the stimulation and inhibition levels were similar in all groups concerning maximal Ca²⁺. Basal Ca²⁺ and basal Ca²⁺ x PTH profiles obtained were different in the different histological groups. For AD forms maximal and minimal PTH were lower than the other 2 groups (p<0.04). The basal Ca in this group was higher than the set-point. This curve would express a relative hypoparathyroidism with a basal inhibition status. In HPT, by contrary, basal Ca was under the set-point, being higher in severe HPT (p<0.02) showing a permanent stimulation. In the studied pts, the slope did not show significant differences that could discriminate different bone pathology forms. In the 2 HPT groups the maximal and minimal PTH values were higher in severe forms, but they did not showed significant differences, and the inhibition level obtained measured by absolute and percentual PTH was lower, although this fact did not show significant differences either.

Conclusions: the functional parathyroid was used to discriminate the glab response grade in different forms of ROD, obtaining different results in the set-point in the 3 groups and in the response grade especially in adynamic forms. The response ranges obtained between mild and severe HPT were different, although they could not discriminate both groups, maybe due to the grade of dispersion and the low number of pts studied.
RENAL OSTEODISTROPHY IN HEMODIALYSIS (HD). EPIDEMIOLOGICAL ASPECTS.


The spectrum of renal osteodystrophy (ROD) has changed in the last decade. Adynamic bone disease (ABD) has increased while Osteomalacia (OM) has reduced their frequency. We have studied a population of 68 patients (pts) on HD (age 48.1±14 years old, 33 males, time on HD: 85±47 months). Bone biopsies were performed and static and dynamic histomorphometric indices were calculated. The distribution of bone diseases was: Mild Osteodystrophy 8 pts (11.7%); Osteitis fibrosa (OF) 35 (51.4%); Mixed 5 (7.3%); ABD 18 (26.4%); OM 2 (2.9%).

The relation to clinical parameters was:

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>OF</th>
<th>Mixed</th>
<th>ABD</th>
<th>OM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>6</td>
<td>19</td>
<td>3</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>46±15</td>
<td>45±14</td>
<td>49±9</td>
<td>51±15</td>
<td>41±15</td>
<td>NS</td>
</tr>
<tr>
<td>Time on HD (m)</td>
<td>81±52</td>
<td>91±45</td>
<td>80±24</td>
<td>71±96</td>
<td>108</td>
<td>NS</td>
</tr>
</tbody>
</table>

Five of the 68 pts were diabetics and all had low remodelling bone disease (4 ABD, 1 OM). Aluminum staining above 25% the trabecular surface was present in 15 pts (22%): 2 OM, 6 ABD, 1 Mild, 4 Mixed and 2 OF. Osteitis fibrosa was the most frequent bone disease in our pts followed by ABD. Age and time on HD were not related to any type of ROD. Aluminum was found in every form of bone disease and could be an etiologic factor in only 6 (33%) pts with ABD.

RENAL OSTEODISTROPHY. ELEVEN YEARS OF BONE BIOPSY.


* San Pablo, BRASIL.

We analyzed different histological forms of renal osteodystrophy (ROD), frequency and evolution with the data of the Uruguayan Registry of Bone Biopsy (BB) between 1985 and 1996. 150 hemodialysis patients had been submitted to the study (170 BB). 68 men, 82 women. age 54±13 years, time on HD 53±33 months. We considered serum Ca, P, AP, PTH, time on HD, and aluminium (Al) exposure by the water or por os, histological diagnosis and percentage of bone Al in the mineralization front. 46.7% (n=70) corresponded to osteitis fibrosa (OF), 16% (n=24) to adynamic forms (AD) (22 with Al), 13.3% (n=20) to aluminium osteomalacia (OMa); 18.7% (n=28) to mixed forms (MX) and 5.3% (n=8) to carciolna osteomalacia (CM). The 5 M rises of blood bone forms and (OF) were different between...