SERUM LEVELS OF PTH, Mg, Ca, INORGANIC PHOSPHATE AND ALKALINE PHOSPHATASES IN URAEMIC PATIENTS ON DIFFERENTIATED Mg DIALYSIS

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Abstract

The serum levels of PTH, Mg, Ca, inorganic phosphate (P_i) and alkaline phosphatases (AlkPase) were determined in 22 uraemic patients on chronic haemodialysis with different Mg levels in the dialysate, in an attempt to clarify the pathogenesis of uraemic osteodystrophy.

Baseline levels of all the considered parameters were obtained over a four month period whilst on standard Mg concentration in the dialysis solution (1.5 mEq/L). Patients were then divided into three groups: 10 patients were dialysed for six months with 0.5mEq/L of Mg, seven patients with 1.5mEq/L and five patients with 2.5mEq/L in the dialysate. At the end of the six months with differentiated Mg dialysis, the three groups had significantly different Mg serum levels, whereas no significant changes were observed in the PTH and Ca serum levels. All the patients on high-Mg dialysis showed a significant reduction of the P_i serum levels, whereas a significant increase of AlkPase was observed in the low-Mg dialysis group.

The overall results obtained in the present study indicate a possible beneficial effect of low-Mg dialysis on the progression of uraemic osteodystrophy of patients on maintenance haemodialysis.

Introduction

Magnesium (Mg) is a normal component of the dialysis solution, where its concentration readily affects the Mg serum levels of uraemic patients undergoing haemodialysis [1–5]. It has been suggested that hypermagnesaemia suppresses parathyroid activity [6, 7], thus reducing the severity of secondary hyperparathyroidism of chronic uraemia; however, this conclusion has not been confirmed in other studies [8–12]. Although the precise role of Mg in the regulation of parathyroid hormone (PTH) secretion still remains controversial, Mg concentration
in the dialysate is usually such as to maintain the uraemic patients frankly hypermagnessaemic as compared to normal.

The purpose of this study was to assess the changes in the serum levels of PTH, Mg, Calcium (Ca), inorganic phosphate (P\textsubscript{i}) and alkaline phosphatases (AlkPase) in uraemic patients treated with different Mg concentrations in the dialysis fluid.

Materials and methods

The study included 22 steady-state uraemic patients on regular dialysis for at least four years; the patients were dialysed 4–5 hours thrice a week, using parallel flow dialysers, against a dialysate containing 1.5mEq/L of Mg and 3.5mEq/L of Ca. All were on a free protein intake and received Ca-carbonate and aluminium hydroxide, whereas all treatment with vitamin D supplementation had been discontinued for six months before and throughout the study, and no Mg-containing drugs were being administered.

Three baseline levels for serum Mg, Ca, P\textsubscript{i}, AlkPase and PTH were obtained over a control period of four months whilst on standard Mg dialysis (1.5mEq/L). The patients were then divided into three groups, and put on dialysis protocols with different Mg levels in the dialysate for the subsequent six months, as follows: Group I (10 patients) 0.5mEq/L, Group II (7 patients) 1.5mEq/L, and Group III (5 patients) 2.5mEq/L. Blood samples for the same biochemical parameters as above were obtained every month (every two months for PTH).

Serum concentrations of Mg and Ca were measured by atomic absorption spectrophotometry; the inter-assay coefficient of variation for Mg was 1.8% (n = 54), with a mean normal value of 1.67 ± 0.07mEq/L, and it was 2.1% for Ca (n = 45), with a mean normal value of 4.80 ± 0.19mEq/L (total Ca concentration). Serum PTH was measured by radioimmunoassay, using commercial kits that utilise an antibody against the C-terminal (CIS-Sorin); the normal range is 1 to 6mU/ml by this method, the sensitivity of the assay is 0.5mU/ml, and the inter-assay coefficient of variation is 9.4% (n = 10). Serum concentrations of P\textsubscript{i} and AlkPase were determined by standard methods, and the normal ranges were, respectively, 1.70 to 2.80mEq/L and 20 to 40mU/ml.

Results

The mean values of serum Mg, PTH, Ca, P\textsubscript{i} and AlkPase obtained in all the patients studied, both during the control period and at the end of the six month period on differentiated Mg concentration dialysis are reported in Table I.

Mean Mg serum levels in the control period were markedly higher than normal in the three groups of patients (patients of Group III were selected among those with the lowest basal Mg serum levels, in order to avoid excessive Mg increases in plasma during the high-Mg dialysis period). After the first month on differentiated Mg level dialysis, Mg concentrations fell and, respectively, rose significantly in the patients on low-Mg (0.5mEq/L) and high-Mg dialysate (2.5mEq/L), whereas they were unchanged in those kept on standard-Mg dialysis (1.5mEq/L); thus, at the end of the six month period, the three groups of patients had significantly different mean Mg serum levels when compared one to each other.
TABLE I. Comparison between baseline values (average of four months) and final values of Mg, PTH, Ca, P_i, and AlkPase serum levels in the three groups on different Mg concentration dialysates

<table>
<thead>
<tr>
<th>Group</th>
<th>Serum Mg, mEq/L</th>
<th>Serum PTH, mU/ml</th>
<th>Serum Ca, mEq/L</th>
<th>Serum P_i, mEq/L</th>
<th>AlkPase, mU/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>baseline</td>
<td>final</td>
<td>baseline</td>
<td>final</td>
<td>baseline</td>
</tr>
<tr>
<td>Group I</td>
<td>2.59</td>
<td>2.05†</td>
<td>17.8</td>
<td>17.2</td>
<td>4.78</td>
</tr>
<tr>
<td>± 1 SD</td>
<td>0.25</td>
<td>0.33</td>
<td>6.4</td>
<td>6.3</td>
<td>0.19</td>
</tr>
<tr>
<td>Group II</td>
<td>2.44</td>
<td>2.59‡☆</td>
<td>17.4</td>
<td>17.2</td>
<td>4.78</td>
</tr>
<tr>
<td>± 1 SD</td>
<td>0.34</td>
<td>0.26</td>
<td>5.3</td>
<td>6.0</td>
<td>0.15</td>
</tr>
<tr>
<td>Group III</td>
<td>2.26*</td>
<td>3.01+</td>
<td>19.3</td>
<td>21.6</td>
<td>4.74</td>
</tr>
<tr>
<td>± 1 SD</td>
<td>0.18</td>
<td>0.17</td>
<td>6.6</td>
<td>5.4</td>
<td>0.19</td>
</tr>
</tbody>
</table>

* significantly different from Group I (p < 0.02); † significantly different from baseline value (p < 0.001); ‡ significantly different from Group I (p < 0.01); • significantly different from Group III (p < 0.005); ○ significantly different from Group I (p < 0.001); ☆ significantly different from Group III (p < 0.001); ◊ significantly different from Group III (p < 0.01).

SEM
The PTH serum levels were markedly higher than normal in all the patients studied, as expected, and there were no significant variations in the three groups after the six month period on different Mg concentration dialysis. Mean serum levels of Ca were within the normal limits in the three groups, and no significant variations were observed during the differentiated Mg concentration dialysis period. High Mg dialysis induced a significant, marked reduction of the P_i serum levels, so much so that in three of these patients administration of aluminium hydroxide was reduced, while it was discontinued in the remaining two patients.

The serum AlkPase levels in the control period were markedly higher than normal in two patients of Group I, and in three patients of both Group II and Group III. During differentiated Mg dialysis, the values of serum AlkPase rose above the normal range in four patients on low Mg dialysis, whereas they remained essentially unchanged in all the other patients submitted to the study. Thus, the mean serum level of AlkPase of Group I after the dialysis test period was significantly higher than the baseline value.

Discussion

In our patients on differentiated Mg concentration dialysis the Mg serum concentrations paralleled the Mg level changes in the dialysis bath, thus confirming previous findings reported by others [1–5]. Although the changes in the Mg serum levels were statistically significant, and lasting for as long as six months, they were not associated with any significant variation of the PTH serum levels; as a matter of fact, the only detectable change in serum PTH, though statistically not significant, was a slight increase of the PTH levels in the high Mg dialysis group.

The significant fall in the serum concentrations of P_i in the high Mg dialysis patients may possibly be explained by an increased apposition of Mg in the bone [14, 15] as Mg-phosphate; this may lead to reduced P_i serum levels, since it has been shown that changes of bone P_i content are directly correlated also with bone Mg content changes [14].

The rise of serum AlkPase in four patients on low Mg dialysis, though not associated with any detectable variation in the PTH serum levels, may be linked to increased osteoblastic activity, therefore to improved bone calcification. This conclusion is supported by the fact that Mg excess in the bone has been postulated to be responsible for bone mineralisation defects [14–16]; as a matter of fact, bone Mg content is markedly increased in dialysed uraemic patients [1, 14–17], due to their high Mg serum levels linked to the concentrations of Mg usually utilised for the dialysis solution. Therefore, our findings are consistent with the hypothesis that the reduction of the Mg serum levels in dialysed uraemic patients may be followed by a reduction of the Mg content of bone, with consequent possible improvement of the calcification processes of the skeleton.

In conclusion, the data obtained in the present study suggest a beneficial effect of maintaining normal Mg serum levels on the progression of uraemic osteodystrophy, although further studies are necessary to find out the optimal Mg concentration in the dialysis fluid.
References

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