MAGNESIUM RENAL WASTING IN CALCIUM STONE FORMERS WITH IDIOPATHIC HYPERCALCIURIA CONTRASTING WITH LOWER MAGNESIUM:CALCIUM URINARY RATIO

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Summary

Plasma magnesium (PMg) and urinary calcium (UCaV) and magnesium (UMgV) were measured after four days of calcium-restricted diet in 60 controls and 82 patients classified according to their calcium excretion in three groups: normocalciuric (NCa), dietary hypercalciuria (DH) and idiopathic hypercalciuria (IH). When compared to controls, higher UMgV (4.26 ± 0.28mmol/d versus 3.4 ± 0.16, p<0.01), lower PMg (0.79 ± 0.01mmol/d versus 0.84 ± 0.01, p<0.05) and lower UMg/UCa ratio (0.6 ± 0.04 versus 1.68 ± 0.15, p<0.001) were observed only in IH. A significant correlation between UMgV and UCaV was found in controls, in NCa and in DH but not in IH. In conclusion, (1) the coexistence of a higher UMgV and of a lower PMg in IH suggests that there is a magnesium depletion in this group of patients; (2) since the lower UMg/UCa ratio may favour a higher propensity for calcium crystallisation and is seen only in IH, magnesium supplements may be specially indicated in this group.

Introduction

Magnesium accounts for approximately 20 per cent of the total inhibitory activity of the urine with respect to calcium stone-formation. Magnesium depletion has been shown to cause calcification in proximal tubule cells and the tubular lumen in rats [1] and to be responsible for nephrocalcinosis in children. Accordingly a possible magnesium deficiency in the pathogenesis of calcium stone formation has been suspected although it has been observed only rarely [2]. Moreover, data concerning magnesium excretion in stone formers are conflicting, being found normal [3] or increased [4]. These discrepancies could be explained by the fact that dietary calcium and calcium excretion were not taken simultaneously into account since it is well established that in normal individuals magnesium excretion is directly correlated with calcium excretion [5], and that a high calcium intake might induce negative magnesium balance by increasing faecal magnesium in magnesium depleted humans [6].
For these reasons it seemed to us interesting to study magnesium metabolism in various groups of idiopathic calcium stone-formers classified according to calcium excretion during a controlled calcium diet.

Methods

Sixty controls and 82 patients with calcium urolithiasis were studied on an ambulatory protocol. They collected 24-hour urine on a free diet and after four days of a low calcium diet providing approximately 400mg calcium daily because no dairy products were ingested. In both collections, creatinine, calcium, phosphate and sodium were measured. Magnesium was measured only on the urine collection after calcium restriction. The blood samples were drawn after the four days of calcium restriction for calcium, phosphate, magnesium, creatinine, to eliminate patients with specific causes of calcium stone-formation.

Calcium, phosphate and creatinine were analysed by automatic colorimetry (Technicon Auto-Analyzer) and magnesium in urine and plasma was determined by a colorimetric procedure (calmagite method).

Results

Classification of patients

With the data of our controls, we classified the patients according to their urinary calcium excretion:

Sixty were normocalciuric (NCa) on a free diet (urinary calcium <0.1mmol/kg/day).

Seventeen patients who were hypercalciuric on a free diet, presented a diet dependent hypercalciuria (DH), a diagnosis based on the return to normal of urinary calcium excretion after calcium restriction, when compared to controls on the same restricted diet (urinary calcium <0.07mmol/kg/day).

Idiopathic hypercalciuria (IH) was found in 29 patients who were hypercalciuric on a free diet and on a restricted diet (i.e. urinary calcium >0.1mmol/kg/day on free diet, urinary calcium >0.07mmol/kg/day on calcium restricted diet).

Magnesium excretion and serum magnesium in patients and in controls

Table 1 shows the values of the daily urinary excretion of calcium and magnesium in controls and in patients after four days of a low calcium diet. When compared to controls, urinary magnesium and calcium excretion were significantly higher (p<0.01) in patients with idiopathic hypercalciuria. Because of the possible role of magnesium in inhibiting calcium crystallisation we determined for each patient and each control the urinary magnesium/calcium ratio. When compared to controls, this ratio was significantly lower only in patients with IH. Serum magnesium was found significantly lower in controls (p<0.05) only in this group.
TABLE I. Daily excretion of magnesium and calcium; urinary magnesium/calcium ratio and plasma levels of magnesium and calcium in controls and calcium stone-formers on a Ca restricted diet

<table>
<thead>
<tr>
<th></th>
<th>UMgV (mmol/d)</th>
<th>UCaV (mmol/d)</th>
<th>UMg/UCa</th>
<th>PMg (mmol/L)</th>
<th>PCa (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls n = 60</td>
<td>3.4 ±0.16</td>
<td>2.02±0.3</td>
<td>1.68±0.15</td>
<td>0.84±0.01</td>
<td>2.35±0.06</td>
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<tr>
<td>NCa n = 36</td>
<td>3.87±0.17</td>
<td>2.84±0.3</td>
<td>1.36±0.08</td>
<td>0.82±0.09</td>
<td>2.30±0.07</td>
</tr>
<tr>
<td>DH n = 17</td>
<td>3.94±0.3</td>
<td>3.78±0.4</td>
<td>1.04±0.13</td>
<td>0.85±0.01</td>
<td>2.25±0.08</td>
</tr>
<tr>
<td>IH n = 29</td>
<td>4.26±0.28**</td>
<td>7.1 ±0.4***</td>
<td>0.6 ±0.04***</td>
<td>0.79±0.01*</td>
<td>2.28±0.07</td>
</tr>
</tbody>
</table>

Significance of the difference between controls and the stone-formers group: *p<0.05; **p<0.01; ***p<0.001).
NCA=normocalciuria; DH=diet dependent hypercalciuria; IH=idiopathic hypercalciuria.

Correlations between calcium excretion and magnesium excretion in controls and in stone-formers

In controls as well as in the whole group of stone-formers, there was a significant correlation between magnesium and calcium excretion (controls: r=0.37, p<0.01; UMg=1.53±0.37 UCa; patients: r=0.44, p<0.01, UMg=2.55±0.56 UCa).

When the various subgroups of stone-formers are considered separately positive correlations between calcium and magnesium excretions are still found in normocalciuria (r=0.62, p<0.01) and in diet dependent hypercalciuria (r=0.47, p<0.05) but not in patients with idiopathic hypercalciuria (r=0.14, NS).

Discussion

Our data, based on a short-term study, show that magnesium excretion on a low calcium diet is comparable in normocalciuric patients and in patients with dietary dependent hypercalciuria when compared to controls on the same Ca-restricted diet. On the other hand, the coexistence of a higher magnesium excretion and a lower plasma value of magnesium in stone-formers with idiopathic hypercalciuria suggests that there is a renal leak of magnesium leading to magnesium deficiency.

To explain the higher magnesium excretion in idiopathic hypercalciuria, the following hypothesis may be proposed: since there is a well-known competition for tubular reabsorption between calcium and magnesium, an increased filtered load of calcium could explain the increase of magnesium excretion [6]. Against this hypothesis are the following facts: (1) since there is no hypercalcaemia in IH there is no reason to postulate an increased filtered load; (2) the absence
of correlation in IH between calcium and magnesium excretion.

A second hypothesis may be proposed: in most patients with IH there is a relative hypoparathyroidism since the primary disorder is an increased intestinal absorption of calcium [7]. Since PTH stimulates magnesium reabsorption [8], relative hypoparathyroidism could explain an increase of magnesium excretion. This hypothesis is further supported by the independent observation of a lower plasma magnesium in patients with documented absorptive hypercalciuria [9].

Finally, a decreased magnesium absorption consequent to the high calcium intake could be considered as a factor of magnesium depletion. In fact, an increased faecal magnesium excretion during a high calcium intake has been observed only in magnesium-depleted humans [6] and not in normal patients [10]. Because of the lack of magnesium balance studies, this mechanism of magnesium depletion cannot be confirmed with our data, but might be an additive one, on free calcium diet, in patients with idiopathic hypercalciuria, who are already magnesium depleted on calcium restricted diet.

The importance of magnesium in inhibiting calcium crystallisation depends on the concentration of magnesium in relation to calcium rather than on the absolute amount on this ion. The urinary magnesium/calcium ratio represents an index of the propensity to stone-formation related to magnesium and calcium. This ratio is significantly decreased only in idiopathic hypercalciuric patients although absolute magnesium is significantly higher in this group of patients. This suggests that magnesium supplements might be of therapeutic interest, especially in idiopathic hypercalciuria.

References

3. Nicot MJ, Pak CYC. Min Electrolyt Metab 1982; 8: 44