Magnesium Supplementation Does Not Affect Blood Calcium Level in Treated Hypoparathyroid Patients

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Context: Magnesium is involved in the homeostasis of calcium metabolism, and magnesium deficiency may lead to clinically significant hypocalcemia. We have had two cases in our department in which treated hypoparathyroid patients with stable calcium levels developed hypercalcemia in conjunction with supplementary magnesium use. To our knowledge, there has been no prospective study looking at the effect of supplementary magnesium on calcium homeostasis in hypoparathyroid patients.

Objective: The aim of this pilot study was to evaluate whether magnesium treatment affects plasma calcium levels in hypoparathyroid patients.

Design and Setting: We conducted a prospective, two-phase, uncontrolled treatment trial at a referral center of endocrine disorders.

Participants: We enrolled treated (calcium + vitamin D analog) hypoparathyroid patients with normal plasma magnesium levels.

Intervention: Three weeks of treatment with oral magnesium (350 mg/d) were followed by 2 wk off treatment.

Measures: We compared the plasma ionized calcium level after 3 wk of treatment to the pre-treatment value. Plasma calcium, phosphate, magnesium, and creatinine levels were measured before treatment, after 3 wk on magnesium, and 2 wk after stopping magnesium treatment.

Results: Ten patients completed the trial. Supplementary treatment with magnesium for 3 wk did not change calcium levels in these patients. Magnesium supplementation induced a small but statistically significant increase in the plasma magnesium level, but levels of phosphate and creatinine remained stable.

Conclusions: Magnesium supplementation did not influence plasma calcium levels in treated hypoparathyroid patients. (J Clin Endocrinol Metab 97: E2090–E2092, 2012)
TABLE 1. Characteristics of patients

<table>
<thead>
<tr>
<th>Type of hypoparathyroidism</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>46 ± 13</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>29.3 ± 6.4</td>
</tr>
<tr>
<td>Gender (females/males)</td>
<td>8/2</td>
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<tr>
<td>Ca dose (g)</td>
<td>1.5 ± 0.33</td>
</tr>
<tr>
<td>Calcitriol dose (µg)</td>
<td>0.78 ± 0.28</td>
</tr>
<tr>
<td>PTH level (pmol/liter)</td>
<td>0.51 ± 0.63</td>
</tr>
<tr>
<td>L-T₄ dose (µg)</td>
<td>145 ± 80</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.

Exclusion criteria were: 1) concomitant condition possibly affecting plasma Ca level (malabsorption, cancer, etc.); 2) pregnancy; 3) creatinine level greater than 150 µmol/liter; and 4) use of Mg supplement during last 2 months.

All subjects signed an informed consent form. The study was approved by the Committee of Ethics for Human Studies of Tartu University (protocol no. 176/T-2) and complied with the ethical principles of the Declaration of Helsinki. The study protocol was published at www.clinicaltrials.gov (NCT 00824226).

Study design

All participants continued their treatment for hypoparathyroidism. An oral Mg supplement (Magnex 350, containing 350 mg Mg; Vitabalans OY, Hameenlinna, Finland) was administered for 3 wk, followed by 2 wk off treatment.

Plasma parameters were measured at the start of the study, after 3 wk on Mg, and 2 wk after discontinuation of the Mg supplement.

Blood chemistry

iCa, phosphate, Mg, and creatinine levels were determined. TSH and PTH levels were also measured at the beginning of the study. All blood chemistry measurements were performed by the Clinical Laboratory of Tartu University Hospital.

The primary endpoint was a change in iCa levels after 3 wk of Mg treatment. A t test for dependent samples was used to determine the significance of any differences.

Results

The clinical characteristics of patients are shown in Table 1.

Among the 11 patients screened, one was excluded due to concomitant gluten enteropathy. The remainder (eight females and two males, all with postoperative hypoparathyroidism) were recruited into the study, and all completed the study. All patients used calcitriol as a vitamin D analog.

The results are shown in Table 2.

There was no change in iCa, phosphate, or creatinine levels during the study. Mg levels were slightly higher after 3 wk of Mg treatment (P < 0.025).

TABLE 2. Biochemical parameters during the study

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 wk on Mg</th>
<th>2 wk off treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma iCa (mmol/liter)</td>
<td>1.16 ± 0.1</td>
<td>1.17 ± 0.08 (P = NS)</td>
<td>1.14 ± 0.03</td>
</tr>
<tr>
<td>(reference range, 1.16–1.29)</td>
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<tr>
<td>Plasma phosphate (mmol/liter)</td>
<td>1.47 ± 0.25</td>
<td>1.51 ± 0.22 (P = NS)</td>
<td>1.49 ± 0.09</td>
</tr>
<tr>
<td>(reference range, 0.87–1.45)</td>
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<tr>
<td>Plasma Mg (mmol/liter)</td>
<td>0.79 ± 0.06</td>
<td>0.82 ± 0.06 (P &lt; 0.025)</td>
<td>0.80 ± 0.02</td>
</tr>
<tr>
<td>(reference range, 0.7–1.05)</td>
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<tr>
<td>Plasma creatinine (µmol/liter)</td>
<td>83 ± 5.6</td>
<td>76 ± 3.3</td>
<td>79 ± 4.6</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. P value after t test for dependent samples. NS, Not significant.
Discussion

The main finding of the current study was that 3 wk of Mg supplementation did not influence plasma iCa levels in hypoparathyroid patients. All study patients (including the patient excluded after screening) had normal Mg levels without additional Mg use. This is consistent with a previous study showing that hypoparathyroid patients had increased Mg levels in blood cells but normal plasma levels (10). In contrast, Winer et al. (1, 3) reported that in their study populations many patients needed Mg supplementation to maintain normal Mg levels. Low levels of Mg were noted not only in children with hereditary forms of hypoparathyroidism but also in adult postsurgical patients (1, 3). We speculate that at least some of the discrepancy may derive from possible differences in the dietary pattern of patients.

Although there are various possible sites at which Mg may interfere with the metabolism of Ca, most studies suggest that the key process in which Mg is involved is in the secretion of PTH. Other possible sites involve the renal clearance of Ca and the renal effects of PTH. Thus, given that our patients were deficient in PTH, it is not surprising that Mg treatment had no effect on plasma Ca levels.

The small, but statistically significant increment in Mg levels demonstrates that patients were compliant with the treatment. The reason why the two index patients developed hypercalcemia remains obscure. One of them participated in the current study and had no change in iCa level after 3 wk on Mg. It seems possible that hypercalcemia was induced by erroneous dosing of vitamin D analog by the patients and the use of Mg supplementation was a mere coincidence.

The study has several limitations. The main limitation is that it was designed as a pilot study, and therefore we did not use a placebo group. However, because the plasma iCa level is a robust endpoint and the study included an off-treatment period during which no changes in any parameter were detected, we believe that the study results are relevant. Because it was a pilot study, we did not perform power calculation in advance. However, post hoc analysis showed that the study had 80% power to detect a change of 0.1 mmol/liter in iCa level. Another limitation of the study is the relatively short period of Mg supplementation. Again, because there was not even a trend toward hypercalcemia, it seems reasonable to believe that a longer period of treatment with Mg would not induce hypercalcemia.

We conclude that 3 wk of oral Mg treatment does not influence plasma Ca levels in treated hypoparathyroid patients.

Acknowledgments

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Disclosure Summary: The authors have nothing to disclose.

References

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