Urological Research 8, 197-200 (1980)

Urological Research

ORIGINALS

Urine Composition in Patients with Urolithiasis During Treatment with Magnesium Oxide

Hans-Göran Tiselius[1], Christer Ahlstrand[1] and Lasse Larsson[2]

[1]Department of Urology and [2]Department of Clinical Chemistry, University Hospital, Linköping, Sweden

Accepted: June 16, 1980

Summary. Fifteen patients with recurrent renal stone formation were treated with 400 mg magnesium oxide daily. Urine composition was analyzed before the start of treatment and after 6 - 12 months. The urinary excretion of magnesium before and during treatment was 321 ± 120 (mean ± SD) and 409 ± 140 mmol per mol creatinine respectively, a difference that was not statistically significant. Urinary calcium increased from 473 ± 186 to 662 ± 213 mmol per mol creatinine ($p < 0.05$). All patients who increased their excretion of magnesium also increased the urinary output of calcium and, as a result of this, the calcium/magnesium-quotients were unaffected by the treatment. No significant effect was observed on urine oxalate excretion. Serum concentrations of calcium, magnesium and urate all remained at the pre-treatment level. From the results obtained in this study, magnesium oxide in this dosage cannot be recommended for use in treatment of patients with urolithiasis.

Key words: Renal stone disease, Magnesium oxide, Calcium, Magnesium, Oxalate, Urine composition.

INTRODUCTION

Several authors have demonstrated the beneficial effect of magnesium in prevention of calcium oxalate and calcium phosphate stone recurrence (10, 9, 12, 1, 2).

In many investigations it has also been shown that the urinary excretion of magnesium appears to be slightly lower in stone formers than in control subjects (5, 7, 13, 15) whereas no differences in magnesium excretion or magnesium metabolism were found by Backman (1, 2).

The biochemical effects responsible for the prevention of renal stone formation during magnesium administration are not completely understood. The purpose of the present study was to obtain information on the changes in urine composition during prophylactic treatment with magnesium oxide in a group of calcium oxalate stone formers.

MATERIAL

Fifteen patients with a history of recurrent calcium oxalate stone disease were given prophylactic treatment with 200 mg magnesium oxide twice daily (400 mg magnesium oxide = 241 mg Mg^{++}). The substance was administered orally in capsules. During the study the patients ate their ordinary diet and urine collections were performed on an out-patient basis.

METHODS

Urine was collected as 24 h urine samples before and after 6 - 12 months of treatment.

Urinary magnesium, calcium and oxalate were analyzed in urine samples collected in bottles containing 90 mmol of hydrochloric acid as a preservative, whereas urate was analyzed in 24-hour-urine without additives. The analytical procedures were as described previously (14, 15).

Wilcoxon's test was used for the statistical analysis.

RESULTS

No significant changes were observed in serum concentrations of calcium, magnesium and urate (Table 1).

0300-5623/80/0008/0197/$01.00

Table 1. Serum concentrations (mean ± SD) of calcium, magnesium and urate, before and during administration of 400 mg magnesium oxide daily

	Before therapy	During therapy	Significance of difference
Calcium mmol/l	2.45±0.09	2.52±0.05	N.S.
Magnesium mmol/l	0.82±0.08	0.83±0.06	N.S.
Urate μmol/l	268 ± 57	317 ± 50	N.S.

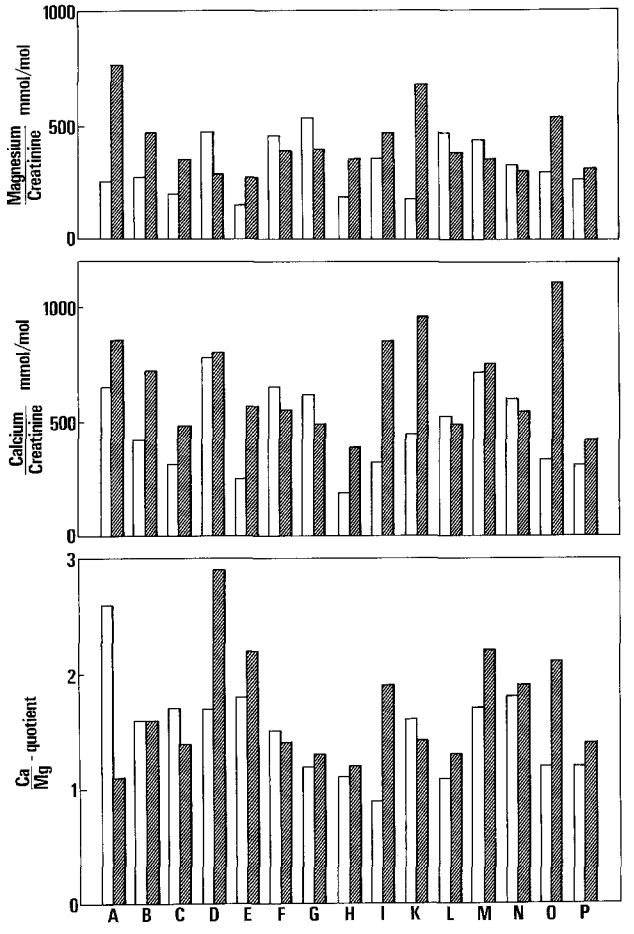

Fig. 1. Urinary excretion of calcium and magnesium expressed as mmol substance per mol of creatinine and calcium/magnesium quotients in 15 patients with calcium oxalate stone disease before (□) and during (■) administration of 400 mg magnesium oxide daily

Urinary excretion of calcium and magnesium are shown in Fig. 1. A higher magnesium excretion during treatment was found in 9 patients, whereas 6 patients had lower magnesium levels in urine during treatment. The urinary excretion of magnesium (mean ± SD) was 321 ± 120 mmol per mol creatinine before and 409 ± 140 during therapy, but this difference was statistically not significant.

The excretion of calcium increased in 11 of the 15 patients during treatment and excretion of calcium (mean ± SD) increased in the group from 473 ± 186 to 662 ± 213 mmol per mol creatinine. This difference was statistically significant ($p < 0.05$).

However, it is also apparent from Fig. 1, that there is a correlation between changes in magnesium excretion and changes in calcium excretion. Thus in the 9 patients who increased their magnesium excretion between 40 and 510 mmol per mol creatinine, the calcium excretion increased by 106 to 765 mmol per mol creatinine. By contrast, the remaining 6 patients who did not increase their magnesium excretion showed no significant increase in calcium excretion. This correlation was not explained by variations in creatinine excretion. As a result of the changes in calcium and magnesium - excretion, a lower value of the calcium/magnesium ratio could be recoreded in only 4 subjects, and in the whole group of patients no significant difference was obtained with respect to this ratio (Table 2).

Urinary excretion of oxalate decreased in 5 of the patients studied (Fig. 2) but increased in 10 patients. Mean excretions (± SD) before and during therapy were 29.4 ± 8.5 and 29.2 ± 9.3 mmol per mol creatinine respectively; the difference was not statistically significant. There was no significant difference in the calcium x oxalate/magnesium x creatinine ratios before and during treatment (Table 2).
The creatinine excretion was unchanged during the study, 12.8 ± 3,5 mmol/d (mean ± SD) before and 12.5 ± 3.5 mmol/d during magnesium oxide administration, and as is evident from the figures in Table 2, no significant changes in urate excretion were recorded.

DISCUSSION

In the present study we administered magnesium as magnesium oxide, 400 mg in two divided doses. This is a magnesium supplement at the same level as that used by Moore and Bunce (10), higher than the dose given by Prien and Gershoff (12) but lower than the doses given by Backman (1, 2) and Fetner (6).

A significant effect on the urinary excretion of magnesium was not obtained in this group of patients. However, further analysis of the results disclosed two subgroups, one comprising 9 patients with an increased excretion of both magnesium and calcium and another group of 6 patients in whom treatment had no effect on magnesium or calcium excretion.

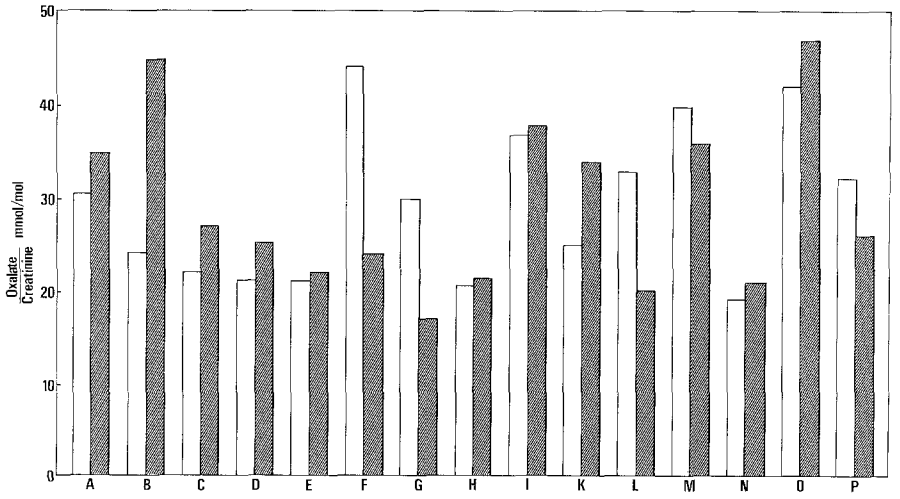

Fig. 2. Urinary excretion of oxalate expressed as mmol per mol of creatinine in 15 patients with calcium oxalate stone disease before (□) and during (■) administration of 400 mg magnesium oxide daily

Table 2. Ca/Mg - and Ca x Ox/Mg x Cr - quotients, urate and creatinine excretion (mean ± SD) in 15 patients with calcium oxalate stone disease before and during administration of 400 mg magnesium oxide daily

	Before therapy	During therapy	Significance of difference
$\frac{Ca}{Mg}$	1.51±0.42	1.69±0.50	N.S.
$\frac{Ca \times Ox}{Mg \times Cr}$ mmol/mol	43.3±15.7	49.8±22.8	N.S.
U-$\frac{Urate}{Creatinine}$ mmol/mol	257 ± 85	250 ± 80	N.S.
U-Creatinine mmol/d	12.8±3.5	12.5±3.5	N.S.

The reason for the failure to increase magnesium excretion by the latter group is not fully apparent, but either these patients had not followed the regimen, and omitted to take the drug or, for one reason or another, magnesium was incompletely absorbed from the intestine. The normal serum magnesium concentration argues against a defect in the renal excretion of magnesium.

In the first group, where we assume that the supply of magnesium was adequate, the increase of both magnesium and calcium excretion were significantly correlated ($p < 0.01$). An increased excretion of calcium has been demonstrated by other authors (6, 3). The mechanism for this is not completely understood but might be attributable to a shift between Ca^{++} and Mg^{++} in the skeleton (11), or to different reabsorption kinetics in the kidney (8) or to effects on the intestinal absorption of calcium. In contrast to these findings no increase in calcium excretion was found during administration of magnesium hydroxide (1, 2).

It is possible that a higher dose of magnesium would further significantly increase the magnesium excretion, but since the calcium increased to such an extent we refrained from increasing the magnesium dose. Besides the benefit of a higher urinary magnesium excretion, magnesium might have other important effects in the prevention of renal stoneformation. It has been suggested that magnesium decreases the oxalate excretion either by affecting its absorption (3) or by regulating the endogenous synthesis. The magnesium ion is a co-factor in the decarboxylation of glyoxylate and an excess of Mg^{++} might stimulate this reaction. Unfortunately no decrease in oxalate excretion was found in these patients, which is in contrast to the findings by von Berg (4).

Magnesium might affect crystal aggregation and crystal growth, but in a recent paper Fetner (6) failed to demonstratethese effects.

The effects of magnesium therapy on urine composition and renal stone formation need to be studied further, but on the basis of the results obtained in this investigation it appears reasonable to use magnesium oxide with care in patients with recurrent stone disease and, if used, it should probably be combined with some calcium reducing regimen.

REFERENCES

1. Backman, U., Danielson, B. G., Johansson, G., Ljunghall, S., Wikström, B.: Magnesium metabolism in renal stone disease. Scandinavian Journal of Urology and Nephrology. Suppl. 51 (1979a)

2. Backman, U., Danielson, B.G., Fellström, B., Johansson, G., Ljunghall, S., Wikström, B.: Biochemical and clinical effects of the prophylactic treatment of renal calcium stones with magnesium hydroxide. Scandinavian Journal of Urology and Nephrology. Suppl. 51 (1979b)
3. Barilla, D.E., Notz, C., Kennedy, D., Pak, C.Y.C.: Renal oxalate excretion following oral oxalate loads in patients with ileal disease and with renal and absorptive hypercalciuria. American Journal of Medicine 64, 579 (1978)
4. Berg, von, W., Schneider, H.-J., Vogel, E.: Die Oxalatausscheidung im Harn bei oraler Oxalsäure- und Magnesiumzufuhr. Deutsche Zeitschrift für Verdauungs- und Stoffwechselkrankheiten 31, 241 (1975)
5. Evans, R.A., Forbes, M.A., Sutton, R.A.L., Watson, L.: Urinary excretion of calcium and magnesium in patients with calcium-containing renal stones. Lancet II, 958 (1967)
6. Fetner, C.D., Barilla, D.E., Townsend, J., Pak, C.Y.C.: Effects of magnesium oxide on the crystallization of calcium salts in urine in patients with recurrent nephrolithiasis. Journal of Urology 120, 399 (1978)
7. Hodgkinson, A.: Relations between oxalic acid, calcium, magnesium and creatinine excretion in normal men and male patients with calcium oxalate kidney stones. Clinical Science Molecular Medicine 46, 357 (1974)
8. Massry, S.G., Coburn, J.W.: The hormonal and non-hormonal control of renal excretion of calcium and magnesium. Nephron 10, 66 (1973)
9. Melnick, I., Landes, R.R., Hoffman, A.A., Burch, J.F.: Magnesium therapy for recurring calcium oxalate urinary calculi. Journal of Urology 105, 119 (1971)
10. Moore, C.A., Bunce, G.E.: Reduction in frequency of renal calculus formation by oral magnesium administration. A preliminary report. Investigative Urology 2, 7 (1964)
11. Pak, C.Y.C., Diller, E.C.: Ionic interaction with bone mineral. Effect of Mg^{2+}, citrate $^{3-}$, F^- and SO_4^{2-} on the solubility, dissolution and growth of bone mineral. Calcified Tissue Research 4, 69 (1969)
12. Prien, E.L., Gershoff, S.N.: Magnesium oxide - pyridoxine therapy for recurrent calcium oxalate calculi. Journal of Urology 112, 509 (1974)
13. Takasaki, E.: Urinary magnesium and oxalic acid excretion in patients with recurrent oxalate urolithiasis. Investigative Urology 12, 251 (1975)
14. Tiselius, H.-G.: Excretion of 4-pyridoxic acid and oxalic acid in patients with urinary calculi. Investigative Urology 15, 5 (1977)
15. Tiselius, H.-G., Almgård, L.E., Larsson, L., Sörbo, B.: A biochemical basis for grouping of patients with urolithiasis. European Urology 4, 241 (1978)

Dr. H.-G. Tiselius
Department of Urology
University Hospital
S-581 85 Linköping
Sweden