The urinary magnesium/calcium ratio inadequately reflects magnesium excretion under conditions of changing calcium output

M. Labeeuw, N. Pozet, A. Hadj-Aissa and P. Zech

Zusammenfassung
Die Wertigkeit des Verhältnisses von Mg: Ca im Urin als Maß für die Mg-Ausscheidung wurde bei 12 Kontrollpersonen und 64 Steinbildnern mit normalen Ausscheidungsmustern von Mg und Ca untersucht. Die Ca-Ausscheidung wurde durch orale Ca-Gaben erhöht. Der Mg: Ca-Quotient und ein neuer Parameter, nämlich dMg: Cr, wurden ermittelt. Im Gegensatz zum Verhältnis dMg: Cr zeigte der Mg: Ca-Quotient falschlicherweise an, daß eine erhöhte Ca-Ausscheidung mit erniedrigter Mg-Ausscheidung einherging.

Summary
The value of the urinary Mg/Ca ratio as an index of magnesium excretion relatively to calcium excretion under conditions of varying calcium output was investigated in 12 normal and 64 normocalcicuric male stone formers. Calcium excretion was increased by an oral calcium load. Mg/Ca and a new parameter, dMg/Cr were calculated. Unlike dMg/Cr, Mg/Ca erroneously suggested that increasing calcium excretion was associated with abnormally low magnesium excretion.

Résumé
La capacité du rapport Ca/Mg urinaire à exprimer les modifications conjointes des excretion de magnesium et de calcium dans des conditions de calciurie variable a été étudiée chez 12 sujets témoins et 64 lithiasiques normomagnésuriques et normocalciuriques. Mg/Ca et un nouveau paramètre, dMg/Cr ont été calculés avant et après une charge calcique orale. dMg/Cr apparaît préférable à Mg/Ca dont les valeurs suggèrent à tort que l'élévation du débit de calcium est associée à une magnésurie inadéquate.

Methods and Subjects
After a 14 hours fast, urine was collected on a 2 hours basis, before and after a 16 mmol calcium load in a standardized meal (magnesium content = 2.8 mmol). Urinary excretions were expressed as the concentration ratio to creatinine (Cr). d Mg/Cr was calculated as previously reported [5]: the normal correlation between Mg/Cr (y) and Ca/Cr (x) was established in 12 controls (C) and the deviation from this correlation along the y axis (d Mg/Cr) was calculated for each experimental point.

Since Desgrez showed in 1958 that the urinary magnesium/calcium ratio (Mg/Ca) was lower in stone formers than in controls [1], Mg/Ca has been widely used in evaluating the magnesium-calcium relationship in urine (see ref. in [3, 5]). However, while it is significantly correlated with calciuria, it bears no direct correlation with both 24 hours [2] and fasting magnesium excretions [5]. Its value as an index of magnesuria should therefore be questioned, particularly when comparing subjects with different calciuria or when evaluating therapeutic regimen susceptible to interfere with the excretion of the two ions, such as calcium restriction, magnesium supplementation or chronic treatment with thiazides.

Recently a new parameter was described in normal subjects to obviate these drawbacks [5]. This paper reports the first part of a study of magnesium excretion in stone formers and intends to compare the Mg/Ca ratio to this parameter under conditions of changing urinary calcium excretion.

Results
During fast
In SF, the correlation between Mg/Cr and Ca/Cr was: Mg/
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\[ Cr = 0.088 + 0.394 \text{ Ca/Cr}, \quad r = 0.45, \ p < 0.001, \text{ not different from} \]

the correlation in controls (see below) indicating that Mg/Cr was indeed normal for the calcium excretion. Mg/Ca was however lower in SF (tab. 1) than the values previously reported in normal subjects [2, 5]. As shown in figure 1, Mg/Ca and Ca/Cr were correlated in SF in the same way as in normal subjects during fasting. Therefore the low Mg/Ca value recorded in SF was only due to their slightly elevated (although in the normal range) fasting calcium excretion, while Mg/Cr was not statistically different from controls (tab. 1).

After the calcium load

In control subjects, the oral calcium load induced a significant increase in magnesium excretion. The overall correlation (fasting + post Ca load), was: Mg/Cr = 0.093 + 0.365 Ca/Cr, \( r = 0.85, \ p < 0.001 \) (not shown). This correlation expresses the normal expected changes in Mg/Cr for the increase in Ca/Cr induced by the load. In SF, the increases in Mg/Cr and Ca/Cr were normally correlated as indicated by the slope of the overall correlation: Mg/Cr = 0.096 + 0.372 Ca/Cr, \( r = 0.62, \ p < 0.001 \) (fig. 2), similar to that of C. Therefore the changes in Mg/Cr were normal for the variations in Ca/Cr. In spite of this normal increase in Mg/Cr, Mg/Ca decreased significantly (tab. 1).

\[ \frac{d \text{Mg/Cr}}{d \text{mg/Cr}} \]

During fasting, this parameter averaged zero both in C and SF, indicating an homogeneous distribution of the points along the correlation line. As expected from the similar correlation between Mg/Cr and Ca/Cr in C and SF (fig. 2) its value did not vary after the load, indicating no trendancy for Mg/Cr to deviate in SF from the normal correlation.

Comments

The initial finding of a low Mg/Ca urinary ratio in stone formers has been amply confirmed on both 24 hours and fasting urine (see ref. in [3, 5]). However the rationale of using the Mg/Ca ratio rests on both physiologic data of the renal tubular reabsorption of the two ions, and on epidemiologic studies of stone disease. The urinary excretions of calcium and magnesium are positively correlated in normal and stone forming subjects [7, 9, 10], mainly due to the interrelations in their renal tubular transport.

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Tab. 1: Excretions (mmol/mmol). Fasting vs post Ca load; * \( p < 0.01 \)

<table>
<thead>
<tr>
<th></th>
<th>Ca/Cr</th>
<th>Mg/Cr</th>
<th>Mg/Ca</th>
<th>dMg/Cr</th>
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<tr>
<td>C</td>
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<tr>
<td>C</td>
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<td>p C vs SF</td>
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</tr>
</tbody>
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Fig. 1: Correlation between Mg/Ca and Ca/Cr in fasting stone formers (\( y = 0.244 \times 0.322, \ r = 0.70 \). The normal correlation (5) is: \( y = 0.223 \times 0.809, \ r = 0.86 \)

Fig. 2: Correlation between Mg/Cr and Ca/Cr in stone formers (\( y = 0.096 + 0.372 x, \ r = 0.62 \). The normal correlation is: \( y = 0.093 + 0.365 x, \ r = 0.85 \)
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[8]. Therefore comparing magnesium of subjects with different calcium output requires some correction for calcium excretion. The Mg/Ca ratio intends to allow for such a correction but although a very simple one, is probably not the best parameter to be used: since the correlation line between the two excretions does not go through the origin (fig. 2), Mg/Ca is not constant over the whole range of calcium excretion. The Mg/Ca ratio intends to allow for calcium-mediated changes in magnesium excretion. Data from our laboratory confirm that it actually expresses non calcium-induced variations in magnesium observed after diuretics [6] or administration of waterborne magnesium [4].

The Mg/Ca has also been considered as a simple index of risk of calcium stone formation (see ref. in [3]). Ljunghall [7] showed that, at similar calcium excretion rates, the prevalence of stones was the highest when the Mg/Ca ratio was below 0.67. The difference was however evident only for high calcium excretion rates, which might be explained by the use of a simple fixed discriminant value when a variable value (see fig. 1) would have been more appropriate. This finding suggested that for a given urinary calcium, magnesium could exert a protective effect, in accordance with experimental data (see ref. in [3]). It was beyond the scope of the present study to look for a correlation between the value of d Mg/Cr and the activity of stone disease. However, since d Mg/Cr does not correlate with calcium but strongly correlates with magnesium excretion [5], it might help to evidence in vivo the importance of magnesium as a protective factor of stone formation.

It is obvious from these results that the changes in the Mg/Ca ratio do not allow any conclusion on the changes in magnesium excretion in face of changing calcium. The newly proposed parameter, d Mg/Cr, which expresses individual deviation from the normal correlation shows no difference between the controls and this intentionally selected subgroup of normomagnesuric stone formers. It does not vary after the calcium load indicating that it reflects only non calcium mediated changes in magnesium excretion.

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References


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