On Formulas for Daily Oral Magnesium Supplementation and Some of Their Side Effects

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Zusammenfassung

Es scheint festzustehen, daß der tägliche Magnesiumbedarf von Osteoporosepatienten bei 800 mg liegt. Die orale Zufuhr von Magnesium kann eine Rolle bei der Verhütung von Osteoporose, Kalzifikation der Arterienwände und Chondrokalzinose der Gelenke spielen. Die meisten Magnesiumpräparate verursachen jedoch bei Einnahme in den empfohlenen Dosen Durchfälle. Hydriertes Magnesiumglyzerophosphat dagegen verursacht keine Durchfälle, aber es hat den Nachteil, den Urin mit Phosphor-Ammonium-Magnesiumverbindungen zu überlasten. In dieser Studie konnten wir beobachten, daß Mischungen von hydriertem Magnesiumglyzerophosphat und Magnesiumhydroxycarbonat zu gleichen Teilen (1 : 1) eine annehmbare Zusammensetzung zur täglichen Magnesiumzufuhr darstellen, die nicht die obigen Nachteile haben.

Summary

There are indications that osteoporotic patients need a daily intake of 800 mg magnesium. Oral magnesium supplementation might prevent osteoporosis and also arterial wall calcification as well as chondrocalcinosis. Most magnesium compounds cause diarrhea, when used daily in the indicated amounts. However, magnesium glycerophosphate hydrate does not cause diarrhea. The disadvantage of these compounds is that it makes the urine supersaturated with struvite. In this study it was found that a 1 : 1 mixture of magnesium glycerophosphate hydrate and magnesium hydroxycarbonate is an acceptable formula for daily oral magnesium supplementation without the above mentioned disadvantages.

Résumé

Il semble bien établi que les besoins quotidiens en magnésium des patients atteints d'ostéoporose se situent à 800 mg. Une supplémentation en magnésium par voie orale peut jouer un rôle dans la prévention de l'ostéoporose, de la calcification des parois artérielles et de la chondrocalcinose articulaire. La plupart des préparations à base de magnésium sont responsables de diarrhées après administrations quotidiennes aux posologies recommandées. Le glycérophosphate de magnésium hydraté ne provoque pas de diarrhée mais présente cependant l'inconvénient de sursaturer les urines en cristaux phospho-ammoniaco-magnésiens. Cette étude nous a permis d'observer que le mélange à parts égales (1 : 1) de glycérophosphate hydraté et d'hydroxycarbonate de magnésium représente une formulation acceptable pour la supplémentation orale quotidienne en magnésium, qui n'entraîne pas les désagréments mentionnés ci-dessus.

Introduction

In a previous study [3] we have hypothesized that magnesium deficiency would be the cause of osteoporosis and pathological calcifications of old age. More recently we have demonstrated [2] that the therapeutic value of magnesium supplementation to severely osteoporotic patients was limited. However, a clinical study on perimenopausal women carried out in Israel [7] showed beyond doubt that oral magnesium supplementation increases the density of trabecular bone and therefore, has a big potential for the prevention of osteoporosis.

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In the above mentioned study [2] we have found that the serum magnesium level in a group of severely osteoporotic patients was normal (patients 0.90 ± 0.07 mmol/l, controls 0.87 ± 0.05 mmol/l). However, the erythrocyte magnesium content in patients (1.91 ± 0.20 mmol/liter cell) was significantly lower than that of controls (2.60 ± 0.25 mmol/liter cell). Hence, this quantity may be the best indicator in a blood test for identification of patients at risk to osteoporosis. We have also shown that daily oral magnesium supplementation with magnesium lactate raised the erythrocyte magnesium level in patients significantly without raising the serum magnesium level. By linear extrapolation we found that a daily dose of 500 to 800 mg Mg would be necessary for these severely osteoporotic patients to restore the erythrocyte magnesium level to normal.

In tab. 1 a survey is given of our and other studies, in which daily oral magnesium loads were applied in order to restore the normal intracellular magnesium level in erythrocytes in patients with latent magnesium deficiency. From these data it can be concluded that indeed a daily dose of up to 800 mg Mg may be necessary in order to restore the normal intracellular magnesium level, whereby the quantity probably also depends on the type of magnesium compound.

In the present study we investigated the incidence of diarrhea as a side effect of daily oral magnesium consumption for the most common magnesium containing compounds in order to find a formula most suitable for daily oral use.

Tab. 1: Erythrocyte magnesium content Mg_{RBC} (mmol/liter cell) in certain groups of patients before and after daily oral magnesium supplementation (as compared with Mg_{RBC} in controls).

Mg_{RBC}		Dose	Duration	Reference
Before treatment	After treatment	(mmol Mg/day)		
1.91 ± 0.20	2.11 ± 0.12	7.4	2 years	2
1.95	2.11	14.7	2 months	1
1.84 ± 0.31	2.41 ± 0.35	2.5	3 months	4

Diarrhea should be avoided because in such a state the balance of most minerals becomes negative.

Material and Methods

Twenty volunteers (10 women and 10 men) in age varying between 42 and 75 years were offered a daily dose of a certain magnesium compound comprising 400 mg Mg during four weeks. The magnesium compound was consumed in the form of a suspension in water. The volunteers registered the number of days on which they had diarrhea, from which we calculated the total percentage of days on which diarrhea occurred averaged over the twenty volunteers. In this way eleven different magnesium compounds were tested in addition to a placebo (mais flower).

The same volunteers tested in the same way several mixtures of magnesium compounds which looked most promising. In this way 1 : 1 mixtures (by weight) of magnesium glycerophosphate-hydrate with six different magnesium compounds and 1 : 1 mixtures (by weight) of magnesium glucose-1- phosphate with three different magnesium compounds were tested.

Tab. 2: Incidence of diarrhea (%) in 20 volunteers upon the oral use of different magnesium compounds in the amount of 400 mg Mg during 28 days.

Mg compound	Incidence
Sulfate	96
Chloride	78
Oxide	47
Hydroxide	45
Carbonate	40
Hydroxycarbonate	37
Lactate	32
Gluconate	27
Phosphate	20
Glycerophosphate	7
Glucose-1-phosphate	7
Placebo	7

Results

In tab. 2 the results are given for the eleven different magnesium compounds, in tab. 3 those for the mixtures with magnesium glycerophosphate-hydrate and in tab. 4 those for the mixtures with magnesium glucose-1-phosphate. It appears from tab. 2 that the side effect of diarrhea did not occur in our group of volunteers with magnesium glycerophosphate-hydrate and with magnesium glucose-1-phosphate. From tabs. 3 and 4 it is evident that these compounds also diminish the incidence of diarrhea in mixtures with other magnesium compounds which on themselves give a fairly high incidence.

Tab. 3: Incidence of diarrhea (%) in 20 volunteers upon the oral use of 1 : 1 mixtures (by weight) of magnesium glycerophosphate hydrate with different magnesium salts in the amount of 400 mg Mg during 28 days.

Mg-glycerophosphate 1 : 1 with	Incidence
Mg oxide	15
Mg hydroxide	12
Mg carbonate	8
Mg hydroxycarbonate	7
Mg lactate	7
Mg gluconate	7
Placebo	7

Tab. 4: Incidence of diarrhea (%) in 20 volunteers upon the oral use of 1 : 1 mixtures (by weight) of magnesium glucose-1-phosphate with different magnesium salts in the amount of 400 mg Mg during 28 days.

Mg glucose-1-phosphate 1 : 1 with	Incidence
Mg oxide	14
Mg hydroxycarbonate	7
Mg gluconate	7
Placebo	7

Discussion

At first sight it might seem that it is most safe to use either magnesium glycerophosphate-hydrate or magnesium glucose-1-phosphate for daily oral magnesium supplementation. However, from the data of *Robertson* and *Nordin* [5] on the ion activity product of struvite ($MgNH_4PO_4.6H_2O$) in urine and from the expected increase of the amounts of magnesium and phosphate ions which will be excreted in the urine, we estimate that the daily consumption of these compounds in the desired amounts will increase the risk of renal calculi formation of struvite from about 3% of the people (which it is in healthy groups) to at least 14% of the people. If we estimate this risk for the 1 : 1 mixtures of tabs. 3 and 4, it is found that these mixtures give a risk for struvite formation for not more than 4% of the people, which seems acceptable to us in view of the fact that it is already 3% without magnesium supplementation.

Tab. 5: Price of the most common magnesium compounds (DM) of the quality of food additives as based on the Merck catalogue 1987.

Magnesium product	per kg product	per kg Mg
Acetate-tetrahydrate	82	722
Glycerophosphate-hydrate	121	970
Hydrogenphosphate-trihydrate	41	294
Hydroxide	43	101
Hydroxycarbonate	22	87
Oxide	59	98

Before patients are advised to apply daily oral magnesium supplementation, one should ask whether their renal function is normal (glomerular filtration rate about 120 ml/min) or one should measure their renal function. Daily magnesium supplementation should be avoided in patients having a glomerular filtration rate of less than 30 ml/min, because otherwise their serum magnesium level will rise to undesirably high levels, by which muscle, heart and nerve function are impeded [6].

Finally, the cost aspect. Tab. 5 gives a survey of the price of the most common magnesium compounds with the quality of food additives as based on the Merck Catalogue 1987. In combination with tab. 2 it can be concluded that for more than 60 % of the people magnesium hydroxycarbonate is the best choice and that a treatment with a daily dose of 400 mg Mg would cost less than DM 13 per person per year. In combination with tab. 3 it is found that for the other people the best combination is a 1 : 1 mixture of magnesium glycerophosphate with magnesium hydroxycarbonate which would cost not more than DM 71 per person per year.

Unfortunately we did not have the possibility in this study to collect and analyze 24-hr samples of urine for magnesium. Otherwise we could have included the aspect of efficiency of the magnesium intestinal absorption from the different magnesium compounds.

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