Comment on "Magnesium supplementation in the treatment of pseudoxanthoma elasticum": Is magnesium oxide the best choice?

Loukman Omarjee, Karine Unger, Guillaume Mahé

Comment on: **Magnesium supplementation in the treatment of Pseudoxanthoma Elasticum: Is magnesium-oxide the best choice?**

Loukman Omarjee, MD-MSc[1,2,3], Karine Unger, MSc[4], Guillaume Mahe, MD-PhD[1,2]

1: Univ Rennes, CHU Rennes, INSERM CIC1414, Vascular Medicine Unit, Rennes, France

2: PXE Vascular Consultation Center, CHU Rennes, 35000 Rennes, France

3: Vascular Medicine Unit, Redon Hospital, 8 Rue Etienne Gascon, 35600 Redon, France

4: PXE France Association, 19 Rue Hippolyte Bousquet, 35170 Bruz, France

Correspondence to:

Dr Loukman OMARJEE, MD-MSc
Vascular Physician and Clinical Immunologist
PXE Vascular Consultation Center
Department of Vascular Medicine and Investigation
Pôle imagerie médicale et explorations fonctionnelles
Hôpital Pontchaillou – Rennes University Hospital
2 rue Henri Le Guilloux Rennes, F-35033. France.
Contact Phone Number: +33 (0) 2 99 28 43 21
Contact Mobile Number: +33 (0) 6 27 49 70 51
Contact Email: loukmano@yahoo.fr
Twitter: @LoukmanOmarjee

Word Count: 497

Dear Editor,

Rose et al. conducted the randomized controlled trial "Magnesium supplementation in the treatment of Pseudoxanthoma Elasticum (PXE)"[1] that we read with great interest. Indeed, magnesium is effective against elastic tissue calcification in PXE mouse models[1]. However, in this study, we regret that magnesium treatment results only in a trend towards improvement[1]. So, various factors may account for lack of statistical effect beyond a small sample size. Magnesium supplements or magnesium-salt, a combination of magnesium and other minerals, come in four different forms: i) insoluble inorganic-salts (oxide-carbonate-hydroxide); ii) soluble inorganic-salts (chloride-sulfate); iii) soluble organic-salts (citrate-lactate-gluconate); and iv) soluble organic complexes (glycinate-bisglycinate)[2]. Importantly, magnesium-element amount is depending from its form[2]. Magnesium bioavailability corresponding to the absorbed quantity is the most relevant pharmacological parameter in magnesium-salt selection[2]. The authors used magnesium-oxide, one of the cheapest available salts, with a relatively high content in magnesium, but with a low bioavailability[2]. Indeed, excessively high magnesium content may have a laxative effect. Hence, the necessity for dose-splitting[2]. Magnesium-citrate has the highest bioavailability of all magnesium-salts, compared to chelated forms and magnesium-oxide[2]. In a randomized, placebo-controlled study 46 healthy subjects received daily 300 mg doses of magnesium-citrate or magnesium-oxide[3]. Saliva, blood, and 24-hour urine samples were taken at baseline, 24-hours and 60-days[3]. At 60-days urinary magnesium excretion was higher with magnesium-citrate than with magnesium-oxide. Magnesium-citrate induced higher mean serum magnesium concentration than magnesium-oxide following 24-hour (p=0.026) and 60-day (p=0.006) supplementation[3]. This study showed that magnesium-citrate is more soluble than magnesium-oxide[3], hence its higher absorption rate as demonstrated by higher plasma concentration and urinary excretion outcomes than magnesium-oxide at various time-points after administration[3]. Thus available

data suggest that magnesium-citrate is better suited to therapeutic and supplementary use[3]. Furthermore citric acid, as a low molecular weight organic acid, promotes magnesium absorption by increasing its solubility[3,4]. Additionally, citrate is a major substrate in cellular energy metabolism and other cellular processes, binding calcium and inhibiting nucleation and calcium crystal growth[4] which is the desired outcome for PXE. A recent study found that citrate inhibited calcification in CKD patient urine[4]. Also, potassium-magnesium-citrate is an effective prophylaxis against recurrent calcium-oxalate nephrolithiasis[4], a complication frequently observed in PXE patients. Furthermore, magnesium-citrate has been shown in a recent study to protect against vascular calcification in an adenine-induced chronic renal failure rat model[4].

Magnesium should remain a new treatment way for PXE calcification, yet larger studies are required. We suggest considering magnesium-citrate, the highest bioavailable magnesium-salt for treatment of PXE calcification, in future clinical trials. Since vascular calcification is a well-known predictive risk factor of subsequent cardiovascular mortality[5], changes in vascular calcification could constitute a trial endpoint.

Magnesium balance in PXE patients should additionally constitute a secondary endpoint. Therefore, serum magnesium concentration, red-blood cell magnesium concentration and 24-hours urinary magnesium excretion are potentially useful biomarkers of magnesium status[5].

Given the rarity of PXE and the few patients involved, it is time to combine efforts for a cure and we call for international multicenter trials encompassing all PXE patient associations.

Acknowledgements

The authors wish to thank the Patients' Association "PXE France", the "Fondation Groupama" and the "CHU de Rennes – Corect" for their support for our work.

The authors wish to thank Ms Hazel Chaouch (hctranslationservices@outlook.com) for the formatting of the article and English language correction.

Ethics Approval

Not Applicable

Funding

No specific funding was received for this work.

Conflict of Interest

All authors declare they have no conflict of interest to disclose.

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