Letter to the Editor

Measurement of erythrocyte magnesium: what is its real value?

Dosagem do magnésio eritrocitário: Qual é o seu real valor?

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ABSTRACT

Magnesium is a cation with location predominantly intracellular and of great importance in several metabolic functions. It is possible that it plays an important role in pain and inflammatory processes. It's serum dosage possibly does not represent the reality of it's body concentration. The measurement of erythrocyte magnesium may represent an advance in its better evaluation.

Keywords: Erythrocyte magnesium; Pain; Inflammation; Osteoarthritis; Rheumatoid arthritis.

RESUMO

O magnésio é um cátion de localização predominantemente intracelular e de grande importância em várias funções metabólicas. É possível que tenha uma participação importante em processos álgicos e inflamatórios. Sua dosagem sérica possivelmente não representa a realidade de sua concentração corporal. A mensuração do magnésio eritrocitário talvez possa representar um avanço na sua melhor avaliação.

Palavras-chave: Magnésio eritrocitário; Dor; Inflamação; Osteoartrite; Artrite Reumatoide.

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Introduction

Motivated by the observation of the performance of an expressive number of serum magnesium (Mg) measurements performed daily, we seek a more precise form for its determination and we intend with the text to alert the reader to some aspects that are not always remembered, thereby avoiding unnecessary expenses that lack scientific basis. Thus, we believe it is necessary to disclose the preliminary results of this pilot study, contributing, perhaps, to a more rational decision-making or, at least, giving rise to a reflection on the subject.

Our presentation begins with the probable relationship between Mg and pain. Chronic pain is one of the great scourges that plague humanity. The search for an effective, safe and permanent treatment is incessant, however, the complexity of this subject makes this intention far from straightforward. This situation causes great suffering for patients who present such condition and for health professionals who assist them.

Osteoarthritis (OA) and rheumatoid arthritis (RA), are highly prevalent diseases that present chronic pain as an important and frequent symptom. In recent years, several studies have sought to correlate the role of magnesium (Mg) in the pain and inflammation process, not only in the diseases mentioned, but also in other diseases.[1-7]

Magnesium is the second most abundant intracellular cation and acts as a cofactor in more than 300 metabolic reactions. The body of a healthy adult has, on average, 21 to 28 g of Mg. Bone tissue is the largest reservoir of Mg in the body (approximately 50%), followed by muscle tissue. Only about 0.3% of the total body Mg is in the blood.[8-10]

Thus, the dosage of serum Mg may not accurately reflect its total amount in the body. Conversely, the intra-erythrocyte concentration of Mg is slightly higher than its sérum concentration, corresponding to approximately 0.5% to 1.5% of the total body reserves.[8,10]

Considering the distribution of Mg in the intra and extracellular compartments, we understand that its intra-erythrocyte dosage - because it is an intracellular measure - is more physiological than the serum dosage. To test this hypothesis, we conducted a pilot study to verify a possible correlation between serum Mg levels and erythrocyte Mg levels, as well as to evaluate a possible association of Mg with inflammatory parameters. Later, we will present the preliminary results of our study. Before, we will describe the results of some similar studies published in the recent medical literature.

Ulger et al. (2010) assessing intra-erythrocyte Mg, demonstrated a high prevalence of hypomagnesemia in geriatric patients, based on intra-erythrocyte Mg measurements, although all patients had normal serum measurements and there was no correlation between serum and intra-erythrocyte Mg levels.[11]

In a recent study Sitzia et al. (2020) showed the importance of assessing intra-erythrocyte Mg, suggesting that laboratory measurement of intracellular magnesium is necessary to detect hidden magnesium deficiency in the elderly population at risk for cognitive impairment due to cerebrovascular disease, finding a significant difference compared to concentration of serum Mg.[12]

Regarding the relationship between Mg and OA, there is a possibility that subjects with a higher content of Mg may be less likely to develop the disease. Shmagel et al. (2018) described that insufficient Mg intake was highly prevalent among individuals with radiographic knee OA and was also associated with a greater report of pain. Moreover, a reduction in synovial inflammation was seen in patients with OA who received magnesium sulfate. As a result, it appears that the administration of magnesium sulfate could improve the condition of patients with OA.[1,4,6]

Li et al. (2016), concluded that Mg deficiency could influence several pathways involved in the pathogenesis of OA, including progressive loss of joint cartilage, abnormal bone formation and tissue inflammation, which, together, could increase pain and loss of joint function.[1]

Shahi et al. (2019) going further to report the possibility of Mg insufficiency in RA, they recommended that serum Mg in RA patients could potentially be used to control cardiovascular risk, claiming that the Mg level had a negative correlation with total cholesterol and LDL. In contrast, the correlation of Mg levels was positive with HDL cholesterol in patients with RA.[9]

About the pilot study that we performed, we carried out a cross-sectional study with 65 volunteers, 32 with RA and 19 with OA (according to the criteria of the American College of Rheumatology), in addition to 14 healthy controls. RA patients were interviewed in order to obtain the Health Assessment Questionnaire (HAQ), Visual Analog Pain Scale (VAS) and Disease Activity Score 28 (DAS28) indexes. In patients with OA, the HAQ, EVA and Westerm Ontario McMaster Universities (WOMAC) indexes were evaluated. All were submitted to a medical interview and collect of blood samples (after a 12-hour fasting) to assess inflammatory tests and to measure serum and erythrocyte levels of Mg. The erythrocyte Mg was measured by the atomic absorption spectrophotometry method. The study was approved by the local ethics committee.

The statistical analysis of the data showed that the levels of serum and erythrocyte Mg did not show any correlation. There was also no statistically significant relationship between Mg levels (serum and erythrocyte) and the following parameters: pain, inflammatory tests, functional and activity indexes in both diseases. The non-association between serum and erythrocyte Mg levels and the parameters evaluated in the study, can be explained by the fact that serum and erythrocyte Mg represent very small fractions of all body Mg (serum Mg is equivalent to 0.3%, while erythrocyte Mg equivalent to 0.5% to 1.5% of the total Mg reserve). Therefore, even though there is an improvement in the search for a real role for Mg in a place where it is more concentrated than in plasma (i.e., in the erythrocyte), it still represents a very low fraction of the total Mg of the whole organism.

It should be noted that the results of our pilot study are still insufficient to reach more robust conclusions. Therefore, we believe it is not appropriate to present our preliminary findings in the form of a full paper. Nevertheless, we understand that it could be interesting to disclose our preliminary results in order to arouse the interest of other researchers to carry out further studies on this topic, due to its clinical relevance.

Albeit magnesium is a very important cation, it seems to us that its serum dosage is of little value, since the plasma dosage seeks magnesium where it is not found, that is, in the extracellular (intravascular) compartment. It is plausible, therefore, to surmise that the erythrocyte (intracellular) dosage, although not ideal (since there is little Mg in the red

blood cells), it would be a more appropriate strategy, however, we consider that it would not yet be a reliable form, since it would probably only show changes in serious deficiencies. New studies should continue in the search for a more accurate, easier to perform and less costly evaluation, observing with critical judgment the values found today both in serum and intra-erythrocyte levels. While a method to quantify Mg in bone and muscle tissue is not available at the clinical level, perhaps another less laborious and less costly way would be an indirect analysis as recently proposed by Schutten et al. (2020), it could be useful perhaps in investigating more serious disabilities and not as a method used in routine[13]. In conclusion, we must follow the search for an ideal method of evaluating this cation, which is of great importance in physiological and perhaps pathological processes such as pain.

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