Review article

From Epsom Salt to a Beneficial Mineral ; Magnesium

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Abstract:

Introduction: One of the most popular medical drugs with healing ability is Epsom salt that is hydrated magnesium sulphate;MgSo4.7H2o. Magnesium is the fourth most in the body and the second intracellular cation after potassium. In minute abundant mineral necessary for body's proper metabolism and function. Magnesium homeostasis amounts it is delicate is maintained by interplay among intestinal absorption, skeletal in the body а cellular reabsorption and urinary excretion. At level magnesium is resorption, renal а well as an in almost all enzymatic systems that regulates diverse cofactor as activator biochemical reactions. In addition, magnesium is essential for the conversion of vitamin D into its active form which in turn activated vitamin D can increase intestinal absorption of calcium influencing the growth and maintenance of magnesium and bones. Serum magnesium concentration estimation is а poor predictor of intracellular magnesium content not accurately reflect the status of body's total magnesium content. The present and may article will review magnesium deficiency and its role in vitamin D activations.

Methods: An integrated review format was chosen for present article and many medical literature on magnesium and its essential role in health and interaction/s and scientific with vitamin D were reviewed.

Findings: Results indicated that chronic magnesium deficiency is common among the wide hospitalized patients. It may general population as well as in the induce a range of clinical indicated complications. Investigations have that the activities of three major binding vitamin D converting enzymes and vitamin D proteins are magnesium dependent. deficiency leads reduced 1,25(OH)2 vitamin impaired Furthermore, magnesium to D and response. In general, the effectiveness vitamin D significantly reduced parathyroid of is when magnesium homeostasis in the body is not maintained.

Conclusion: concluded that It is chronic magnesium deficiency should always be considered beneficial different clinical complications. Taking magnesium supplementations could be in to prevent recurrence of the diseases. Moreover. the general population should be encouraged consume magnesium-containing foods to reduce disease burden. Further to in regard vitamin D investigations are necessary to and magnesium interaction/s. They may include observations to determine the adequate magnesium dose as well as studies on the more effective type of magnesium supplementation for vitamin D processing.

Keywords: Epsom salt. Chronic magnesium deficiency. Vitamin D. Magnesium Supplementation.

Introduction:

Magnesium relationship and its important role with humans health have been recognized for many years even before it was identified as an element. In 1618 a farmer in "Epsom, Surrey- England" dug out few wells in his farm for his cattle to drink. His thirsty animals refused to drink the water because of its bitter taste. Interestingly, the well's water had the ability to rapidly heal scratches, sores and rashes both in animals and humans (1). The fame of the healing ability of this water became spread by the word of mouth and others tried it. It was found that this water contained a salt /a pure mineral compound of magnesium and sulfate that attributed to its benefits. Later a factory was established in London (1) for the world-wide marketing of this salt. In England this salt was (and still is) known as " Epsom Salt" and in continental Europe as "Salt Anglicum". Late in the 17th century and thereafter, salt (hydrated magnesium Epsom sulphate;MgSo4.7H2o) was one of the most popular medical drugs. The people who used it did not know exactly why it was so beneficial, but they did understand that in some way it was good for health (1). In 1755 the Scottish Chemist Joseph Black in Edinburgh identified magnesium as an element. Although magnesium biology became clearer during the 20th century, in 21th century the importance of the magnesium in health remained overlooked or even ignored(1). Magnesium (Mg) is the fourth most abundant mineral in the body after calcium, sodium, and potassium and the second intracellular cation after potassium(1). While the pathophysiological calcium, sodium, and importance of potassium are well known and understood, the importance of magnesium is neither commonly known nor perceived as a

clinically important mineral. Magnesium is widely distributed in plant and animal foods, most green vegetables, sea foods, nuts, and grains. Whereas oils, fats, many highly-refined flours, corn flour and sugars have extremely low magnesium contents(2). Water is also a useful source of magnesium with some hard tap water containing more magnesium than soft water (2). The recommended daily allowance (RDW) of magnesium for adults is 310 to 420 mg/day and the required amount increases during pregnancy and regular strenuous exercise (3). Total Mg in the average 70Kg adult with 20% (w/w) fat is ~ 1000 to 1120 mmol or ~ 24g (4-5).

The most important reservoir for magnesium in the body is the bone and teeth (about 60% of total body magnesium) and 39% is in intercellular tissues (skeletal muscle and soft tissue). Remaining 1% is in serum and red blood cells, and from this only 0.3% is primarily found in serum (6-7). Therefore, serum magnesium concentration estimation poor predictor of intracellular a is magnesium content (6-7) and it may not accurately reflect the status of body's total magnesium content (8-9). Red blood cells magnesium concentration is three times higher than in serum, however, it has not been established as a reliable marker for magnesium determination at present (6). The normal reference range for the magnesium in blood serum is 0.76-1.15 mmol/L (8,10-11). Serum magnesium is present in three states: two-thirds is in ionized form, onethird is protein bound mostly to albumin, and a very small amount is complexed to anions. Magnesium is a cofactor as well as an activator in almost all enzymatic systems that regulates diverse biochemical reactions in the body. It is essential for the fundamental processes such as protein muscle contraction, synthesis, nerve function, blood pressure regulation, energy production, nucleic acid synthesis and repair, vitamin D activation, bone formation, electrolyte homeostasis and influence on extracellular calcium levels (4). The magnesium content of bone decreases with age and magnesium that is stored in this way, is not completely bioavailable during its deprivation (6-7).

In regard to laboratory tests and assessment of magnesium status, determination of magnesium concentration in nonhaemolysed serum is a useful routine test. However, as mentioned less than 1% of the total magnesium is present in serum (6-7) and this amount does not reflect bound intracellular or total body magnesium status. Intracellular magnesium content are moieties that account for its biological role in the body. Therefore, serum should not be used to exclude magnesium deficiency (8.12) and in patients with chronic magnesium deficiency a serum magnesium could remain within concentration the normal range (4,8,12). To exclude а deficiency, oral or intravenous magnesium loading tests would be appropriate. This procedure physiologically is considered to be the gold standard for assessing body magnesium content (12). Patients who are to undergo this test should have normal kidney function, not be taking medication that affects renal excretion of magnesium, and not have disturbances in cardiac conduction or advanced respiratory insufficiency(12).

Magnesium homeostasis in the body is maintained by a delicate interplay among intestinal absorption, skeletal resorption, renal reabsorption and urinary excretion. It is mainly absorbed in the small intestine, although some is also taken up via the large intestine (4,10,13-14). It is worth noting that intestinal absorption is not directly proportional to magnesium intake but is dependent mainly on magnesium status. The lower the magnesium level, the more of the mineral is absorbed in the gut, thus relative magnesium absorption is high when intake is low and vice versa. The kidneys are crucial in magnesium homeostasis as serum magnesium concentration is primarily controlled by its excretion in urine (5). Even when the skeletal or intracellular magnesium content of soft tissue may be depleted, the circulating levels of magnesium could remain within the normal range because of its tight homeostatic control (8,11-12). Moreover, various clinical results have shown that there is a direct link between magnesium deficiency, and impaired glucose tolerance, osteoporosis ,muscular spasms, electrolyte disturbances, excessive alcohol intake, and abnormalities in cardiac (15-16). In addition, interactions rhythm between magnesium and vitamin D are necessary for vitamin D metabolism. They directly regulate bone and muscle metabolism and are also essential for the absorption of dietary calcium and phosphorus (12,17).

Methods:

An integrated review format was chosen for this article and many medical and scientific literature on magnesium and its essential role in health and vitamin D metabolism were reviewed.

Findings and Discussion:

The healing ability of Epsom salt is related to its pure mineral compound as hydrated MgSo4.7H2o. magnesium sulphate; Magnesium as the second intracellular cation after potassium, is a critical mineral in the body. It facilitates cellular energy production process(18) as well as it is necessary for DNA synthesis and repair (19-21). Previous studies have indicated that hypermagnesemia magnesium or intoxication is very rare in humans. Such conditions only occur in severe renal insufficiency (22). Furthermore, it has been shown that hypomagnesemia or magnesium deficiency in healthy individuals who are consuming a balanced diet is quit rare because kidneys are able to limit prolonged excretion of magnesium when intake is low (5,13). In addition, several studies have found that elderly people have relatively low intakes of magnesium because of inadequate dietary consumption. Furthermore, intestinal absorption tends to decrease and urinary magnesium excretion tends to increase in the older individuals (23-24). Hypomagnesemia or magnesium deficiency is defined as serum magnesium concentration <0.75 mmol/L with nonspecific early signs that include loss of appetite, lethargy, nausea, vomiting, fatigue, and weakness (25). It is estimated that at least 42% of young adults have an ongoing magnesium deficiency primary (26).Clinically magnesium deficiency may present acutely or with chronic manifestations. Acute hypomagnesemia

represented by clinical features such as severe cramps, refractory hypokalaemia, refractory hypocalcaemia, eclampsia in pregnant woman, and cardiac arrhythmias (15). Response to IV magnesium in these cases is rapid. Chronic magnesium deficiency is an important underlying risk factor for many clinical conditions of a host such as osteoporosis, muscular spasms, electrolyte disturbances, and abnormalities in cardiac rhythm (15-16,24-25). It reflects reduced levels of magnesium within cells and bones in the setting of normal serum magnesium, which is erroneously perceived to exclude magnesium deficiency. Its clinical presentation may vary from nonspecific symptoms to causing wide range of diseases (25).

Investigations have also indicated that magnesium deficiency, leads to reduced 1,25(OH)2 vitamin D and impaired parathyroid response (7,27). Previous studies conducted among patients with rickets showed magnesium supplementation substantially reversed the resistance to vitamin D treatment (17,,27-28). The results indicated that have magnesium supplementation can increase the effectiveness of vitamin D activity (17,29). Indeed, magnesium plays a critical role in the synthesis and metabolism of parathyroid hormone and vitamin D (18,26). Vitamin D; either D3 (animal source) or D2 (non animal source) does not have significant biological activity. Rather it needs to be processed further in the liver and kidneys to generate the biologically active form 1.25dihydroxyvitamin D (1,25[OH]2 D). In addition, absorbed vitamin D is transported in blood bound to the carrier proteins. Earlier studies have indicated that the activities of three major vitamin D converting enzymes and vitamin D binding proteins are magnesium dependent. These three enzymes are 25- hydroxylase in the liver and 1α hydroxylase and 24hydroxylase in the kidneys (30-32). Vitamin D also plays a key role in the intestinal absorption of phosphate and magnesium to influence eventual skeletal mineralization process (33,18). Magnesium deficiency are often associated with vitamin D resistant hypocalcemia as well (15,17), which can only be corrected after the proper replacement of magnesium. Calcium and magnesium are important for maintaining bone health and preventing osteoporosis. It is recommended that calcium supplements always be taken with magnesium to ensure that the calcium intake is properly metabolized (17).In general, the effectiveness of vitamin D is significantly reduced when magnesium homeostasis in the body is not maintained (34).

Conclusion:

Chronic magnesium deficiency is common in general population particularly in the elderly and in the hospitalized patients. It can induce a wide range of clinical complications (6-7). Its etiology is summarized in Figure 1. Assessment of serum magnesium status does not reflect reduced levels of magnesium within cells and bones. Therefore, serum should not be used to exclude chronic magnesium deficiency (8,12). It is concluded that chronic magnesium deficiency should always be considered in different clinical magnesium conditions and taking supplementations could be beneficial to

prevent recurrence of the diseases. Moreover, the general population should be encouraged to consume more magnesiumcontaining foods to reduce disease burden. Further investigations are necessary in regard to vitamin D and magnesium interaction/s. They may include observations to determine the adequate magnesium dose as well as studies on the more effective type of magnesium supplementation for vitamin D processing. Since there are very limited data on the bioavailability of different magnesium supplementation salts (35)

References:

1. Ismail AAA , Ismail NA. Magnesium: A mineral essential for health yet generally underestimated or even ignored. J Nutr Food Sci. 2016; 6:4.

2. Jiang L, He P, Chen J. et al. Magnesium levels in drinking water and coronary heart disease mortality risk: a meta-analysis. Nutrients. 2016;8(1).

3. Institute of Medicine. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D and fluoride. Washington, DC: National Academy Press; 2010.

4. Jahnen-Dechent J, Ketteler M. Magnesium basics. Clin Kidney J. 2012; 5: i3–i14.

5. Swaminathan, R. Magnesium metabolism and its disorders. Clin Biochem Rev. 2003; 24: 47–66.

6. Ismail AAA. Ismail AA. Ismail Y. Chronic magnesium deficiency and human disease; time for reappraisal? QJM: an inter J Med.

2017;1-5.har

7. Faheemuddin A . Abdul M . Magnesium: The forgotten electrolyte—A review on hypomagnesemia. Med Sci. 2019; 7(4): 56.
8. Ismail Y, Ismail AA. The underestimated problem of using serum magnesium measurements to exclude magnesium deficiency in adults; a health warning is

needed for "normal" results. Clin Chem Lab Med. 2010; 48: 323–327. 9. Seo JW, Park TJ. Magnesium

9. Seo JW, Park IJ. Magnesium metabolism. Electrolyte Blood Press. 2008;6(2):86-95.

10. Romani AM. Cellular magnesium homeostasis. Arch Biochem Biophys. 2011; 512:1-23.

11. Elin RJ. Assessment of magnesium status for diagnosis and therapy. Magnes Res. 2010;23(4):S194-S198.

12. Ismail AAA, Ismail AA, Ismail Y. Clinical assessment of magnesium status in the adult: an overview. In: Watson RR.

Preedy V. Zibadi S. eds. Magnesium in Human Health and Disease. New York, Humana Press, Springer Science. USA. 2013;3–34.

13.Beggs MR, Appel I, Svenningsen P, Skjodt K, Alexander RT, Dimke H. Expression of transcellular and paracellular calcium and magnesium transport proteins in renal and intestinal epithelia during lactation. Am J Physiol Renal Physiol. 2017;313(3):F629-F640.

14. de Baaij, JH, Hoenderop, JG, BindelsRJ. Regulation of magnesium balance:Lessons learned from human

genetic disease. Clin Kidney J. 2012; 5: i15–i24.

15.Vierling W, Liebscher DH, Micke O, Von Ehrlich B, Kisters K. Magnesium deficiency and therapy in cardiac arrhythmias: Recommendations of the German society for magnesium research. Dtsch Med Wochenschr. 2013; 138: 1165–1171.

16. Castiglioni S, Cazzaniga A, AlbisettiW, Maier JA. Magnesium and osteoporosis:Current state of

knowledge and future research directions. Nutrients .2013; 5: 3022–3033.

17. Reddy P, Edwards LR. Magnesium Supplementation in Vitamin D Deficiency. Am J Ther. 2019 ;26(1):e124-e132.

18. Chen HY, Cheng FC, Pan HC, et al. Magnesium enhances exercise performance via increasing glucose availability in the blood, muscle, and brain during exercise. PLoS One. 2014;9(1):e85486.

19.Gao Y, Yang W. Capture of a third Mg(2)(+) is essential for catalyzing DNA synthesis. Science. 2016; 352(6291):1334-7.

20.Petrovic J, Stanic D, Dmitrasinovic G, et al. Magnesium supplementation diminishes peripheral blood lymphocyte DNA oxidative damage in athletes and sedentary young man. Oxid Med Cell Longev. 2016;2016:2019643.

21. Chen Y, Gao T, Wang Y, et al. Investigating the influence of magnesium ions on p53-DNA binding using atomic force microscopy. Int J Mol Sci. 2017;18(7).

22. Tokmak F, Kisters K, Hausberg M, Rump LC. Buffer function of the cell membrane for magnesium in chronic kidney disease. Trace Elem Electrol. 2008; 25: 234–235.

23. Killilea DW, Maier JA . A connection between magnesium deficiency and aging: new insights from cellular studies. Magnes Res. 2008; 21: 77-82. 24. Veronese N, Berton L, Carraro S, et al., "Effect of oral magnesium supplementation on physical performance in healthy

elderly women involved in a weekly exercise program: A randomized controlled trial". Am J Clin Nutrition. 2014;100(3): 974–981.

25. Spätling L, Classen HG, Külpmann WR, Manz F, et al. Diagnosing magnesium deficiency. Current recommendations of the society for magnesium research. Fortschr Med Orig. 2000; 118:49–53.

26. Hermes Sales C, Azevedo Nascimento D, Queiroz Medeiros AC, Costa Lima K, et al. There is chronic latent magnesium deficiency in apparently healthy university students. Nutricion Hospitalaria .2014; 30(1): 200–204.

27. Castiglioni S. Cazzaniga A. Albisetti W. Maier, JA. Magnesium and osteoporosis: Current state of knowledge and future research directions. Nutrients. 2013; 5: 3022–3033.

28. Ozsoylu S, Hanioğlu N. Serum magnesium levels in children with vitamin D deficiency rickets. Turk J Pediatr. 1977;19(3-4):89-96.

29. Brown RB, Haq A, Stanford CF, Razzaque MS. Vitamin D, phosphate, and vasculotoxicity. Can J Physiol Pharmacol. 2015;93(12):1077-1082.

30. Risco F, Traba ML. Possible involvement of a magnesium dependent mitochondrial alkaline phosphatase in the regulation of the 25-hydroxyvitamin D3-1 alpha-and 25-hydroxyvitamin D3-24Rhydroxylases in LLC-PK1 cells. Magnes Res. 1994;7(3-4):169-178.

31. Risco F, Traba ML. Influence of magnesium on the in vitro synthesis of 24,25-dihydroxyvitamin D3 and 1 alpha, 25-dihydroxyvitamin D3. Magnes Res. 1992; 5:5–14.

32. Aliasgharpour M. Technical points in vitamin D measurement assays. Int J Med Invest .2019; 8(2):1-5.

33. Dusso AS. Update on the biologic role of the vitamin D endocrine system. Curr Vasc Pharmacol. 2014;12(2):272-277.

34. Elin RJ. "Re-evaluation of the concept of chronic, latent, magnesium deficiency". Magnes Res.2011; 24(4):

225-227.

35. Coudray C. Rambeau M. Feillet-Coudray C. Gueux, E. et al. Study of magnesium bioavailability from ten organic and inorganic mg salts in mg-depleted rats using a stable isotope approach. Magnes Res. 2005; 18: 215–223.



Figure 1: Etiology of Chronic Magnesium Deficiency (11). GI- Gastrointestinal tract, Mg-Magnesium