

Mini Review

Magnesium and Oxidative Stress during Menopause Stage

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Abbreviations

Mg: Magnesium; OS: Oxidative Stress

Introduction

The menopause process

Menopause is a stage that occurs in women's life characterized by a great change at hormonal level in which the ovarian secretion ceases, producing a hormonal fall in the levels of estrogens and progestogens, [1] that could generate a series of cardiovascular, bony, adipose and urogenital modifications [2,3] and frequent associated symptoms such as hot flashes, depression, insomnia, headache, dizziness, irritability, loss of sexual interest, weight gain, vaginal dryness, urinary incontinence, breast symptoms, and changes in skin and hair [4-10]. Moreover, in the longer term, are common the development of some pathologies such as Osteoporosis (OP) and Cardiovascular Diseases (CVD), which are the main causes of death in women in the world, due to the hormonal changes [11,12].

At this stage, since there is a redistribution and increase in fat mass, as well as a chronic stress that favors the synthesis of cortisol (a hormone that stimulates appetite), there is an easier tendency to gain weight that could make women to restrict the diet [13,14]. Therefore, if the menopausal woman does not follow a balanced diet rich in micronutrients, a situation of mineral deficiency could be reached, compromising minerals such as Magnesium (Mg) [15-17].

Importance of magnesium

Mg, which is the fourth cation of the organism, is a major mineral in the human organism which regulates a wide range of biological mechanisms. With respect to intake, absorption and metabolism of Mg, this mineral needs to enter to the body through the diet. It is estimated that an amount of 300 mg/day of this mineral is necessary to cover all physiological needs. Of this amount ingested, about 200 mg/day will be excreted in the feces, absorbing 100 mg/day. Once the intestinal barrier is passed, hormones such as Paratohormone

Abstract

Menopause is a natural process that could lead to pathological if it is not controlled. During this stage, key minerals such as magnesium may be decreased due to the fall of estrogen that promotes weight gain, which is related to magnesium deficiency. During menopause, an increase in oxidative stress has been seen due to a decrease in antioxidant defense, which could be improved by ensuring adequate magnesium status. Therefore, menopausal women should monitor their magnesium status by increasing dietary magnesium intake and assess the intake of magnesium supplements, in order to prevent the symptoms that occur in menopause

Keywords: Magnesium; Menopause; Woman; Oxidative Stress

(PTH) and Calcitonin (CT), will favour the tubular reabsorption of Mg. Moreover, hormones such as androgens and estrogens, which are decreased in menopause, will stimulate Mg excretion in the urine, expelling about 100 mg/day, thus maintaining a balance between dietary Mg and Mg expelled both at renal and fecal level [19].

Among its functions, at bone level, it is part of the mineral structure next to Calcium (Ca) and Phosphorus (P). It is estimated that there is 30% of Mg that will be forming the internal structure of the bone, maintaining fixed without suffering alterations. The remaining 70% will be in constant remodeling and renovation, being regulated for plasmatic Mg. Mg is essential too for the functioning of PTH and vitamin D, therefore, a possible deficiency in a risky group like menopausal women, could make bone health look compromised, suggesting a possible supplementation with Mg in case of deficiency [20,21]. It also plays a great role in brain tissue, as it intervenes in the transmission of nerve impulses, reducing the excitability in the Central Nervous System (CNS). Mg inhibits the release of acetylcholine and has an antioxidant effect on those factors that are prooxidants in the motor plate [19]. At muscular level, it is related to normal muscle excitability. In addition, it regulates the contractility of the heart and intestinal peristalsis, so it seems to be necessary to prevent CVD as well as intestinal problems [22]. In global terms, because of having an effect on ATP, it is involved in all mechanisms dependent on this molecule that occur throughout the body and is also a cofactor of various enzymatic systems of energy metabolism, protein synthesis and nucleic acids [23].

Magnesium Deficiency and Menopause

When Mg is not ingested enough, a situation of hypomagnesemia occurs, as it is a water soluble mineral which has to be assured every day in the diet. Mg deficiency will lead to weakness, ataxia, cramps, tetany, seizures and arrhythmias [24]. Other situations that could generate hypomagnesemia are proton pump inhibitors, the use of diuretics, hypercalcemia, nephrotoxins, alcohol consumption, as well as diseases such as uncontrolled Diabetes Mellitus (DM) and

pancreatitis [25-29].

In menopausal women, due to the hormonal alteration, there will be an imbalance in the phosphorous-calcium metabolism, directly related to the status of Mg [30]. Chronic Potassium (K) and Calcium (Ca) deficiency often leads to a Mg deficiency. Mg regulates K and is necessary for Na-K ATPase to function properly. In addition, hypomagnesemia

inhibits release of PTH, leading to hypocalcaemia, which could result in an accentuation of the characteristic symptoms of menopause that are modulated by Mg activity, which, although in the short term are anorexia, nausea, vomiting, lethargy and weakness, when this Mg deficiency is prolonged, it is manifested generating complications at neuromuscular, cardiovascular and metabolic level [19,31].

Therefore, due to this possibility of hypomagnesemia in this risky group, it is necessary monitoring the status of those minerals related to phosphorous-calcium metabolism such as Ca, K, Phosphorous (P) and Mg, since these minerals keep a close relationship to achieve their homeostasis. Thus, the inclusion of Mg supplements in menopausal women is suggested, because it seems to improve the menopausal symptoms and avoids consequences at longer-term systemic level [32].

Oxidative stress during menopause. Role of magnesium

The human organism is in contact with prooxidant and antioxidant compounds. When there is an imbalance in favor of those factors that are prooxidants, the production of Free Radicals (FR) increases, generating Oxidative Stress (OS). This situation has multifactorial etiology and increases the probability of developing cancers, neurodegenerative and respiratory diseases [33-35]. FR are very unstable chemical species because they have a missing electron. They are generated by the addition of an electron to a molecule, by the loss of a hydrogen atom or by the rupture of a covalent bond. This free radical can be neutralized by sharing electrons or reacting with other molecules that become FR of less instability and that end up becoming stable. There is a wide range of FR such as oxygen, nitrogen, carbon, sulfur, chlorine and quinones [36,37]. The sources of FR can be endogenous (the electronic transport chain, enzymes, hemoproteins and phagocytosis) and exogenous (toxic, drugs, xenobiotics and alcohol) [38,39]. FR will act on lipids, causing lipid peroxidation of membrane lipids, on proteins, oxidizing structural proteins and enzymes, on carbohydrates and on nucleic acids. To combat this effect, we use enzyme defense systems such as Superoxide Dismutase (SOD), Catalase and Glutathione Peroxidase (GPX), as well as non-enzymatic antioxidant defense systems such as glutathione (GSH), vitamin E, vitamin C, coenzyme Q, carotenoids, polyphenols and uric acid [40-42].

Estrogens are sexual hormones that also function as antioxidants, facing OS. In menopause, when estrogens decrease, an increase in OS occurs, favoring the activity of FR on various biomolecules of the organism, thus increasing the pathologies and symptoms associated with the menopausal process [43]. On the other hand, it has been observed that the menopausal woman will have the levels of antioxidant enzymes such as SOD and GPX altered [44]. In addition, during the menopausal process, the redistribution and increase of fat mass, will increase the probability of earning weight, which has been associated with OS [45], being Mg deficiency a risky factor of

obesity [46]. To combat OS, several authors propose physical activity of moderate intensity that reduces FR, because it controls weight and increase the antioxidant activity, due to the reduction of stress and anxiety [47-49].

It has been observed that Mg is related to OS, since it has been shown that its deficiency decreases antioxidant status through the accumulation of products derived from lipid peroxidation, as well as by a decrease of GPX [44]. When the human body detects that there is a low Mg status, it sends signals to reduce both the expression and the activity of various antioxidant enzymes such as catalase, GPX and SOD, decreasing the antioxidant defense and producing hydrogen peroxide and superoxide anion, which will increase the inflammatory response, developing a low-grade pro-inflammatory state [50,51], which, if it is not corrected, could lead to some pathologies that occur with a prolonged inflammation over time, such as obesity and metabolic syndrome [52]. Therefore, Mg status in menopausal woman must be controlled very well, being necessary to take food of high nutritional density in Mg. Likewise, the use of Mg supplements is recommended as long as the menopausal woman does is not able to achieve an adequate status of Mg through the diet, or due to pathologies that alter the intake and metabolism of this mineral [32,53,54].

Conclusion

Menopausal women are a risk group with a high prevalence of magnesium-deficient status, which is related to both short- and long-term symptoms, making special emphasis on a decreased antioxidant status that could be corrected by monitoring magnesium status and ensuring its optimal intake through food or Mg supplements.

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