MAGNESIUM SUPPLEMENTATION IN CARDIOVASCULAR DISEASES : - A SYSTEMATIC REVIEW

Review Article

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ABSTRACT

OBJECTIVES: The aim of this study was to clarify the role of Mg^{2+} in diseases linked to cardiovascular risks.

METHODS: A retrospective systematic review of the Medical Literature Analysis and Retrieval System Online and Latin American (MEDLINE) and Caribbean Literature in Health Sciences (LILACS) databases was performed. The following keywords were used for queries: "magnesium supplementation," "diabetic," and "lipid profile." The inclusion criteria for the selection of papers were as follows : original articles or systematic reviews with and without meta-analyses, published between January 2007 and April 2017. Studies that were unrelated to magnesium replacement and cardiovascular function as well as case reports were excluded.

RESULTS: Initially, 472 articles were obtained. After applying the inclusion and exclusion criteria, 13 articles were evaluated. Overall, Mg^{2+} supplementation had a favorable effect on glycemic and lipid indexes in patients with diabetes and/or pre-diabetes. Two studies demonstrated that Mg^{2+} did not have a significant effect on laboratory test results. In these studies, 62.5% of patients had uncontrolled hbA1c and dyslipidemia, 41% were obese, and 82% had HOMA-IR $\geq$ 2.5.

CONCLUSION: Mg^{2+} supplementation may contribute to reductions in the risks of cardiovascular diseases. However, owing to the conflicting results, additional complementary studies are needed, not only to improve our understanding of the beneficial pathways involving Mg^{2+}, but also to facilitate the development of robust guidelines for clinical practice.

KEYWORDS :

Cardiovascular disease, Magnesium, Treatment.

I. INTRODUCTION

Magnesium (Mg) is an important cofactor in biochemical reactions and the second most abundant intracellular cation. Mg coupled with enzymes is involved in the oxidation of carbohydrates, and it is also involved in insulin secretion, binding, and activity at several levels, consequently affecting glucose and lipid metabolism [1-3]. In adults, normal levels of Mg^{2+} are 1.7–2.4 mg/dL (1.5–2.4 mEq/L, 0.7–1 mmoL/EU). Hypomagnesemia is clinically defined as serum Mg^{2+} concentrations of ≤1.6 mg/dL or <0.66 mmol/L, or ≤2 standard deviations below the general population mean [4]. Magnesium deficiencies have been reported in patients with metabolic disorders, such as type 2 diabetes mellitus, pre-diabetes, hyperlipidemic, hypertension, and chronic kidney disease, and are concomitantly associated with cardiovascular diseases [5,6].

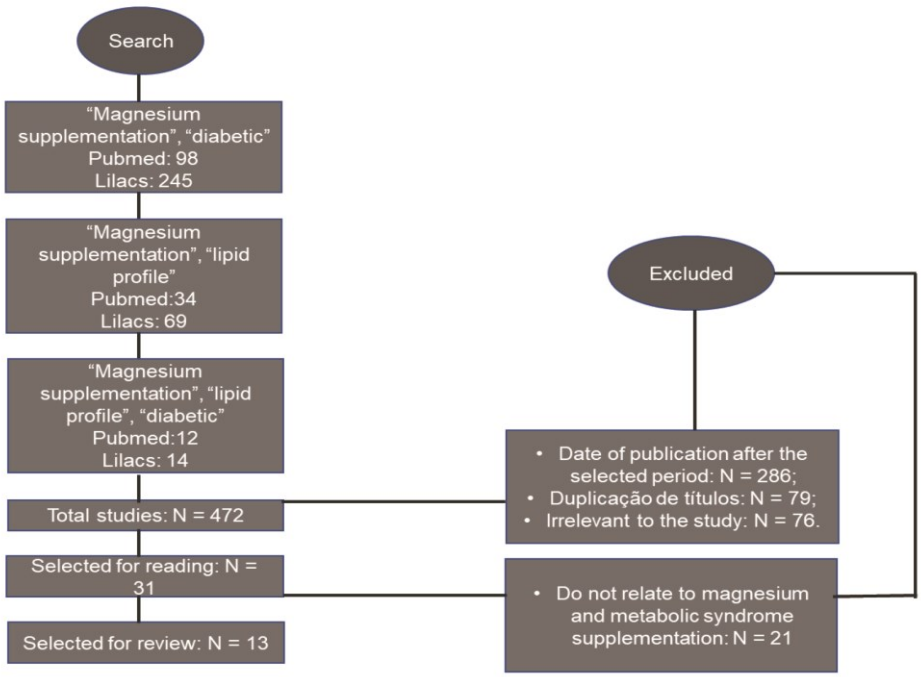
Hypomagnesemia is a common condition in patients with type 2 diabetes due to increased renal excretion, accounting for 1/3 of the population, and may be involved in the development of other complications of macro and microvascular diabetes. However, the relationship between type 2 diabetes mellitus and Mg^{2+} deficiency has not yet been fully elucidated [1, 7-9]. Furthermore, studies have suggested that magnesium supplementation may be effective in patients with diabetes.

With respect to cardiovascular factors, Mg^{2+} is routinely measured in the blood and has many functions in the cardiovascular system; it acts as a sodium potassium ATPase activator, has antiarrhythmic effects, and is associated with cardiovascular risk [10]. Its cardioprotective role extends to modulation, calcium uptake, and distribution in vascular smooth muscle cells, and it affects vascular restriction, thereby reducing peripheral resistance. Recent studies have shown that Mg^{2+} also reduces the levels of triglycerides and low-density lipoproteins and increases high density lipoproteins [11]. Dyslipidemia is the main risk factor for atherosclerosis, which can be improved by magnesium therapy. Studies have shown that by significantly reducing parathyroid hormone levels, vascular calcification is hindered; however, more studies are needed to elucidate the complete pathophysiological mechanism [12, 13]. We aimed to clarify the role of Mg^{2+} in the context of diseases related to cardiovascular risks.

II. METHODOLOGY

A retrospective systematic review was performed using the Medical Literature Analysis and Retrieval System Online (MEDLINE) and Latin American and Caribbean Literature in Health Sciences (LILACS) databases. For the search, the following terms were used: magnesium, supplementation, diabetics, and lipid profile. The inclusion criteria were as follows: original articles, systematic reviews with or without meta-analyses, and published between January 2007 and April 2017. The exclusion criteria were as follows: studies that did not relate to magnesium replacement therapy with cardiovascular function, case reports, letters to the editor, and publications in congresses (Figure 1).

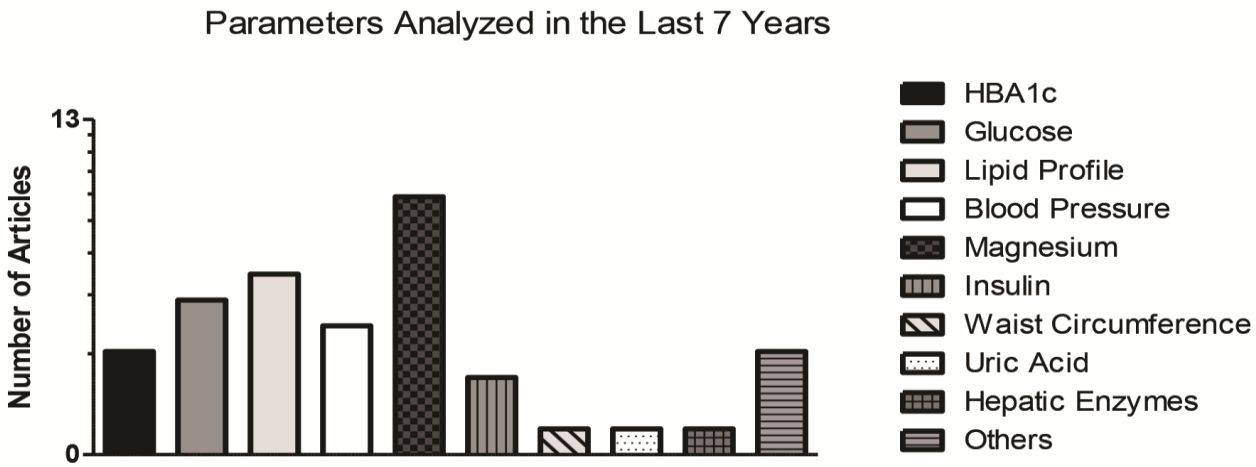
Figure 1



III. RESULTS

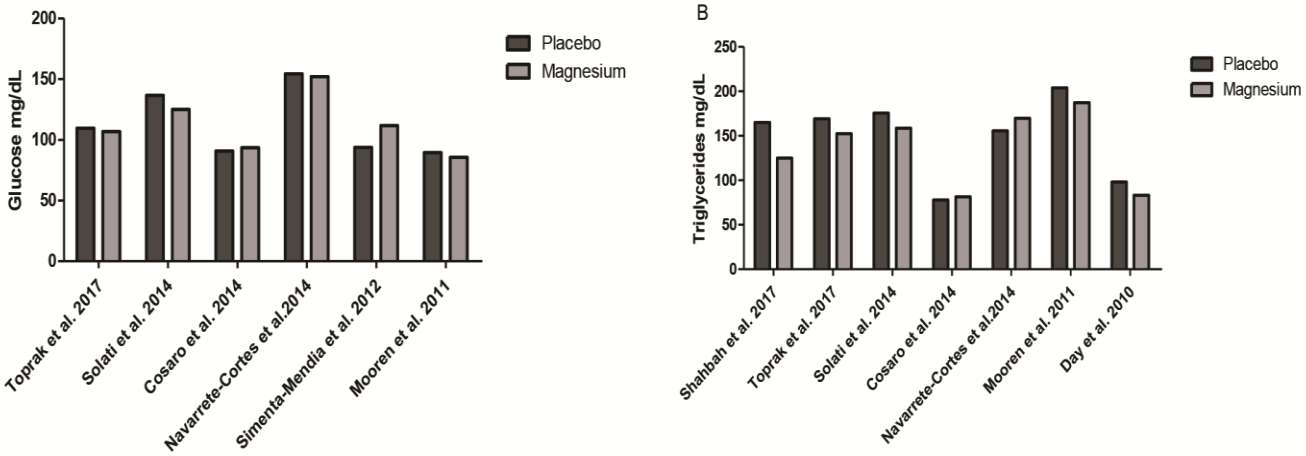
Initially, 472 articles were obtained. The final sample size was 13 articles after applying the inclusion and exclusion criteria. Table 1 presents the characteristics of the 13 articles selected in the present review, including the authors, year of publication, type of study, and experimental model. The reported parameters differed among studies (Figure 2).

Figure 2



Magnesium supplementation had a favorable effect on glycemic and lipid levels in patients with diabetes and/or pre-diabetes. However, Mg^{2+} had no significant effect on the laboratory parameters (Figure 3 a–b) [14] Shahbah et al.[15] performed Hba1c, lipidogram, and magnesium tests using serum from 71 children (32 boys and 39 girls). Children who presented with hypomagnesaemia had values of less than 1.7 mg/dL and were subjected to supplementation with 300 mg of Mg^{2+} per day for 3 months, resulting in improvements in glycemic and lipid control.

Figure 3



In another study by Toprak et al.[16], 128 obese and pre-diabetic patients with hypomagnesemia (<1.8 mg/dL) were enrolled, and Hba1c, glucose, waist circumference, uric acid, Mg^{2+}, and systolic and diastolic pressure were evaluated. These individuals were divided into two groups: a group consisting of 57 people that received 365 mg of Mg^{2+} per day for 3 months and a control group consisting of 61 patients that received a placebo. An improvement in metabolic syndrome was observed in patients who received Mg^{2+} supplementation when compared to the control group, including reduced glycemic, lipid, insulin, and uric acid levels. In addition, Mg^{2+} supplementation resulted in reduced glycemic indexes in 4 out of 6 studies. Furthermore, 5 out of 7 studies reported reduced triglyceride levels after Mg^{2+} supplementation when compared to those of the control group.

Figure 4 summarizes glucose and serum triglyceride levels before and after treatment with magnesium and the placebo. The first two graphs in the upper portion identify the glycemia values and the final triglyceride levels. These parameters were selected based on their large sample sizes. The articles summarized in graph 5 used the baseline methodology, i.e., baseline values were collected from the control and test groups. The triglyceride levels were lower in subjects who were administered Mg^{2+} than in those administered the placebo, but glycemia did not differ between groups. As shown in Figure 5, 69% of studies focused on adults, 15% used lineage cells, 8% included children, and 8% used rats.

Figure 4

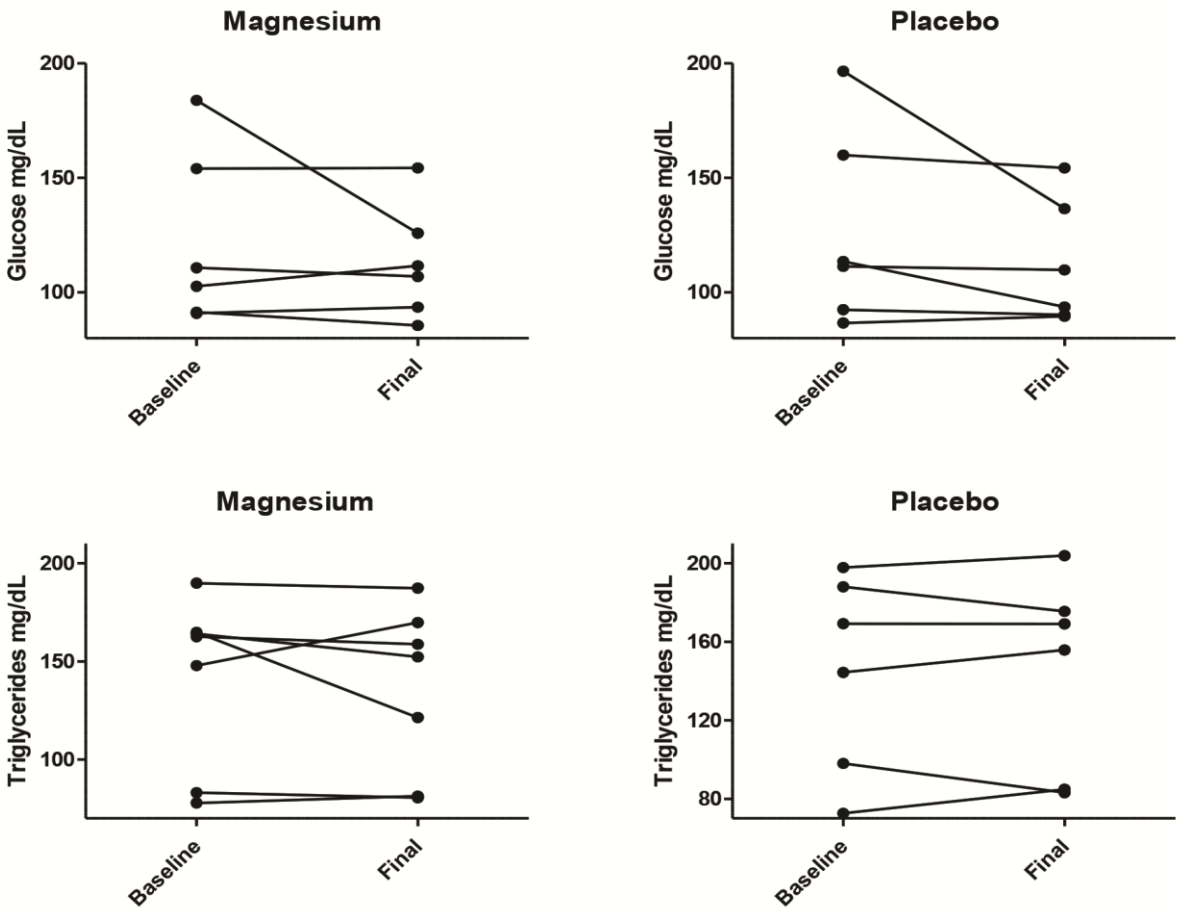
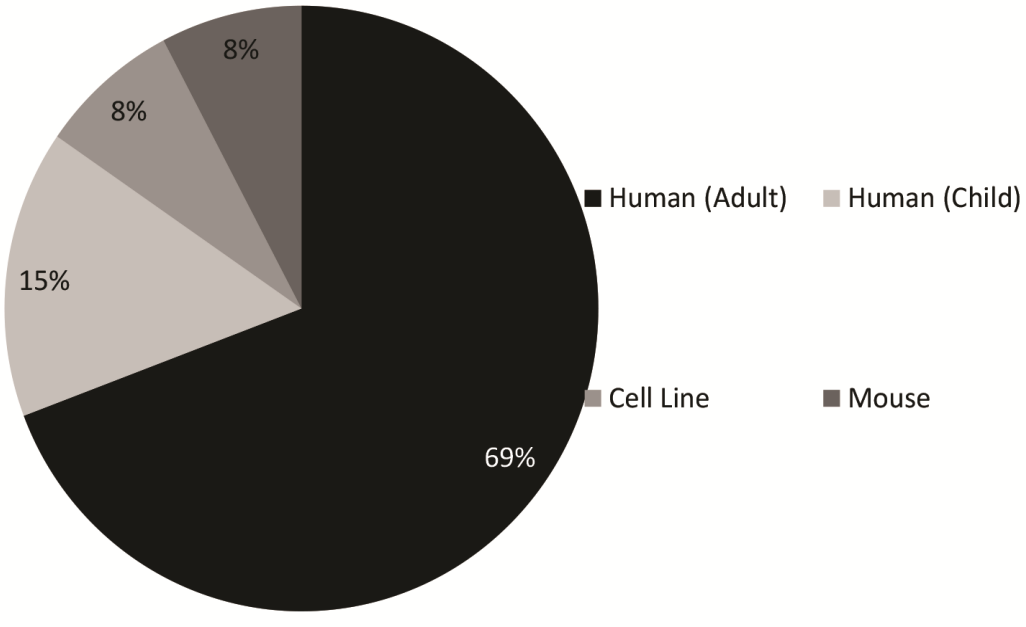


Figure 5



IV. CONCLUSION

Mg^{2+} supplementation may be useful for reducing the risk of cardiovascular diseases. However, owing to conflicting results, additional complementary studies are needed to improve our understanding of the beneficial pathways involving Mg^{2+} and to develop robust guidelines for clinical practice.

V. ACKNOWLEDGMENTS

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VI. AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

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