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A narrative review on the role of magnesium in immune regulation, inflammation, infectious diseases, and cancer

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Abstract

Background

Magnesium (Mg) has gained much importance recently because of its unique range of biological functions. It is one of the most significant micronutrients in biological systems. This review aims to outline the immune-regulating actions of Mg and its crucial role in regulating inflammation and immune response to infectious agents and malignancies.

Methods

We conducted a literature review on MEDLINE, PubMed, EMBASE, Web of Science to determine the impact of Mg on immune regulation in three settings of inflammation, infection, and cancer. We thoroughly examined all abstracts and full-text articles and selected the most relevant ones for inclusion in this review.

Results

Mg has long been associated with immunological responses, both nonspecific and specific. It plays a pivotal role in diverse immune responses by participating in multiple mechanisms. It facilitates substance P binding to lymphoblasts, promotes T helper, B cell, and macrophage responses to lymphokines, and facilitates antibody-dependent cytolysis and immune cell adherence. Besides, Mg

serves as a cofactor for C'3 convertase and immunoglobulin synthesis. It additionally boasts a significant anti-cancer effect. Chronic Mg deficiency leads to enhanced baseline inflammation associated with oxidative stress, related to various age-associated morbidities. A deficiency of Mg in rodents has been observed to impact the cell-mediated immunity and synthesis of IgG adversely. This deficiency can lead to various complications, such as lymphoma, histaminosis, hypereosinophilia, increased levels of IgE, and atrophy of the thymus. The immunological consequences of Mg deficiency in humans can be influenced by the genetic regulation of Mg levels in blood cells. Mg can also mediate cell cycle progression. There has been a renewed interest in the physiology and therapeutic efficacy of Mg. However, the in-depth mechanisms, their clinical significance, and their importance in malignancies and inflammatory disorders still need to be clarified.

Conclusions

Mg is essential for optimal immune function and regulating inflammation. Deficiency in Mg can lead to temporary or long-term immune dysfunction. A balanced diet usually provides sufficient Mg, but supplementation may be necessary in some cases. Excessive supplementation can have negative impacts on immune function and should be avoided. This review provides an update on the importance of Mg in an immune response against cancer cells and infectious agents and how it regulates inflammation, oxidative stress, cell progression, differentiation, and apoptosis.

Keywords: Magnesium, Cancer, Immune modulator, Infectious diseases

Introduction

Magnesium (Mg) is the second-most abundant cation inside the body's cells, after potassium, and the fourth-most abundant element in the human body (Ca^{2+} > K^{+} > Na^{+} > Mg^{2+})". At birth, the human body possesses an initial Mg content of 760 mg, which subsequently undergoes an increase to approximately 5 g at the age of 4–5 months. The total amount of Mg^{2+} in the body exhibits variation ranging from 20 to 28 g. The majority of Mg^{2+} in the human body, exceeding 99% of the total amount, is found within the intracellular compartment. Its primary storage site is the skeletal system/bones, accounting for approximately 50–65% of the total body Mg^{2+}. In conjunction with calcium and phosphorus, Mg^{2+} contributes to the structural composition of the skeleton. Additionally, Mg^{2+} is distributed among muscle tissue, soft tissues, and organs, constituting approximately 34–39% of the total body Mg^{2+}. Conversely, a small fraction of Mg^{2+}, less than 1–2%, is present in the bloodstream and extracellular fluids [1]. Mg serves as a crucial cofactor in a wide range of biological processes, encompassing over 600 activities. These include the regulation of "cell cycle progression, differentiation, and apoptosis". Additionally, it plays a structural role in nucleic acids through its ability to form complexes with negatively charged compounds like phosphates [2]. Mg plays a role in various biochemical processes, including oxidative phosphorylation, energy generation, protein and nucleic acid synthesis, and glycolysis [3, 4]. This fundamental ion also impacts the excitability of neurons, the reduction of muscle function, and the maintenance of regular heartbeats through its active transport of other ions across cell membranes [5]. According to a recent study conducted by researchers at Basel University, it has been found that immune T cells, which play a crucial role in combating cancer cells and infectious agents, necessitate an adequate amount of Mg in order to effectively detect, activate a response against, and eliminate