INTRODUCTION

Obesity represents the most prevalent nutritional problem, with growing rates of morbidity and mortality in the latest decades. The ongoing rise in obesity reflects changes in lifestyle but the genetic background is also involved [1,2].

Magnesium plays a crucial role in several fundamental cellular reactions. A large number of clinical disorders have been found to be associated with magnesium deficiency [3,4]. One of these disorders is obesity. The common link between obesity and magnesium deficiency may be sustained by the inflammatory response which is the major origin of the oxidative stress (OS).

The implication of OS generated by magnesium deficiency – induced inflammation in obesity state will be discussed in the subsequent paragraphs.

OBESITY AND MAGNESIUM DEFICIENCY: IS OXIDATIVE STRESS INVOLVED?

ANDREEA LIANA RÂCHIȘAN, NICOLAE MIU, MARIANA ANDREICA

Clinica Pediatrie II, UMF „Iuliu Hațieganu” Cluj-Napoca

Abstract

Obesity – the “epidemic” of our century, an energy-rich condition, is associated with a chronic inflammatory reaction in adipose tissue. There is a controlled interaction between metabolic and immune systems in the over or under-nutrition states. Magnesium deficiency contributes to immune stress response and the oxidative stress is its consequence. There are similar pathways associated with the development of obesity-induced inflammation and magnesium deficiency in this state. The pivotal role is supported by the stress response.

Keywords: obesity, magnesium deficiency, inflammation, oxidative stress.

OBEZITATEA ȘI DEFIENȚA DE MAGNEZIU: ESTE IMPLICAT STRESUL OXIDATIV?

Rezumat


Cuvinte cheie: obezitate, hipomagneziemie, inflamație, stres oxidativ.

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OBESITY – A LOW-GRADE INFLAMMATORY DISEASE

Chronic stress is known to be a threat to the metabolic homeostasis and can lead to complications caused by the stressor and the delay of the adaptative response [5]. Obesity impairs metabolic homeostasis and elicits stress response [6]. The associated secretion of proinflammatory cytokines by the adipose tissue may act as an additional chronic stimulus which maintains the chronic stress reactions.

The inflammatory status in obesity is indicated by the presence of tumor necrosis factor α (TNFα) in the adipose tissue. This was a major discovery and contributed to a better understanding of the relation obesity – inflammation [7,8].

Adipose tissue is the site of secretion for several proinflammatory factors such as interleukine 6 (IL-6), C – reactive protein, serum amyloid A, plasminogen activator inhibitor – 1 [9,10]. In obese states, adipose tissue is infiltrated by macrophages and there is a shift between alternatively activated M₂ type to the classically activated M₁ type [11,12]. This shift results in changes in secreted cytokines from anti – inflammatory M₂ to proinflammatory
The secretion of proinflammatory factors by adipose tissue and their regulation sustain the hypothesis of a low-grade inflammation during obesity.

In addition to the proinflammatory cytokines that are expressed in fat, specific factors are produced from adipocytes and are generally named adipokines. In 1994 Zhang et al. isolated a hormone, the leptin, from the adipose tissue [14]. This elucidated the fact that adipose tissue is not only a lipid storage, but is involved in the regulation of energy homeostasis. The principal function of leptin is to signal the energy state of the organism. In obesity, there is a leptin resistance that promotes the vicious circle of regulation of energy homeostasis. The direct contribution of leptin resistance in the development of obesity—inflammation has not yet been elucidated [15,16]. Circulating levels of adipokines in humans reflect the degree of their adiposity.

Obesity is a low-grade inflammatory disease, and the expression of proinflammatory cytokines is the first pathway in the generation of reactive oxygen species. The exposure to stress conditions in obesity is a result of metabolic overload [17]. Mitochondria and endoplasmic reticulum are the most sensitive organelles to metabolic stressors. The development of oxidative stress in adipose tissue activates several kinases [18].

The proinflammatory mediators, intracellular processes and their pathways are linking obesity to inflammation and therefore to intense reactions of oxidative stress.

**MAGNESIUM DEFICIENCY INDUCED INFLAMMATION-OXIDATIVE STRESS**

Several lines of evidence support the role of inflammation in magnesium deficiency states. The following pathways should be considered [19,20,21]:

- Cellular entry of calcium and priming of phagocytic cells;
- Opening of calcium channels and activation of specific receptors;
- Release of neurotransmitters: substance P;
- Membrane oxidation and activation of nuclear factor kappa B (NFkB).

The inflammatory response is probably secondary to a modification in the extracellular magnesium level because of the decline in plasma magnesium. The intracellular level of magnesium does not fall at all in the first time of magnesium deficiency [22,23].

Magnesium is a physiological calcium antagonist, so decreased extracellular magnesium leads to increase intracellular calcium [24]. Therefore, increasing extracellular levels of magnesium may have anti-inflammatory effect [25,26].

Thus, the mechanism of immune stress in magnesium deficiency may consist of a reduced extracellular magnesium/calcium antagonism as the result of decreased plasma magnesium level.

Neuromediators play a major role in inflammation and in the production of OS. Nervous and immune systems interact bidirectionally. Magnesium deficiency leads to a stress response by releasing neurotransmitters such as substance P.

Another important pathway in magnesium deficiency— inflammation cascade is the activation of NFkB, which is a crucial factor in regulation of immune and inflammatory responses. NFkB is present in cytoplasm in an inactive form, and can be activated during the response to different stress conditions [27]. Low serum levels of magnesium induce activation of NFkB in cultured canine cerebral vascular smooth [20]. This supports an important role of the activation of NFkB in magnesium deficiency induced inflammation.

The inflammatory response is linked to oxidative damage during magnesium deficiency. There are several proofs indicating the presence of OS reactions in magnesium-deficient animals: enhanced tissue, lipoprotein peroxidation, reduced antioxidant status and increased plasma nitric oxide [28,29]. The macrophages and neutrophils generate superoxide anions, and are more responsive to activation by immune stimuli. This kind of activation is blocked by administration of a substance P receptor blocker, so the neurogenic inflammation linked to oxidative stress is present during magnesium deficiency [30].

**CONCLUSION**

Almost all clinical entities associated with a low magnesium status are being characterized by a chronic inflammatory stress condition. Magnesium deficient state generate an inflammatory response: macrophage activation, release of inflammatory cytokines and production of free radicals.

The interplay of obesity, a chronic low-grade inflammatory condition, with magnesium deficiency vastly enhances the noxious influence of inflammation, promoting deleterious immune adaptations and ultimately increasing oxidative stress reactions.

The adverse role played by inflammation in the etiology of the most prevalent disease in modern society may support nutritional advise for the population to maintain a good bodyweight index and also an adequate intake of magnesium.

**References**

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