Asthma and magnesium

Bronchial asthma affects approximately 334 million people worldwide. It is a chronic condition that is characterized by airway inflammation and recurrent bronchospasm, which comes about as a result of reversible bronchial hyper-responsiveness. This airway hyper-responsiveness is thus termed because it occurs in response to stimuli that do not normally produce airway narrowing in most individuals.

Asthma has been strongly linked to magnesium deficiency and insufficiency in the medical literature. Magnesium deficiency has been shown to contribute to increased inflammation within the body by several known mechanisms, including activation of phagocytic cells, opening of calcium channels, activation of the N-methyl-D-aspartate (NMDA) receptor, and activation of nuclear factor (NF)-κB.[1] The resulting increased inflammation leads to an increased risk for a variety of inflammatory conditions, including asthma. Several studies demonstrate low serum magnesium levels in children[2] and adults[3-4] with low bronchial asthma control. In one particular study, mean serum magnesium values were found to be lower in asthmatics than in healthy controls. Specifically, 58.8% of asthmatic patients had hypomagnesemia (<1.7 mg/dL).[4] As a statistical group, Asians were found to have the greatest disparity, with significantly lower serum magnesium levels in Asian asthmatics than in healthy Asian controls.[5] Another study demonstrated that mean serum magnesium levels were significantly higher in the "well-controlled" group when compared to the "uncontrolled" group. The "partly controlled" group also had higher magnesium levels than the uncontrolled group, but lower levels than the "well-controlled" group.[3] While the difference in magnesium values among the groups was statistically significant, most values fell within their cited reference range, suggesting that values within the lower portion of the reference range may be insufficient or suboptimal. Researchers concluded that serum magnesium levels may be an important biomarker in the assessment of control of asthma severity.

Research demonstrates a relationship between mean serum magnesium values and asthma severity, attack frequency, and asthma exacerbation. Mean serum magnesium values in individuals with chronic, stable asthma were negatively correlated with asthma severity[4] and were found to be lower in those with severe persistent asthma (1.53 ± 0.09 mg/dL) than in those with moderate persistent- (1.70 ± 0.07 mg/dL) and mild persistent asthma (1.86 ± 0.07 mg/dL).

Some pulmonary function test values were positively correlated with magnesium levels in individuals with chronic stable asthma. Specifically, FEV1, FEV1%, PEF, and PEF% were significantly lower in asthmatic patients with hypomagnesemia compared to asthmatic patients with normal magnesium levels,[6] suggesting that asthma is less likely to cause hypomagnesemia, but rather it is more likely that hypomagnesemia increases the risk of asthma and of symptom severity in asthmatics. To the contrary, some suggest[4] that hypomagnesemia in asthmatics could be due to chronic β_2-agonist inhalation or nebulization, which in turn leads to vitamin D deficiency, which then increases the risk of severe asthma exacerbation.[7] Magnesium studies on treatment-naïve asthmatics would be required to determine whether conventional treatment is the cause of hypomagnesemia in asthmatics.

Research demonstrates varied efficacy with the most common forms of magnesium utilized for prevention and treatment of asthma attacks, namely oral, nebulized, and intravenous. A systematic review and meta-analysis that examined the efficacy of oral magnesium in the management of stable bronchial asthma found that FEV1 improved after 8 weeks of oral magnesium therapy, but there was no significant improvement in this value at other follow-up periods.[8] Additionally, there was no significant change in FVC, Methacholine challenge test, bronchodilator use frequency, or symptoms score.

Similarly, researchers reported minimal bronchodilatory effect in asthmatics treated with nebulized magnesium sulfate,[9] noting that treatment efficacy may be dependent upon the cause of the bronchospasm. In another study, short-term treatment with nebulized magnesium in stable, severe asthma patients with persistent airflow limitation did not result in significant bronchodilation.[10] Again, researchers did observe heterogeneity in response, but noted that this may have been the result of variations in treatment intensity. One study did note that adding nebulized magnesium sulfate to standard therapy in patients with moderate to severe asthma attacks led to favorable results, including greater and faster improvement in peak expiratory flow rate (PEFR), oxygen saturation, and respiratory rate, as well as reduced hospitalization rate.[11] Overall, the medical literature suggests that while nebulized magnesium may result in improvements in pulmonary function test values when used adjunctively, the confidence level of the evidence is low.[12] High-quality studies do not demonstrate significant benefit with the use of nebulized magnesium alone in the treatment of asthma. Some subgroups of asthmatics may

receive greater benefits than others, but further high-quality research is necessary to elucidate more concrete conclusions.

While two very early studies failed to demonstrate favorable results[13-14], the vast majority of research demonstrates that intravenous magnesium is beneficial as an adjunctive therapy in the treatment of acute asthma. Research demonstrates that it reduces the likelihood of hospital admission in those with severe acute asthma[15] and by up to 68% in all categories of asthmatics[16-17], reduces bronchial hyper-reactivity[18] and significantly improves respiratory function.[19]

The majority of studies analyzed the efficacy of intravenous magnesium sulfate in the treatment of acute asthma exacerbations and not necessarily prophylactically. Researchers noted that this may be because emergency department physicians restrict its use to patients with severe exacerbations.[20] Others noted that this inconsistent use of intravenous magnesium may be due to a lack of consensus. Nevertheless, most of the researchers seem to agree that the efficacy and favorable side-effect profile of intravenous magnesium sulfate justifies its use in those presenting to the ED with acute severe asthma.[21] One case-series reported that weekly or biweekly maintenance therapy consisting of magnesium and other nutrients resulted in enhanced asthma control.[22]

Regarding adverse effects, one study reported hypotension as a possible mild adverse effect of intravenous magnesium administration,[23] but overall, researchers did not report any significant side effects in asthmatics who were administered intravenous magnesium therapy.[16]

In conclusion, asthmatics have been found to have higher incidences of magnesium deficiency and insufficiency than healthy controls, with serum magnesium levels correlating negatively with asthma symptom severity. As such, oral magnesium has been found to result in minimal improvements, while nebulized magnesium provided somewhat greater benefit and intravenous magnesium administration resulted in the greatest benefit, including in individuals who did not respond favorably to conventional treatment. The cost-benefit profile of intravenous magnesium was favorable, with magnesium resulting in no significant adverse effects. These facts make intravenous magnesium a highly advantageous and efficacious treatment in the management of acute asthma exacerbations. Additional research is needed to support the idea of prophylactic intravenous magnesium therapy, however, preliminary research is promising.

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