

Magnesium for treatment of asthma in children

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ABSTRACT

QUESTION Magnesium is considered adjuvant therapy for moderate to severe asthma exacerbations in adults, but can it be used to treat children?

ANSWER Magnesium seems to be beneficial in the treatment of moderate to severe asthma in children. It is a safe drug to administer, but there have been minor side effects reported, such as epigastric or facial warmth, flushing, pain and numbness at the infusion site, dry mouth, malaise, and hypotension. Owing to its bronchodilating and anti-inflammatory effects, magnesium is an encouraging adjuvant therapy for pediatric patients who do not respond to conventional treatment in acute severe exacerbations. Future studies should focus on establishing the optimal dosage for maximal benefits and the best route of administration. Magnesium should also be considered as a prophylactic treatment.

RÉSUMÉ

QUESTION Le magnésium est considéré comme une thérapie adjuvante pour les exacerbations de l'asthme de modérées à graves chez l'adulte, mais peut-il être utilisé pour traiter les enfants?

RÉPONSE Le magnésium semble bénéfique dans le traitement de l'asthme modéré à grave chez l'enfant. C'est un médicament sécuritaire à administrer, mais on a signalé des effets secondaires mineurs, comme une chaleur épigastrique ou faciale, des bouffées vasomotrices, de la douleur et de l'engourdissement au site d'infusion, la sécheresse de la bouche, une sensation de malaise et de l'hypotension. Compte tenu de ses effets bronchodilatateurs et anti-inflammatoires, le magnésium est une thérapie adjuvante encourageante pour les patients pédiatriques qui ne répondent pas au traitement conventionnel dans les exacerbations aiguës graves. Les études futures devraient porter sur l'établissement de la dose optimale pour un maximum de bienfaits et sur le meilleur mode d'administration. Le magnésium devrait aussi être considéré comme un traitement prophylactique.

Asthma is one of the most common conditions among adults and children. In 2005, 15.7 million adults (7.2%) and 6.5 million children (8.9%) had asthma in the United States. In 2004 in Canada, asthma resulted in 1.8 million emergency department visits, with a 10% to 25% admission rate to hospital and 3780 deaths. Asthma is responsible for millions of lost school days every year.¹⁻⁴

Canadian recommendations for the management of asthma, including in children and youth, were published in 2005.⁵ They suggest the use of short-acting β_2 -agonists for symptom relief. Oral or inhaled corticosteroids should be administered to reduce inflammation. Anticholinergics (eg, ipratropium bromide) can be added, which act synergistically with β_2 -agonists to reduce hospitalizations.⁶

Magnesium and asthma

Magnesium is the fourth most abundant ion in the human body, with a distribution of 50% in bones, 49% intracellularly in all body organs, and 1% in blood serum. Magnesium is absorbed by the small intestine, and is eliminated through renal excretion and perspiration.⁷

Magnesium has a role in several enzymatic reactions, helping maintain cellular homeostasis.^{4,8} Its role in asthma has not been clearly defined, but there have been studies to explain its mechanisms of action.

In 1912, Trendelenburg observed magnesium's bronchodilator effects in cows; in 1936, Rosello

and Pla demonstrated the same on patients. In vitro studies demonstrated the role of magnesium in the relaxation of bronchial cells.⁹ In smooth muscle, magnesium decreases intracellular calcium by blocking its entry and its release from the endoplasmic reticulum and by activating sodium-calcium pumps. Furthermore, inhibition of calcium's interaction with myosin results in muscle cell relaxation. Magnesium also stabilizes T cells and inhibits mast cell degranulation, leading to a reduction in inflammatory mediators. In cholinergic motor nerve terminals, magnesium depresses muscle fibre excitability by inhibiting acetylcholine release. Lastly, magnesium stimulates nitric oxide and prostacyclin synthesis, which might reduce asthma severity.^{9,10}

Clinical trials

A total of 9 trials—8 randomized double-blinded studies^{9,11-17} and 1 retrospective chart review¹⁸—were published in the literature. The retrospective chart review identified 40 asthma patients between the ages of 2 months and 15 years that were admitted to a pediatric intensive care unit in Florida. Before the use of magnesium, 15 of the 40 patients with severe asthma needed intubation. After magnesium was used, no patients required additional ventilation. There were no cardiovascular adverse events reported.¹⁸

Five randomized trials studied the use of 25- to 75-mg/kg doses of intravenous (IV) magnesium sulfate,^{11-13,15,17} with a total of 182 patients between the ages of 1 and 18 years. Some children received concurrent medications, such as steroids, aminophylline, and albuterol. Four of the trials found IV magnesium to be effective.^{12,13,15,17} Outcome measures were different in these studies and included improved clinical asthma score,^{13,15} percentage of peak expiratory flow rate (PEFR),^{12,13,15} oxygen saturation, forced expiratory volume in 1 second, and forced vital capacity.¹² A decrease in hospital admissions was also found.¹² A more recent study¹⁷ concluded that using a higher dose of magnesium sulfate resulted in a faster and longer improvement in pulmonary function (ie, pulmonary function test results and PEFR), and a higher discharge rate in children who did not respond to β_2 -agonists. One study found no evidence to support the use of IV magnesium sulfate as an adjuvant therapy for moderate to severe asthma exacerbations; there was no difference in the clinical improvement and hospitalization rates between the placebo and magnesium groups.¹¹

Inhaled magnesium sulfate has also been investigated in 2 randomized double-blinded trials with 102 children in total. In one trial participating children were between 5 and 17 years of age,¹⁴ and in the other the children had a mean age of 10.8 years.¹⁶ Patients in one trial received concomitant therapy with β_2 -adrenergic receptor agonists and corticosteroids,¹⁴ and in the second trial, only the control group received β_2 -adrenergic receptor agonists.¹⁶ Nebulized magnesium sulfate was found to provide short-term bronchodilation.^{14,16}

Of interest, asthma exacerbations have been related to magnesium deficiency. In one study⁹ 300 mg of oral magnesium daily was given for asthma prevention for 2 months to 37 patients between the ages of 7 and 19 years. Both the treatment and placebo groups received inhaled fluticasone and salbutamol as needed. Children in the magnesium group had fewer asthma exacerbations and used less salbutamol compared with the placebo group. Bronchial reactivity to methacholine and the allergen-induced skin responses were also reduced.

To evaluate the effectiveness of IV magnesium sulfate in children, a meta-analysis¹⁹ analyzed 5 trials,^{11-13,15,17} with a total of 182 patients. There were favourable effects with the use of magnesium sulfate in addition to β_2 -agonists and systemic steroids. It appears effective in relieving symptoms, and there was no evidence to suggest that the greater the dosage the better the results. The outcome showed that IV magnesium sulfate was effective in reducing hospitalization rates with an absolute risk reduction of 0.26 (95% confidence interval 0.12 to 0.39); when used as an adjunct therapy there was a reduction in asthma symptoms and an 85% reduction in risk of persistent bronchoconstriction, with a PEFR of less than 60%.


Several clinical trials in adults and children were summarized in 2 recent reviews.^{4,8} Rowe et al⁴ examined the effect of IV magnesium sulfate and Blitz et al⁸ studied its inhaled form in the treatment of asthma exacerbations. Both included randomized or pseudo-randomized trials in patients presenting with acute asthma. Patients experiencing severe exacerbations benefited from inhaled or IV magnesium sulfate as an adjuvant therapy to inhaled β_2 -agonists.

Safety

Magnesium sulfate is generally a safe drug to administer. In one trial there were some minor side effects reported, such as epigastric or facial warmth, flushing, pain and numbness at the infusion site, dry mouth, and malaise.¹³ Hypotension was also documented with rapid infusion. Toxicity might result in abnormalities in cardiac conduction, absent reflexes, muscle weakness, and respiratory depression.²⁰

Magnesium sulfate seems to be beneficial in the treatment of moderate to severe asthma in children. Its bronchodilating and anti-inflammatory effects are encouraging as an adjuvant therapy for pediatric patients who do not respond to conventional treatment in acute severe exacerbations.

Conclusion

The role of magnesium in the bronchial tissues is not completely understood. Current recommendations do not support the addition of magnesium as part of the management of children with mild or moderate asthma. Future studies should focus on elucidating the role of magnesium in children, while for severe asthma there is a need to establish the optimal dosage and the most effective route of administration. 

Competing interests

None declared

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