Allergol Immunopathol (Madr). 2017;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

The effect of nebulised magnesium sulphate in the management of childhood moderate asthma exacerbations as adjuvant treatment

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Received 11 December 2015; accepted 31 October 2016

KEYWORDS
Adjuvant treatment;
Asthma exacerbations;
Childhood;
Nebulised magnesium sulphate

Abstract
Background: After the bronchodilator effect of magnesium was shown, the use of magnesium in treatment of asthma exacerbations became common. With the results of recent studies, the use of intravenous magnesium in severe asthma exacerbations took its place. We aimed to examine the effects of adding isotonic magnesium sulphate instead of isotonic saline into nebulised salbutamol on the Modified Pulmonary Index Score (MPIS) and the hospitalisation rate in moderate asthma exacerbations.
Methods: Our study population included 100 children age between 3 and 15 years with asthma admitted to emergency department due to moderate asthma exacerbations. The patients were randomised to placebo or magnesium, with 50 patients in each arm. All patients received 1 mg/kg of systemic methylprednisolone at the beginning of treatment and thereafter received either nebulised salbutamol (0.15 mg/kg/dose) and 1 ml magnesium sulphate (15%) + 1.5 ml isotonic saline on three occasions at roughly 20 min intervals (Magnesium group) or nebulised salbutamol (0.15 mg/kg/dose) and 2.5 ml isotonic saline mixture on three occasions at roughly 20 min intervals (Placebo group). The MPIS of patients on 0th min, 20th min, 40th and 120th min were calculated and compared. The primary outcome was to compare MPIS values at the end of 120th min.
Results: Both groups have similar demographic, allergic characteristics and baseline MPIS scores. When the MPIS scores in the 120th min and admission rates in the 200th min, there was no significant difference between the two groups.
Conclusions: The use of nebulised magnesium sulphate in moderate asthma exacerbation as adjuvant treatment showed no benefit to standard treatment in our study.

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http://dx.doi.org/10.1016/j.aller.2016.10.003

Please cite this article in press as: Turker S, et al. The effect of nebulised magnesium sulphate in the management of childhood moderate asthma exacerbations as adjuvant treatment. Allergol Immunopathol (Madr). 2017. http://dx.doi.org/10.1016/j.aller.2016.10.003

Introduction

Asthma, which is common all over the world, is a chronic respiratory disease affecting 1–18% of the population in different countries. Exacerbations of asthma are episodes characterised by a progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function. Severe exacerbations can be potentially life-threatening, and require early evaluation and careful follow-up. The main characteristic of asthma exacerbation is airflow obstruction in the respiratory tract. The aim of treatment is to rapidly relieve airflow obstruction and hypoxaemia, address the underlying inflammatory pathophysiology, and prevent relapse. Oxygen, short-acting beta$_2$-agonist (SABA), and systemic corticosteroids (oral/iv) are used in the first step of treatment of asthma exacerbation in the emergency department. In patients who do not respond to initial treatment; ipratropium bromide, aminophylline or theophylline, IV magnesium, helium and high dose inhaled corticosteroid treatments are applied.[1]

Magnesium plays a role as a co-factor in more than 300 enzymatic reactions, including in particular, glycolysis and oxidative phosphorylation. Magnesium is accepted as the physiological antagonist of calcium.[2] In addition to these functions, magnesium has also bronchodilatory and anti-inflammatory effects.[2–6] The mechanism of bronchodilation consists in making dose-dependent relaxation in bronchial smooth muscle.[3] The inhibition of histamine from mast cells, acetylcholine from cholinergic nerve terminals and the release of calcium into the cytoplasm play a role in this formation.[4–7] In children, the anti-inflammatory and bronchodilatory effect of magnesium is promising as an adjuvant treatment for patients who do not respond to treatment in severe asthma exacerbation. In GINA 2015, intravenous magnesium sulphate (MgSO(4)) treatment is not recommended for routine use in acute asthma exacerbations. However, it has been reported that the application of 2 g magnesium as a single dose within 20 min intravenous infusion reduces hospitalisation in adult patients with FEV1 <25–30% at admission to hospital, in adult and paediatric patients who fail to respond to initial treatment and have persistent hypoxaemia, and in paediatric patients who do not reach FEV1 60% predicted after 1 h of care.[1] Cochrane meta-analysis reported no signs of evidence that inhaled MgSO(4) can be used as a substitute for inhaled SABA. While this drug is used in addition to inhaled SABA (with or without inhaled ipratropium), no overall clear evidence for improved pulmonary function or reduced hospital admissions are stated.[8] Studies investigating the usage of Mg in asthmatic children are rare.[9–12] In these studies, mostly mild to moderate or moderate-to-severe asthmatic children were evaluated. This study has aimed to investigate the clinical findings and the effects of hospitalisation of nebulised isotonic Mg given in addition to standard asthma exacerbation treatment in children who come to the emergency room with moderate asthma exacerbations.

Methods

Study design

Our study population included 100 consecutive children whose age ranged between 3 and 15 years with asthma and who admitted to the emergency department due to moderate asthma exacerbations between February 2014 and September 2014. This study was designed as randomised controlled double-blind. Before starting the study, the ethical approval of Zeynep Kamil Woman and Children's Diseases Training and Research Hospital was taken and also the aim and procedures of the study were explained to children and their families and their verbal and written approval was taken. The study adhered to the principles of Helsinki Declaration.

Study population

Patients were asked to fill in a questionnaire during the first assessment. This questionnaire included the following: the demographic characteristics of patients, whether they used preventive medicine or not, if they used how long and in which dose, the presence of upper respiratory tract infection symptoms before exacerbations, whether they took salbutamol and/or inhaled corticosteroids at home, the number of exacerbations in the last one year and the number of hospitalisations, history of atopy, and whether cigarettes are smoked at home. Those patients are included in the study: patients over three years old being followed-up in paediatric allergy clinic with the diagnosis of asthma, and children admitted to the emergency department due to moderate asthma exacerbations.[1] Patients with any associated chronic diseases such as cystic fibrosis, bronchiectasis were excluded from this study.

Study interventions

The 100 patients were randomised to placebo or magnesium, with 50 patients in each arm. The patients selected for the magnesium group received nebulised salbutamol (0.15 mg/kg/dose) and 1 ml magnesium sulphate (15%) + 1.5 ml isotonic saline on three occasions at roughly 20 min intervals, and 1 mg/kg methylprednisolone IV with the first dose of treatments applied. For those patients who did not respond adequately, nebulised salbutamol treatment was continued, on three occasions at roughly 40 min intervals.

The patients selected for the placebo group received nebulised salbutamol (0.15 mg/kg/dose) and 2.5 ml isotonic saline mixture on three occasions at roughly 20 min intervals, and 1 mg/kg methylprednisolone IV with the first dose treatments applied. For those patients who did not respond adequately, nebulised salbutamol treatment was continued three times with 40 min intervals (Fig. 1).

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