Intravenous Magnesium Sulfate in Acute, Life-Threatening Asthma

Magnesium, a physiologic calcium antagonist, is known to have a direct effect on calcium uptake in smooth muscle, resulting in smooth muscle relaxation. Studies of magnesium sulfate infusions in patients with mild or moderate-to-severe acute asthma have shown that it may have a significant bronchodilatory effect, similar to that of salbutamol (albuterol). We present the case of a patient with acute severe life-threatening asthma (initially in cardiorespiratory arrest) who responded to an IV infusion of magnesium sulfate after aggressive pharmacologic management failed to result in clinical improvement. [Kuitert LM, Kletchko SL: Intravenous magnesium sulfate in acute, life-threatening asthma. Ann Emerg Med November 1991;20:1243-1245.]

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INTRODUCTION

Conventional therapy for moderate-to-severe asthma includes β_2-sympathomimetics, steroids, and aminophylline. Most asthmatics respond to this combination therapy, yet a small group fail to improve and require hospitalization and often ongoing management in an ICU. Two patients with acute asthma described in a 1940 report who failed to respond to conventional therapy (subcutaneous and intramuscular adrenaline) improved significantly after an infusion of magnesium sulfate.[1]

More recently, an open study reported symptomatic improvement and improved peak expiratory flow rates in ten patients with mild asthma given 1.2 g magnesium sulfate by infusion.[2] In a placebo-controlled, double-blind trial of 38 patients with moderate-to-severe acute asthma, a significant increase in peak expiratory flow rate was demonstrated in the magnesium sulfate-treated group, and there was a significant reduction in the number of patients requiring hospitalization.[3]

We present the case of a patient with acute severe life-threatening asthma who was treated with an infusion of magnesium sulfate after conventional therapy failed and in whom it was thought that magnesium was instrumental in relieving bronchospasm.

CASE REPORT

A 56-year-old woman was brought to the emergency department of Middlemore Hospital by her relatives. She was in cardiorespiratory arrest, and resuscitation was begun immediately. She was defibrillated successfully, but manual ventilation was difficult because of high airway pressures, and wheeze was audible throughout the lung fields. Therefore, it was assumed that she had acute severe asthma. This was later confirmed by her medical history. The patient had lifelong mild-to-moderate asthma (according to American Thoracic Society criteria) with several admissions, although none recently. She was a nonsmoker.

During the next one and one-half hours, the patient received 100% inspired oxygen, a total of 19.5 mg parenteral salbutamol, a stat dose of 250 mg aminophylline followed by an infusion of 45 mg/hr, 200 mmol sodium bicarbonate for severe and persistent mixed metabolic and respiratory acidosis, 200 mg hydrocortisone, and 2 mg adrenaline parenterally for episodes of bradycardia and hypotension, in addition to volume expansion.

There was little improvement, and manual ventilation continued to be difficult because of severe persistent bronchospasm, necessitating transfer

to the ICU. On a mechanical ventilator, the airway pressures were in excess of 60 mm Hg end-tidal CO_2 ($ETCO_2$), recordings were less than 3 kPa, and only maximum tidal volumes of 250 mL could be achieved. Dobutamine was required once she was ventilated because of hypotension.

Three hours after the arrest, there was still no improvement despite maximum therapy, and magnesium sulfate infusion was started. The patient received a total of 100 mmol (24.6 g) over 20 minutes.

There was a dramatic physiological and clinical improvement in her asthma with a decrease in airway pressure, an increase in compliance, and an $ETCO_2$ increase to 5 kPa. Tidal volumes were able to be increased to 800 mL without a rise in peak airway pressure. This improvement continued over the next two hours; the patient was awake, ventilating spontaneously, and able to be extubated. The remainder of her hospital stay was uneventful, and she was discharged five days later.

DISCUSSION

We believe that an IV infusion of magnesium sulfate was instrumental in relieving our patient's severe bronchospasm because her improvement was temporally related to the infusion at a time when several hours of aggressive pharmacologic management of her asthma had resulted in minimal, if any, improvement. This improvement was already obvious before the conclusion of the infusion and at a time when there had been no recent changes in the remainder of her asthma management. This report may be the first to describe the beneficial effect of magnesium sulfate in severe life-threatening asthma complicated by cardiorespiratory arrest.

There is little clinical literature available regarding the use of magnesium sulfate in acute asthma. It was first given in 1940 to a small group of patients who had failed to respond to subcutaneous and intramuscular injections of adrenaline, which at that time was the only treatment available for acute asthma.[1] Several of these patients had a dramatic response to their magnesium sulfate therapy, and the effect appeared not to be limited to those with low serum magnesium levels in that only 50% had demonstrably low magnesium levels before the infusion.

More recently, magnesium sulfate infusions have been given to two groups of five patients with mild attacks (mean forced expiratory volume in one second [FEV_1], 58% of predicted).[2] In the first group, the time course of respiratory resistance, forced vital capacity (FVC), and FEV_1 were studied. In the second group, magnesium sulfate dose-response curves were obtained in addition to serum and red blood cell concentrations of magnesium. All patients exhibited a reduction in respiratory resistance and improvements in FEV_1 and FVC, with the effects beginning to appear within two minutes of commencing the infusion and plateauing at 20 minutes. In all patients, dyspnea decreased within two to five minutes of commencement of the infusion, and on auscultation, wheeze had disappeared.

A further study reviewed the results of IV magnesium sulfate in 38 patients suffering from an acute exacerbation of moderate-to-severe asthma.[3] These patients were included in the study if, after two nebulizations of β_2-sympathomimetic agents, they failed to double their initial peak flow. Those who did not double their peak flow were considered to be poor responders to nebulized therapy and eligible for entry into the study. In addition to inhaled β_2-sympathomimetics, they were also given IV methylprednisolone and IV theophylline infusion. At this point, an infusion of 1.2 g magnesium sulfate was administered over 20 minutes; sequential peak expiratory flow rates were recorded.

There was a significant difference in the magnesium sulfate-treated group compared with the placebo-treated group, who had no change in peak expiratory flow rate. The magnesium sulfate-treated group had a sequential rise in peak expiratory flow rate to almost 300 L/min. In addition, there was a significant difference in the admission and discharge rates for the two groups. Those treated with magnesium sulfate were much less likely to require subsequent hospitalization than were the placebo-treated patients.

Intubation and assisted ventilation were contemplated in a 72-year-old man who presented with respiratory failure secondary to acute severe asthma.[4] He had failed to respond to therapy with nebulized β_2-sympathomimetics, aminophylline infusion, and parenteral methylprednisolone. An IV infusion of magnesium sulfate was given with a rapid symptomatic and biochemical improvement, averting the need for assisted ventilation.

The exact mechanism of action of magnesium is controversial but is likely to be due to its effect on calcium homeostasis. Magnesium, a natural antagonist of calcium, blocks the voltage-sensitive calcium channels (also blocked by nifedipine) and the receptor-operated calcium channels in bronchial and vascular smooth muscle, thereby modulating calcium fluxes through cell membranes, which then inhibits smooth muscle contraction. Despite these findings, the results of therapy with calcium channel blockers such as nifedipine in asthma have been disappointing.[5] *In vitro,* magnesium may also antagonize the action of calcium required for histamine release from basophils, release of mediators from mast cells, and acetylcholine secretion at nerve endings.[6]

Serum magnesium levels are known to poorly reflect body stores of magnesium as the large majority of magnesium is intracellular. Previous reports that have looked at serum magnesium levels in patients presenting with acute asthma who subsequently had IV infusions of magnesium sulfate suggest that normal levels do not preclude a response to magnesium sulfate infusion. A pretreatment serum magnesium level was not taken in our patient, but after the completion of the infusion, her serum magnesium rose to 2.39 mmol/L (normal range, 0.8 to 1.0 mmol/L) and fell to 1.54 mmol/L within 12 hours.

SUMMARY

We present the case of a patient with severe asthma who responded to a magnesium sulfate IV infusion after failing to respond to aggressive pharmacologic management. Magnesium sulfate may prove to be a valuable addition to the variety of drugs already available to treat asthma and may be particularly valuable in patients who fail to respond to conventional treatment. Further research is warranted.

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