Paediatric use of IV magnesium sulphate in severe asthma exacerbation: Report of a case and review of literature

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Abstract

Nebulization with B-agonist and administration of systemic corticosteroids are standard treatments for severe asthma exacerbations, but corticosteroids take several hours to become effective. IV magnesium sulphate ($MgSO_4$) acts faster and has both anti-inflammatory and bronchodilating properties. It appears to have played a pivotal role in the successful management of a child with severe asthma exacerbation and atelectasis unresponsive to conventional therapy. A literature review reveals that the results of IV $MgSO_4$ are much greater in children than in adults, and can avoid the need to hospitalize 25% of children presenting with severe asthma. Magnesium sulphate appears safe to use.

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Introduction

Magnesium sulphate ($MgSO_4$) has important bronchodilating and anti-inflammatory effects. It is a physiological calcium antagonist that inhibits contraction of bronchial smooth muscle, decreases histamine release from mast cells, and inhibits acetylcholine release at axon terminals. It stabilizes T cells, reduces thromboxane, and stimulates nitric oxide and prostacyclin synthesis. It has an important role in the management of severe asthma where other medications have not been successful in providing relief.[1-2] The beneficial role of IV $MgSO_4$ in the management of severe asthma in adult asthma exacerbation is well established as shown in the 2000 Cochrane Collaboration systematic review,[3] but is less well established in childhood asthma. Several publications have showed that $MgSO_4$ is effective for use both in emergency departments and intensive care units.[4-5]

This paper reviews the use of IV $MgSO_4$ in acute exacerbation of severe paediatric asthma as illustrated by presentation of a case. This case reports the dramatic resolution of massive pulmonary atelectasis in an asthmatic child following IV $MgSO_4$, after there was no response to standard asthma medical treatment. It also reviews the paediatric literature on the effectiveness of $MgSO_4$ in acute asthma exacerbations in children, the effective dosage, and its possible toxicity.

Case Report

A 5-year-old boy with a past history of asthma, presented with rapidly progressing acute asthma unrelieved by prednisone, multi-dose salbutamol and ipratropium bromide. Examination revealed tachypnea, tachycardia, chest recession, tracheal tug, right tracheal deviation (Figure 1), dullness and decreased breath sounds in the right lower chest, and presence of wheezing in other areas. Percutaneous SpO_2 was 86% (room air), and 95% with oxygen 5 L/min. WBC 27.3 x 10^9/L, neutrophils 25.7 x 10^9/L, lymphocytes 1.1 x19^9/L. CRP was 11.6 (<10mg/L).

Antibiotics were started followed by IV methylprednisone 1mg/kg, and aminophylline 10 mg/kg bolus without any improvement. In view of continuing deterioration in respiratory status and SpO_2 level, a bolus of magnesium sulphate (50 mg/kg) was administered intravenously. The child started improving within 30 minutes following magnesium, and clinical chest findings normalized within 2 hours. SpO_2 improved to 95% on 2 L oxygen/minute. All medications were discontinued save for salbutamol PRN, oral prednisolone (1 mg/kg/day), and MDI fluticasone 50 mcg (BD). On day 2, the child was active and playful, and chest examination was normal. Chest x-ray (AP) view on day 3 showed complete resolution of atelectasis and full expansion of the lungs (Figure 2).

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Figure 1. Chest x-ray (A-P) shows marked deviation of trachea and shift of mediastinum to the right due to gross atelectasis of the right middle and lower lobe.

Figure 2. Chest x-ray (AP view) on day 3 shows complete resolution of atelectasis and full expansion of lungs.

Discussion

Salbutamol and ipratropium bromide are well established bronchodilators, and corticosteroids are powerful anti-inflammatory agents used in the management of severe asthma exacerbations. However, these bronchodilators are limited by their ineffectiveness in the face of obstruction of the bronchial lumen from inflammation and swelling of the bronchial walls. Corticosteroids, although potent anti-inflammatory agents, are limited by the time frame of the several hours that it takes for them to become effective.[1] This situation was present when treatment was initiated in our patient, who continued to deteriorate despite prednisone, nebulized salbutamol and ipratropium bromide, and developed the added complication of atelectasis from a narrowed bronchus with a possible mucus plug. $MgSO_4$, on the other hand, has both bronchodilating and anti-inflammatory qualities, and its effectiveness becomes evident from 30 minutes after infusion of IV $MgSO_4$.[6] Similar improvement was evident in our patient after one hour.

A search of the literature was made for reports on beneficial effects of $MgSO_4$ in patients with acute exacerbation of severe asthma with the added complication of pulmonary atelectasis, but no report of a similar nature with such dramatic response was found. There is little doubt that the favourable outcome in this case was due to the additional effects of IV $MgSO_4$, as the child had deteriorated despite corticosteroids and use of the bronchodilators salbutamol and ipratropium bromide administered earlier.

Both children and adults with asthma unresponsive to standard beta agonist, anticholinergic, and corticosteroid medications have shown variable improvement to magnesium.[7-8] Bichara and Goldman[9] reviewed the use of magnesium for treatment of asthma in children. Their literature survey revealed a total of 9 clinical trials on the use of $MgSO_4$ in asthma – 1 retrospective chart review[10] and 8 randomized double-blinded studies.[6,8,11-15] Glover et al reviewed 40 children with asthma aged 2 months to 15 years in paediatric intensive care.[10] Before use of magnesium, 15 of 40 patients with severe asthma needed intubation. After magnesium, no patients required additional ventilation. There were no adverse cardiovascular complications with use of magnesium. Five of the studies[6,8,12-14] reviewed by Bichara and Goldman used 25- to 75-mg/kg doses of IV $MgSO_4$ on 182 patients aged 1-18 years.[9] Some patients received concurrent steroids, aminophylline and albuterol. Four

trials found IV $MgSO_4$ effective.[6, 13-14] The outcome measures included improved clinical asthma score, percentage PEFR, oxygen saturation, FEV1, and forced vital capacity. A reduction in hospital admissions was also observed. Use of a higher dose of $MgSO_4$ has resulted in faster longer improvement in pulmonary function test results and PEFR, and a higher discharge rate in children who did not respond to ß2-agonists.[8] One study failed to support IV $MgSO_4$ as adjuvant for moderate - severe asthma exacerbations as there was no difference in clinical improvement and hospitalization rates between placebo and MS groups.[12]

A recent study shows that early (within 1st hour) $MgSO_4$ reduces the need for mechanical ventilation, shortens PICU stay, and duration of respiratory support.[16] Studies of children have shown that the optimum dose is 40 mg/kg given as an intravenous bolus with a maximum dose of 2 g. Improvement in forced expiratory volume in 1 second (FEV1) was seen within 20 minutes and continued for up to 110 minutes. Up to 20% improvement in FEV1 may be seen. Patients with an initial FEV1 lower than 25% of what was predicted benefited the most from magnesium sulphate therapy.[17] Torres *et al* have found from a randomized controlled trial study in a tertiary-level university, that IV infusion of magnesium sulphate during the first hour of hospitalization in children with acute severe asthma significantly reduced the percentage of children who required mechanical ventilation support.[18] Ciarrallo *et al* found that IV $MgSO_4$ potentially reduces hospitalization rate by 25%.6

In recent years, several studies have analyzed the effectiveness of intravenous and nebulized $MgSO_4$ given together with bronchodilators in acute severe asthma episodes. Two studies were conducted on inhaled magnesium sulphate in 2 randomized double-blinded trials involving 102 children.[15,19] In the first study, 5-17 year-olds received concomitant ß2-adrenergic receptor agonists and corticosteroids.[19] In the second trial on children with a mean age of 10.8 years, only controls received ß2-adrenergic receptor agonists.[15] Nebulized $MgSO_4$ was found to provide short-term bronchodilation.[15,19] A more recent study found that the use of intravenous MgSO4, in addition to ß2-agonists and systemic steroids, in the treatment of acute asthma appears to produce benefits with respect to improved pulmonary function and reduced number of hospital admissions for children, and only improve pulmonary function for adults. However, the use of nebulized $MgSO_4$ just appears to produce benefits for adults.[20]

Safety of magnesium sulphate therapy

Magnesium sulphate appears to be a safe drug; the risk of major toxicity is very low at standard doses. Minor side effects include epigastric pain, facial warmth, flushing, numbness at infusion site, dry mouth and general malaise.[13] Hypotension, abnormalities in cardiac conduction, muscle weakness, respiratory depression and absent reflexes have been observed.[21] Further studies are needed to confirm the efficacy of $MgSO_4$ in specific situations.

Conclusion

The administration of b2-agonist nebulizations in conjunction with corticosteroids is an effective treatment strategy for severe acute asthma, but corticosteroids require several hours before their effects are appreciated. Review of the literature, and dramatic resolution of severe asthma-related massive atelectasis following intravenous $MgSO_4$ in this case report establish $MgSO_4$ as a safe and useful adjunct to standard therapy in severe, acute asthma exacerbations including atelectasis.

REFERENCES

1. Corbridge TC, Hall JB. Assessment and management of adults with status asthmaticus. Am J Respir Crit Care Med1955; 151(5):1296-316.
2. Silvio Torres et al. Effectiveness of MS as initial treatment of acute severe asthma in children, conducted in a tertiary-level university hospital. A RCT. Arch Argent Pediatr 2012; 110(4): 291-6.
3. Brian H Rowe, Jennifer Bretzlaff, Christopher Bourdon, Gary Bota, Sandra Blitz, Carlos A Camargo. Magnesium sulfate for treating

exacerbations of acute asthma in the emergency department. Editorial Group: Cochrane Airways Group, Published Online: 24 JAN 2000. Assessed as up-to-date: 21 Oct 1999. DOI: 10.1002/14651858. CD001490.
4. NHLBI Guidelines for the diagnosis and treatment of asthma. Available at: http.//www.nhlbi.nih.gov/guide-lines/asthma.
5. Global strategy for asthma management and prevention 2010 (update). Available at: http.//www.ginasthma.org
6. Ciarallo L, Sauer AH, Shannon MW. Intravenous magnesium therapy for moderate to severe pediatric asthma: results of a randomized, placebo-controlled trial. J Pediatr. 1996; 129: 809-14.
7. Corbridge TC, Hall JB. Assessment and management of adults with status asthmaticus. Am J Respir Crit Care Med1955; 151(5): 1296-316.
8. Ciarallo L, Brousseau RS. Higher dose intravenous magnesium therapy for children with moderate to severe acute asthma. Arch Pediatr Adolesc Med. 2000; 154: 978-83.
9. Bichara MD, Goldman RD. Magnesium for treatment of asthma in children. Child Health Update. Canadian Family Physician 2009; 55: 887-9.
10. Glover ML, Machado C, Totapally BR. Magnesium sulfate administered via continuous intravenous infusion in pediatric patients with refractory wheezing. J Crit Care. 2002;17(4): 255–8.
11. Gontijo-Amaral C, Ribeiro MA, Gontijo LS, Condino-Neto A, Ribeiro JD. Oral magnesium supplementation in asthmatic children: a double-blind randomized placebo-controlled trial. Eur J Clin Nutr. 2007; 61(1): 54–60.
12. Scarfone RJ, Loiselle JM, Joffe MD, Mull CC, Stiller S, Thompson K, et al. A randomized trial of magnesium in the emergency department treatment of children with asthma. Ann Emerg Med.2000; 36: 572–8.
13. Devi PR, Kumar L, Singhi SC, Prasad R, Singh M. Intravenous magnesium sulfate in acute severe asthma not responding to conventional therapy. Indian plus albuterol to nebulized albuterol plus saline in children with acute exacerbations of mild to moderate asthma. J Emerg Med. 2004;27(1): 21–5. [PubMed]
14. Gürkan F, Haspolat K, Bosnak M, Dikici B, Derman O, Ece A. Intravenous magnesium sulphate in the management of moderate to severe acute asthmatic children nonresponding to conventional therapy. Eur J Emerg Med. 1999;6(3): 201–5. [PubMed]
15. Meral A, Coker M, Tanac R. Inhalation therapy with magnesium sulfate and salbutamol sulfate in bronchial asthma. Turk J Pediatr. 1996; 38(2): 169–75. [PubMed]
16. Cheuk DK et al. A meta-analysis on intravenous MS for treating acute asthma. Arch Dis Child 2005; 90: 74-7.
17. Silverman RA, Osborn H, Runge J, *et al*. IV magnesium sulfate in the treatment of acute severe asthma. Chest. 2002; 122: 489-97.
18. Torres S, Sticco N, Bosch JJ, Iolster T, Siaba A, Rivarola MR, Eduardo Schnitzler E. Effectiveness of magnesium sulfate as initial treatment of acute severe asthma in children, conducted in a tertiary-level university hospital. A randomized, controlled trial. Arch Argent Pediatr 2012;110(4): 291-6.
19. Mahajan P, Haritos D, Rosenberg N, Thomas R. Comparison of nebulized magnesium sulphate plus albuterol to nebulized albuterol plus saline in children with acute exacerbations of mild to moderate asthma. J Emerg Med 2004; 27 (1): 21-5.
20. Shan Z, Rong Y, Yang W, Wang D, Yao P, Xie J, Liu L. Intravenous and nebulized magnesium sulfate for treating acute asthma in adults and children: a systematic review and meta-analysis. Respir Med. 2013 Mar; 107(3): 321-30.
21. Monem GF, Kissoon N, DeNicola L. Use of magnesium sulphate in asthma in childhood. Pediatr Ann 1996; 25 (3): 136, 139-44.