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ORIGINAL RESEARCH

Effectiveness of magnesium sulphate in acute asthma: a retrospective study

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ABSTRACT

Objective: The recent interest in intravenous magnesium sulphate for using it in many other indications other than control of eclamptic fits lead the researchers to try it as a smooth muscle relaxant in cases of acute bronchial asthma. The results have largely been controversial, so we conducted this study to determine efficacy of intravenous magnesium sulphate in acute asthma based on its terminal outcome.

Methodology: This retrospective study was conducted at Surgical Intensive Care Unit at Peoples University of Medical and Health Sciences for Women, Nawabshah from January 2014-December 2015. We retrospectively reviewed the medical data sheets of all cases of acute asthma admitted during the study period, and extracted the relevant information. All the patients were initially treated with standard therapy for asthma and then given 4ml of 50% MgSO4 (2g) diluted in 250 ml of normal saline intravenously. Outcomes were presented in percentages and frequencies while patient age is presented as mean ± SD.

Results: The mean age of the population was 45.29 ± 20.1 y. We had a female predominance in our population (60.3%). Successfully cured patients were 32.3% whereas those expired were 57.4%. There was not a significant difference between the genders for the outcome ($p > 0.05$).

Conclusions: We found that intravenous magnesium sulphate is ineffective in successfully management of patients with acute asthma in terms of enhanced survival rate.

Keywords: Magnesium sulphate; Bronchial asthma; Efficacy; Emergency management.

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INTRODUCTION

Asthma is a chronic inflammatory disease of the lower airways characterized by respiratory symptoms and variable airway obstruction. Its clinical manifestations include recurrent symptoms, often involving shortness of breath, wheezing, coughing and chest tightness.[1] In developed centuries, asthma is prevalent in 4-5% of the population and almost 27% of patients requiring admission.[2] It is extremely prevalent with up to 1:10 adults worldwide.[3]

In addition to general treatment strategy, standard management of asthma include ß2-agonists, inhaled anticholinergic agents, short-acting bronchodilators, and corticosteroids.[4,5] For patients unresponsive to these initial therapies, magnesium sulfate ($MgSO_4$) may be a treatment option.[1,6] It has also been recommended as an adjunct in treating severe asthma with other mainline drugs.[7,8] In patients who do not respond to initial treatments and those with severe, life-threatening acute exacerbations, current guidelines are suggestive of using $MgSO_4$ as an adjunct therapy for reducing hospital stay and improving pulmonary functions, while the evidence for using nebulized magnesium is still inconclusive.[4,7,9-11] Results have been mixed for several randomized controlled trials (RCTs) using intravenous $MgSO_4$ in acute patients as some studies demonstrate its

benefits,[12-14] while others do not.[2,15,16] Moreover, the studies reporting positive outcomes have shown a benefit predominantly in severe exacerbations as two recent reviews supported its use as an adjunct in severe asthma.[2]

Intravenous $MgSO_4$ has a high safety profile[17] with commonly reported minor side effects including dry mouth, flushing, malaise pain, and numbness at the site of infusion.[1,18] Potential drug interactions include potassium-sparing diuretics and glucagon, which when used simultaneously, increase serum magnesium levels. If concomitant use of both drug groups have to be used, commonly reported problems need to be monitored or the later drug withheld temporarily if possible.[1,19] Contraindications to the use of $MgSO_4$ include myasthenia gravis, myocardial conditions, AV block and renal failure (creatinine clearance less than 30 ml/min).[1,20]

There has not been any study from Pakistan on this topic and there is scarce and conflicting data available on it particularly in Asia.[9] Therefore, this study was conducted to investigate the efficacy of intravenous magnesium sulphate in acute asthma based on its outcomes.

METHODOLOGY

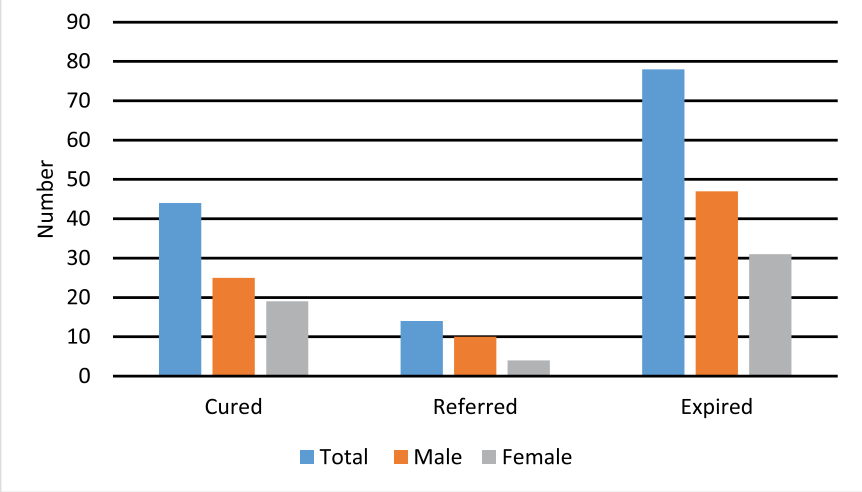
The study was approved by the institutional ethical committee. We conducted a retrospective review of all cases of acute severe asthma transferred to Surgical Intensive Care Unit at Peoples University of Medical and Health Sciences for Women, Nawabshah over a period of 2 years (January 2014-December 2015), and extracted the relevant information from the medical records. We excluded the poisoning cases, post-operative cases, post-trauma and patients on ventilatory support from the analysis. Variables under consideration were age and outcome (expired, cured, and referred). We, however, did not obtain any information on post-referral state of the patients. These patients were referred to hospitals with better treatment facilities on the request of their family or due to the orders of their treating physician.

Moreover, all the patients were initially managed at the Department of Medicine and then shifted to Surgical Intensive Care Unit. Before the current admission, most patients had a history of asthma and were received treatment with maintenance and/or rescue medications at home. In addition, patients received standard therapy (including nebulized salbutamol and ipratropium bromide, and systematic hydrocortisone) for an asthma exacerbation before receiving treatment with intravenous magnesium sulfate. All the patients were initially treated with standard therapy for asthma and then given intravenous magnesium sulphate i.e. received 4 ml of 50% $MgSO_4$ (2 g) diluted in 250 ml of normal saline and given slowly over 20 min as per the recent recommendations.[21] All the patients, after being stable were shifted to the Department of Medicine.

Statistical analysis: The data was recorded and kept on Microsoft Excel 2007 Spreadsheets. We extracted the relevant information and analyzed it on SPSS version 20. Gender and outcomes were presented in percentages and frequencies while age were presented as mean ± SD. Chi square test was used for comparing the outcome between the genders. The significance level was set at $p < 0.05$.

Table 1: Demographic variables and outcomes

Variables	Data
Age (years)	45.29 ± 20.1
Gender	
• Male	54 (39.7)
• Female	82 (60.3)
Outcome	
• Cured	44 (32.3%)
• Expired	78 (57.4%)
• Referred	14 (10.3%)



Graph 1: The outcome of the vpatients based upon gender

RESULTS

A total of 136 patients were enrolled in the study during the study period. There was a female predominance 82 (60.3%) as compared to males, which were 54 (39.7%). The mean age was 45.29 ± 20.1 y. The cured patients were 32.3% whereas those expired were 57.4%. Table 1 shows the demographic variables while Graph 1 shows outcomes based on the gender of the patients. There was not a significant difference between the genders for the outcome; cure rate for males was 25(18.38%) vs. 19(13.87%) ($p > 0.05$). A total of 78 (57.4%) patients expired despite the use of $MgSO_4$.

DISCUSSION

$MgSO_4$ has been used as an adjunct in managing acute asthma but there is still lack of adequate evidence to support its effectiveness. Most of the studies have been conducted in the West and there is a high gap of research in the Asia-Pacific region.[9] The role of $MgSO_4$ in asthma is still unclear, but some studies have helped explain its mode of action. The possible effects of $MgSO_4$ on smooth muscles may include activating sodium-calcium pumps and blocking the entry and release of calcium from the endoplasmic reticulum (ER) which consequently result in decrease in intracellular calcium.[22,23] Moreover, $MgSO_4$ inhibits acetylcholine release and depresses excitability of muscle fiber in cholinergic motor nerve terminals, ultimately generating bronchial smooth muscle relaxation.[24] Furthermore, calcium and myosin interaction is inhibited by magnesium sulphate resulting into muscle cell relaxation. Magnesium also reduces inflammatory mediators by inhibiting mast cell degranulation and stabilizing T-cells.[25] It may also increase the receptor affinity of ß2-agonists thereby, increasing their bronchodilator effect.[9,26] Lastly, it may directly reduce the severity of asthma by stimulating the synthesis of prostacyclin and nitric oxide.[1]

We found that 57.4% patients died even after the management of asthma with magnesium sulphate. However, the use of intravenous $MgSO_4$ improved pulmonary function in adults but did not cause any reduction in the rate of hospitalization.[27,28] Furthermore, a Cochrane review reported the effectiveness of $MgSO_4$ in the treatment of acute asthma,[29] whereas, the recent reviews by Mohammed et al. found that the efficacy of $MgSO_4$ was only marginal on pulmonary function (SMD=0.25, 95% CI= 0.01-0.51).[6] Moreover, the most recent review was unable to draw clear conclusions about effectiveness of $MgSO_4$ in adults. However, it was suggested that intravenous $MgSO_4$ seemed to be effective in children.[30] This shows that there are mixed results and conclusions about the efficacy of magnesium sulphate in management of acute asthma. We tried a different strategy of finding efficacy of magnesium sulphate as compared to the previous studies; they most often were, randomized controlled trials; but we used an outcome-based retrospective review, concluding that magnesium sulphate was ineffective in asthma management.

Strengths and Limitations: This study is the first one from Pakistan on the role of magnesium sulphate in the management of asthma. However, it has its limitations. The study design for this study was retrospective in which charts of the patients were reviewed. Outcome measures were weak and duration of hospital stay, ventilator support, and post-referral status were not obtained and addressed. Nevertheless, this study expands the previous knowledge base on the use of intravenous magnesium sulphate in asthma management.

CONCLUSION

We found that intravenous magnesium sulphate is ineffective in managing patients with acute asthma. However, there is still need of some larger studies, primarily the randomized trials and prospective studies, to draw definite conclusions about the role of magnesium sulphate in the management of asthma.

Conflict of interest: None declared by the authors

Author contribution:
MSK – Manuscript editing
RT – Statistical analysis
AHA – Literature search

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★★★★★

My Most Memorable Patient

What are you afraid of?

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My patient, a 38-year-old lady, of average built, weighing 68 kg, had history of fall from a bike in a road traffic accident, one and half months back. She sustained a subcondylar fracture of her mandible, for which she underwent open reduction and internal fixation with plating in a private hospital. One month after the surgery, she presented to the department of oral and maxillofacial surgery in our hospital with pain in the left preauricular region. The orthopantomogram revealed broken and dislodged plates in the subcondylar region. So, a revision surgery with open reduction internal fixation using facelift approach was planned.

She was then referred to the pre-operative assessment clinic. Airway examination revealed mouth opening of 1.5 fingers with loose lower incisors. Her systemic examination and blood investigations were within normal limits. She had undergone general anesthesia (GA) with endotracheal intubation last time but the anesthetic record was not available, and there was no complaint of any postop complication. GA was planned with nasotracheal intubation after discussion with the surgeons. Anesthetic management and the associated risks were explained and a written, informed consent was obtained.

On the day of surgery, she was found with a dull and anxious look on her face in the preoperative holding area. Somehow, I couldn't ignore that countenance and enquired her as why was she so anxious. Was there anything bothering her? Was she afraid of surgery or pain? She muttered, "No sir. It's not about pain. Sorry, I didn't mention it during my last visit". She took a pause and continued, "I had a very rough time after my previous surgery due to sore throat caused by the tube which had been inserted in my windpipe during surgery". Then all of a sudden, she grasped my hand and pleaded, "Sir, promise me that I won't have sore throat this time". I was taken aback and reassured her. I discussed the role of superior laryngeal nerve block with her and took a separate consent for it.

In the operating room, she was premedicated with midazolam 2 mg and dexamethasone 8 mg slow IV. I performed bilateral superior laryngeal nerve blocks with 2% lignocaine, 3 ml injected on each side after negative aspiration for air or blood. After the block was accomplished, GA was induced by fentanyl 130 μg, propofol 140 mg and vecuronium 6 mg after confirming bag-mask ventilation. After 3 minutes of manual ventilation with 100% of O2, a well-lubricated, size 7 cuffed reinforced endotracheal tube was inserted through the right nostril. Her inter-incisor gap was increased by applying Fergusson mouth gag by the surgeon and the endotracheal tube was glided into the trachea with the help of a magil forceps. Intracuff pressure was maintained at $<$25 cmH2O. Rest of the intraoperative period was uneventful.

The surgery went unremarkably smooth and after three hours she was shifted out to post-anesthesia care unit (PACU). I was busy with the next case on the list and couldn't follow her in PACU. She was shifted to post-operative ward after 2 hours of observation in PACU. As soon as I finished the theatre, I rushed to the ward to see her. While I was approaching her, she looked at me and smiled. I asked her, "How are you feeling? Is there any trouble with your throat?" She replied with a smile, "Sir, I wish I could have you as my anesthetist during my previous surgery as well".

Her nice complement made my day!