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Original Article

Effectiveness of Intravenous Magnesium Sulfate in Children Presenting to the Emergency Department with Acute Exacerbation of Asthma

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ABSTRACT

Asthma is a serious medical condition in the pediatric age group and can have a high mortality, therefore it should be managed effectively. Patients not responding adequately to first line therapy need additional treatment. A few research studies have evaluated the use of intravenous magnesium sulfate in improving respiratory scores in severe acute pediatric asthma but the results have been conflicting. **Objectives**: To determine the benefit of intravenous magnesium sulfate in treating children presenting with worsening of asthma symptoms. **Methods:** A cross-sectional prospective study carried out at the Pediatrics Unit of Zia Uddin University Hospital, Karachi from 1st March 2021 to 1st March 2022. On the whole, 280 children in the age group 2-12 years with acute worsening of asthma of were selected by non-probability purposive sampling technique, however, children in need of invasive ventilation and those having asthma related complications on radiological investigations were omitted. Chi-square was applied for categorical variables and a p-value <0.05 was considered statistically significant. **Results:** Out of 280 patients who came to the Pediatric Emergency Department with acute severe asthma, 236 (84.3%) patients responded to a single dose of intravenous magnesium sulfate manifested by an improvement in clinical asthma score, while 44 patients (15.7%) did not show improvement. The admission rate to the pediatric intensive care unit was only 12.8%. **Conclusion:** Magnesium sulfate infusion helps improve respiratory symptoms in acute worsening of pediatric asthma.

INTRODUCTION

Asthma is a common pediatric illness but if not treated effectively, it can have serious consequences requiring urgent treatment in the emergency setting. In the past two decades, the prevalence of pediatric asthma escalated from 5% to about 20% in Pakistani population [1]. Systemic administration of magnesium sulfate has been advocated by many clinical protocols for treatment of severe asthma not showing improvement to standard therapy. Magnesium sulfate possesses bronchodilator and anti-inflammatory characteristics, and is a beneficial adjunct therapy in children unresponsive to usual medication in acute asthma exacerbation [2]. However, its role in children in acute exacerbation of asthma is yet to be clearly established [3].

First-line therapy in acute severe asthma comprises oxygen inhalation, bronchodilator nebulization (β-2 agonists and anticholinergics), and administration of intravenous steroid therapy [4]. Failure to respond to these warrants the use of alternative agents such as magnesium sulfate (I/V MgSO4) infusion [5]. Very recently, an enormous increase in the number of pediatric asthma cases in Pakistan has been reported and the load on the already over -burdened emergency departments (ED) across the country is surging . Therefore, it is important to conduct randomized controlled trials to elucidate the role of magnesium sulfate as a treatment for improving the management of severe asthma and prevent undue hospital

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admissions [6]. A latest report by a Registry involving pediatric emergency highlighted the fact that a mere 10% of severely asthmatic were treated with intravenous magnesium sulfate [7]. Another current research data emphasized that intravenous magnesium was being administered in barely 36% of pediatric asthma admissions [8] and a link between the use of magnesium sulfate infusion in the ED and decreased hospital admission rates was not observed. However, evidence regarding the effectiveness of magnesium sulfate infusion in pediatric severe acute asthma is restricted [7]. Nebulized magnesium sulfate in pediatric asthma with worsening symptoms has not found to be beneficial, however it has been observed that systemic administration lessens the requirement for severe pediatric asthma cases to be admitted .Furthermore, it is inexpensive, has a good safety profile [9] and severe adverse effects such as respiratory failure and decreased blood pressure attributed to its use in children are infrequent [10]. The dearth of pediatric studies on the systemic use of magnesium sulfate in children are attributed to inconvenience of conducting spirometry to assess the working of lungs as well as their hesitancy to be exposed to this procedure. Therefore, research in this age group focusses on the estimation of betterment in clinical scores, employment of assisted ventilation and the duration of hospital visit [11]. However, results of previous published trials indicate conflicting and unequivocal affirmation of advantage .The British Thoracic Society protocols (2014) declare that utilization of magnesium infusion in acute worsening of pediatric asthma cannot be advocated owing to lack of substantial evidence [5]. This study was therefore undertaken, to determine if intravenous magnesium sulfate could improve clinical symptoms in children with acute worsening of asthma as evidenced by improvement in clinical asthma scores (CAS), and thus reduce the need for invasive ventilation by maximizing medical management.

METHODS

A prospective cross-sectional study was done at Ziauddin University hospital Karachi from 1st March 2021 till 1st March 2022 after approval from Ethical Review committee (Reference code: 2901220SHPED). The sample size was calculated using WHO sample size calculator considering the prevalence of children having successful treatment with magnesium sulphate P=97% with confidence level= 95% and margin of error =2%, the total sample size came out to be 280 patients. Patients in the age group 2-12 years visiting the pediatric Emergency Department of Ziauddin Hospital with acute severe asthma and unresponsive to first line therapy as per standard asthma management protocols were included in the study. A non-probability purposive sampling technique was used. Informed consent from parents or guardians was taken after explaining the advantages and disadvantages of the study. Children requiring immediate intubation, those with asthma related complications on chest X-ray and for whom there was a refusal to consent by parents/caregivers were excluded. The severity of asthma was assessed by the Clinical Asthma Score (CAS) wherein the assessment criteria consists of rate of breathing, wheezing, retractions, dyspnea, and inspiration to expiration (I: E) ratio (minimum 0, maximum 10 points) [12]. All subjects received initial treatment in line with the standard treatment protocols Those patients who failed to respond to the initial treatment were thereafter administered intravenous infusion of magnesium sulphate (50% solution of 50 mg/kg in 30 ml 0.18% saline in D5W) over 20 minutes and a change in the CAS score was recorded at the end of 1 hour and then 2 hours after treatment and compared with the initial score. Data was collected on a pre-designed proforma. A good response to magnesium sulphate infusion was considered if there was an improvement in clinical asthma severity score (CAS) of ≥4 points in 1 hour after starting infusion. Poor response to treatment was considered as no improvement in CAS score after the first hour. SPSS version 20.0 was used to carry out statistical analysis and the results were expressed as frequencies and percentages for qualitative data and mean and standard deviation for quantitative analysis. Categorical variables were analyzed by chi-square and p-value was taken as statistically significant if <0.05.

RESULTS

The study population comprised 280 cases ,151 (53.9%) males and 129 (46.1%) females . Frequency distribution according to age revealed 88 patients (31.4%) to be in the age group 1-6 years and 192 patients (68.6%) to be 7-12 years of age respectively . Mean age, respiratory rate, oxygen saturation, Body mass index , height, weight, systolic blood pressure, diastolic blood pressure , Clinical asthma score (CAS) at baseline, 1 hour and 2 hours in our study was 8.79 ± 4.52 years, 34.72±10.19 breath/min, 82.56±10.63%, 15.7±3.1 kg/m2, 116.7±10.5 cm, 21.9±8.6 kg, 100.4±10.4 mmHg, 62.1±8.7 mmHg, 9.5±2.78, 7.4±2.65 and 4.1±1.21 respectively as shown in Table 1.

Variable	Mean ± SD	Min-Max
Age (years)	8.79±4.52	2-12
Respiratory rate (breaths/min)	34.72±10.19	20-38
Oxygen saturation %	82.5±10.63	69-91
BMI (kg/m2)	15.7±3.1	8.8-17.4
Height (cm)	116.7±10.5	90-125
Weight (kg)	21.9±8.6	17-23
SBP (mm/hg)	100.4±10.4	95-105
DBP (mm/hg)	62.1±8.7	55-70

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CAS score at baseline	9.5±2.78	8-10
CAS score After 1 hour of I/V MgSO4	7.4±2.65	4-8
CAS score After 2 hours of I/V MgSO4	4.1±1.21	1-6

Table 1: Clinical characteristics of the study population (n=280)

It was observed that 236 (84.3%) patients in the study population responded to a single dose of intravenous magnesium sulfate, while 44 patients (15.7%) did not show improvement . The response to treatment was reflected in the improvement of their Clinical asthma score (Table1) . Response with respect to age distribution is shown in Table 2. It was observed that a total of 236 patients responded to treatment and out of these 78 (33.1%) were in the age group 1-6 years while 158 (66.9%) patients were between 7-12 years of age .However ,out of the 44 patients who failed to respond to treatment 10 (22.7%) were in age group 1-6 years and 34 (77.3%) patients were 7-12 years old (p-value 0.11).

Age	Response To I/V Magnesium Sulphate		Total
	Yes	No	
1-6 Years	78 (33.1%)	10 (22.7%)	88 (31.4%)
7-12 Years	158 (66.9%)	34 (77.3%)	192 (68.6%)
Total	236 (100%)	44 (100%)	280 (100%)
P-Value	0.11		

Table 2: Response to treatment according to age (n=280)

Gender distribution with respect to response to treatment with intravenous magnesium sulphate showed that out of a total of 151 male patients ,129 (85.4%) responded to treatment while 22 (14.6%) did not .Whereas, out of a total of 129 females , 107 (82.9%) showed improvement while in 22(17.1%) no response to treatment was observed(p-value 0.34) (Table 3).

Gender	Response To I/V Magnesium Sulphate		Total
	Yes	No	
Male	129 (85.4%)	22 (14.6%)	151 (100 %)
Female	107 (82.9%)	22 (17.1%)	129 (100%)
Total	236 (84.3%)	44 (15.7%)	280 (100%)
P-value	0.34		

Table 3: Response to treatment according to gender (n=280)

Stratification for family history of asthma with respect to response to treatment revealed that a total of 124 patients had a positive family history of asthma and out of these 108 (87.1%) patients showed a clinical response while 16 (12.9%) did not respond (p-value was 0.16)(Table 4). Only 36 (12.8%) patients out of a total of 280 patients who presented with acute asthma in the ED needed admission in the pediatric intensive care unit and 4 (11.1%) out of these admitted patients required mechanical ventilation .Side effects of treatment were minor with flushing and drowsiness observed in only 8 children (2.85%).The average duration of hospital stay was 6.5 ± 1.2 days .

Family history of asthma	Response To I/V Magnesium Sulphate		Total
	Yes	No	
Yes	108 (87.1%)	16 (12.9%)	124 (100%)
No	128 (82.1%)	28 (17.9%)	156 (100%)
Total	236 (84.1%)	44 (15.7%)	280 (100%)
P-value	0.16		

Table 4: Distribution according to response to treatment and family history of asthma(n=280)

DISCUSSION

A stepwise approach is recommended for management of acute severe asthma, initially first-line standard therapy is used followed by additional therapeutic options. Review of literature reveals that a number of studies have been conducted in the adult population regarding the efficacy of magnesium sulfate infusion [13, 14]. Although most studies reporting the potential clinical use of MgSO4 treatment in acute pediatric asthma have observed a beneficial effect, its precise role has still not been fully determined [15, 16]. In this regard, effectiveness of magnesium sulfate infusion in children was evaluated by a meta-analysis that analyzed 5 trials and reported favorable effects with its use when added to β2-agonists and systemic steroid therapy. The results revealed magnesium sulfate infusion to be efficacious in reducing hospital admission rates and when used as an add on treatment to conventional therapy it produced 85% reduction in symptoms [17]. These findings are similar to our study wherein we observed that 82% of the children in the age group 2-12 years presenting to the Emergency Department had an improvement is Clinical Asthma Score following the administration of a single dose of intravenous magnesium sulfate .In a similar study by Özdemir *et al* , systemic use of magnesium sulfate was efficacious in improving spirometry values in children aged 6-17 years with acute worsening of asthma symptoms [18]. Furthermore , a systematic review carried out by Mathew *et al* to assess the effectiveness of intravenous and nebulized magnesium sulfate for acute worsening of pediatric asthma, concluded that injectable magnesium sulfate therapy produced considerable improvement in clinical signs and symptoms and led to a twofold decline in admission rate [19]. In our study we noted that after administration of a single dose of intravenous magnesium sulfate only 36(12.8%) patients needed admission while invasive ventilation was needed in a mere 4 patients. Similar observations were reported in a study by Ciarallo *et al*, wherein more pediatric patients with acute exacerbation of asthma who received intravenous magnesium sulfate in ED went home [20]. Griffith *et al* evaluated the effectiveness of intravenous magnesium sulfate in children with acute symptoms of asthma and observed minimal side-effects with a substantial fall in admission rates by 68% [4]. These findings are also

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supported by our study results . Moreover , Singhi *et al*. compared the efficacy of IV MgSO4 with other systemic treatments such as aminophylline and terbutaline for asthma symptoms unresponsive to standard initial treatment [21].They concluded that using IV MgSO4 as an additional therapy to inhaled bronchodilator therapy was extremely useful and safe as compared to other injectable treatments .Our study findings are in concert with these findings and also those of Tassalapa *et al*. wherein in their study they observed that both intravenous as well as nebulized MgSO4 are effective and harmless in severe pediatric asthma [10]. On the other hand, Alansari *et al* evaluated the usefulness of this treatment in bronchiolitis and reported no particular benefit [22]. We however , observed a clear improvement in clinical asthma scores of our study population after one hour and more so after 2 hours of using intravenous magnesium sulfate.

CONCLUSIONS

Based on the study results acute worsening of pediatric asthma can be effectively treated by intravenous magnesium sulfate when combined with conventional treatment.

Conflicts of Interest

The authors declare no conflict of interest

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