ISSN: 2573-9611

Research Article

Journal of Pediatrics & Neonatal Biology

Magnesium Sulphate as an Adjuvant Therapy in Critically Ill Infants and Children Presenting with Wheezy Chest

Hanaa I Rady*, Hala H Shaaban, Hafez M Bazaraa, Sherif E Abdelmonem and Yasmin S Aly

Department of pediatrics, Faculty of Medicine, Cairo University, Cairo, Egypt

***Corresponding author**
Dr. Hanaa Rady, MD, Department of Pediatrics, Faculty of Medicine, Cairo University, Cairo, Egypt. E-mail: hanaaarady@gmail.com

Submitted: 30 June 2018; **Accepted**: 09 July 2018; **Published**: 25 July 2018

Abstract

Background: *Wheezy chest remains one of the major causes for emergency department visits and admissions at Paediatric intensive care units.*

Objective: *We aimed to determine the efficacy of magnesium sulphate ($MgSO_4$) versus standard treatment in critically ill infants and children with wheezy chest.*

Methodology: *Randomized controlled trial comprised 81 patients suffering from wheezy chest divided into 3 groups. In addition to bronchodilators and systemic steroids, $MgSO_4$ was given by inhalation in Group A, intravenously in Group B, and Group C received placebo. The improvement in our cases was determined by clinical respiratory score (CRS), ventilator setting and arterial blood gases before and after treatment.*

Results: *Median age was 11 months, mean weight 9.3kg and the median of SOFA score was one. After treatment: There was significant improvement of CRS in the three groups. In group A, there was significant reduction in ventilator rate (p=0.017) and improvement of arterial/inspired oxygen ratio (p=0.0056). In group B better mean arterial pH was noted (p=0.009).*

Conclusion: *Magnesium sulphate is a safe and beneficial adjuvant therapy in addition to standard treatment in critically ill infants and children with wheezy chest.*

Keywords: Critically Ill Infants and Children, Inhaled Mgso4, Iv Mgso4, Wheezy Chest.

Introduction

Wheezy chest remains one of the major causes for emergency department visits and admissions at Pediatric intensive care units (PICUs). About 25% to 30% of infants will have at least 1 episode of wheezes, increasing to 40% at 3 years and more than 50% at6 years [1].

Most infants and children with recurrent wheezing have asthma. Other common causes of wheezing in children include infections (bronchiolitis, bronchitis, pneumonia, and upper respiratory tract infection), allergies, gastro esophageal reflux disease and obstructive sleep apnea. Broncho-pulmonary dysplasia, foreign body aspiration, and cystic fibrosis are less frequent causes of wheezing. Oxygen, inhaled beta2 adrenergic agonist, hydration and corticosteroids (CS) remain the first line of treatment in acute wheezing episode. Addition of ipratropium bromide (IB) to short-acting b2-agonists may be considered in patients with severe wheeze [2].Other modes of treatment include intravenous (IV) salbutamol and theophylline. This is not adequate in a significant amount of patients [3].

The use of IV magnesium sulphate ($MgSO_4$) in treating asthma attacks has been shown to improve pulmonary functions as adjunct therapy. The suggested mechanisms of action are airways smooth muscle relaxation secondary to inhibition of calcium influx, its inhibitory effect on methacholine, histamine and sodium metabisulfite induced bronchoconstriction and it increases bronchodilator response to beta2 adrenergic agonist by up regulation of beta 2 receptors [3, 4].

So we aimed to determine the efficacy and safety of inhaled and IV $MgSO_4$ versus standard treatment in critically ill infants and children with diverse causes of wheezy chest in addition to asthma.

Methods

The study was a randomized control clinical trial conducted at PICU of the Cairo University, Children Hospital, between January 2016 and December 2017. The included cases were critically ill infants and children between 2 months and 12 years with severe respiratory distress and / or one or more system failure and suffering from wheezy chest.

Excluded patients were those known to have chronic chest condition like cystic fibrosis, interstitial lung disease and broncho-pulmonary dysplasia and patients known allergic to $MgSO_4$ or whom $MgSO_4$ is contraindicated.

The patients were divided into three groups using sealed envelopes for randomized allocation, Group A: Inhaled $MgSO_4$, Group B: IV $MgSO_4$, Group C: control group. All cases were subjected to clinical assessment on admission including full history and examination and assessment of severity of respiratory illness on admission, using clinical respiratory score (CRS) and determination of illness severity by SOFA score [5, 6].

The three groups received respiratory support according to the patients' condition. Nebulized drugs were given by Atom ultrasonic nebulizer Sanilizer 303 [An ultrasonic nebulizer device designed to create large quantities of fine particles less than 5 microns in diameter at ambient temperatures, Operating temperature: 0°C ÷ 60°C, Nebulisation rate: ≈ 390 ml /h] in the form of salbutamol consisting of 4 ml of sterile saline with 2.5 mg of salbutamol for children ≤ 2 yrs old or 5 mg of salbutamol for children > 2 yrs; every 3 hours. Inhaled IB in a dose 0.25mg added to 4ml of sterile saline every 6 hours added to salbutamol. Inhaled budesonide in a dose 0.25mg every 12 hours added to salbutamol [7]. In travenous hydrocortisone in a dose 4mg/kg/dose every 6 hours and intravenous bronchodilators as salbutamol (5µg/kg/dose) every 6 hours [8, 9].

In severe cases (resistant cases or whom developed respiratory failure); intravenous methyl prednisolone in a dose of 10mg/kg once is given [10]. In addition to the above, Group A received inhaled $MgSO_4$ in a dose of 100mg $MgSO_4$ every 6 hours for 24 hours, Group B received intravenous $MgSO_4$ at a dose of 25mg/kg every 6 hours for 24 hours and Group C Control group received placebo [11].

In all groups follow up within 24 hours after starting treatment by CRS, arterial blood gases (ABG) values, oxygen saturation by pulse oximeter, level of respiratory support and its duration, oxygenation index and airway resistance in ventilated patients.

The protocol was approved by the research committee of the Paediatric department at Children Hospital of Cairo University after an ethical review and a written parental consent was taken and the data were documented on Excel spreadsheet. It was also registered in ClinicalTrials.gov and took the ID: CairoU76.

Data Analysis

Data were tabulated and subjected to computer-assisted statistical analysis using Microsoft excel 2003 and statistical package for social science (SPSS) version 16. Nominal data were described as frequency and percentage and were compared using chi square tests. Numerical data were described as mean and standard deviation and were compared using t tests. Non parametric data were expressed as median and inter-quartile range and compared using Mann Whitney test. Pearson correlations were used to determine the associations between numerical variables. P values less than 0.05 were considered significant. Graphs were prepared using Microsoft excel sheet and SPSS.

Results

The study included 81 patients admitted to PICU and suffering from wheezy chest. (Table 1) showed the characteristics of the studied groups. The median of SOFA score in Inhaled $MgSO_4$ group was higher than the IV $MgSO_4$ group and Placebo.

Table 1: Clinical Respiratory Score. (5)

Clinical Respiratory Score			
Assess	**Score 0**	**Score 1**	**Score 2**
Respiratory Rate	< 2 mo < 50	< 2 mo 50-60	< 2 mo > 60
	2-12 mo < 40	2-12 mo 40-50	2-12 mo > 50
	1-5 yrs < 30	1- 5 yrs 30-40	1-5 yrs> 40
	> 5 yrs < 20	> 5 yrs 20-30	> 5 yrs > 30
Auscultation	Good air movement scattered expiratory wheezing and loose rales/crackles	Depressed air movement, inspiratory and expiratory wheezes or rales/crackles	Diminished or absent breath sounds, severe wheezing, or rales/crackles, or marked prolonged expiration
Use of Accessory Muscles Mild to no	Mild to no use of accessory muscles. Mild to no retractions, nasal flaring on inspiration.	Moderate intercostals retractions, mild to moderate use of accessory muscles, nasal flaring.	Severe intercostals and substernal retractions, nasal flaring.
Mental Status	Normal to mildly irritable	Irritable, agitated, restless	Lethargic
Room Air	Sp02 > 95%	90-95%	< 90%
Colour	Normal	Pale to normal	Cyanotic, dusky

• The weight of patients of IV $MgSO_4$ group was higher than Placebo group.

Table2: Characteristics of studied groups

	Inhaled MgSo4	IV MgSo4	control	P value
Number of cases	25	29	27	
Male/Femle	13/12	15/14	14/13	
Mean weight (Kg)	8.75 ± 4.306	11.79± 9.722	7.07 ± 3.168	(p =0.022)•
Median age (months)	18(6-36)	12(7-29)	9(4-18)	NS
Median SOFA score	1.5(0-2)	1(0-3)	1(0.75-3)	NS

• The weight of group B patients was higher than group C.

SD: standard deviation, Group A: Inhaled $MgSO_4$, Group B: IV $MgSO_4$, Group C: Placebo

The CRS of the three groups improved after treatment. The median of respiratory score change in Group B (median IQ 1-5.5) was better than Group A (median IQ 1.5-4.5) and Group C (median IQ 0-3); however this was not significant, p= 0.55.
There was significant improvement in the mean PH of ABGs of group B after treatment (p=0.009), while there was significant reduction in ventilator rate in group A in comparison to group C (p =0.017).

There was significant improvement of arterial inspired oxygen ratio in Group A after treatment (p = 0.0056). Also there is improvement in Group B and C but it is insignificant. (Figuer.1, 2)

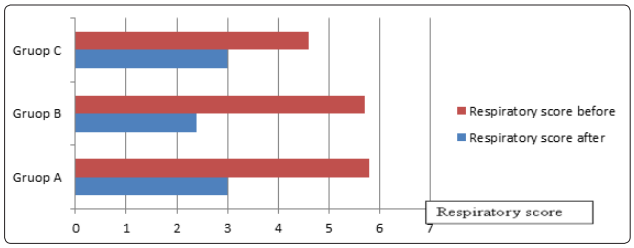

Figure 1: Changes in respiratory score among the 3 groups

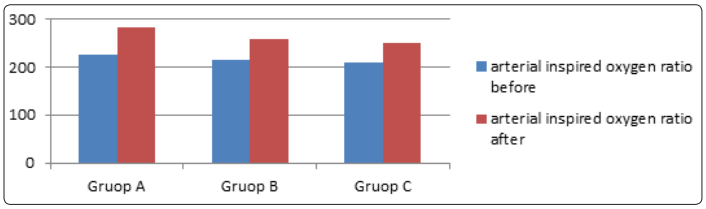

Figure 2: Arterial inspired oxygen ratio in the 3 groups before and after treatment

There was insignificant reduction of FiO2 needs in the three groups; also there is insignificant reduction in ventilator rate in Group A and B after treatment. The mean of ventilator rate in Group A after treatment was significantly lower than that of Group C (p =0.017). (Table, 3, 4)

Table 3: Clinical respiratory score before and after treatment in the 3 groups

Groups	A		B		C		p value		
Respiratory score	Mean	SD	Mean	SD	Mean	SD	A/B	A/C	B/C
Before	5.8	2.2	5.7	3	4.6	2.1	0.9	0.07	0.15
After	3.1	2.8	2.4	1.4	3	2.3	0.32	0.94	0.30
p value before /after	0.0014	<0.0001	0.03						

SD: standard deviation

Table 4: Ventilator settings in the 3 groups before and after treatment

Groups	A		B		C		P value		
	Mean	SD	Mean	SD	Mean	SD	A/B	A/C	B/C
PIP before	19.5	3.6	19.1	4.63	17.9	3.7	0.88	0.44	0.58
PIP after	17.2	2.4	18.4	4	19.2	3.43	0.51	0.27	0.73
PEEP before	5.2	0.4	5.1	1.3	4.4	1.3	0.93	0.20	0.30
PEEP after	5	0	4.4	1.1	4.8	0.8	0.17	0.59	0.38
FiO2 (MV)_ before	53.3	16.3	72.5	18.3	64.3	22.4	0.06	0.34	0.44
FiO2(MV)_ after	42.5	6.1	53.9	18.4	53.3	17.8	0.176	0.189	0.957

p value FiO2_before / FiO2_ after	0.16		0.06		0.36				
RR before	32	6.5	34.1	10.1	35	9.1	0.66	0.51	0.86
RR after	24.5	5.2	31.9	10.5	36	8.4	0.14	0.02	0.45

PIP: peak inspiratory pressure, PEEP: positive end expiratory pressure, FiO2: fraction of inspired oxygen, TI: inspiratory time, RR: respiratory rate, SD: standard deviation.

PIP: peak inspiratory pressure (cmH2O), PEEP: positive end expiratory pressure (cmH2O), FiO2: fraction of inspired oxygen (Vol %), TI: inspiratory time (seconds), RR: respiratory rate, SD: standard deviation.

Discussion

We intended to test the benefits of inhaled and IV $MgSO_4$ in other diseases presenting by wheezes like pneumonia, to verify the bronchodilator effect of $MgSO_4$ and the possibility of its use in other causes of wheezy chest in PICU rather than asthma. Unlike other studies who studied asthmatics only or patients with bronchiolitis [12-16].

We used CRS in our study to assess the improvement of the clinical condition of cases before and after treatment, while most of the other studies assessed pulmonary functions before and after treatment. We couldn't use pulmonary function tests in assessing our patients because they were critically ill, mechanically ventilated and pulmonary functions wasn't available in the same building; so transportation could have endangered their lives.

There was significant improvement in CRS in 3 groups after treatment; the median of CRS change in (IV $MgSO_4$) group B was better than group A and C; however the difference between 3 groups was statistically insignificant. This was in agreement with the study done by Abdelnabi and his colleagues who showed significant reduction in mean final respiratory rate of asthmatic patients divided into 2 groups one received inhaled $MgSO_4$ and the other group received inhaled salbutamol, in addition to IV hydrocortisone in both groups. However patients received nebulized salbutamol showed better improvement when compared to those received inhaled $MgSO_4$ [17].

Also, **Powell** and his colleagues used asthma severity score to reassess the patients after treatment. Mean asthma severity score after 60 min was lower in the $MgSO_4$ group than it was in the placebo group (p = 0•03) [12].

Moreover, the study by **Singhi** and his colleagues, showed significant improvement in modified Clinical Asthma Severity score without adverse events occurred among patients receiving IV $MgSO_4$, and it showed that adding a single dose of IV $MgSO_4$ to inhaled beta2-agonists and CS was more effective, and safer, than using terbutaline or aminophylline when treating a child with acute severe asthma poorly responsive to initial treatment [13]. This was in accordance with our results that didn't show adverse effects (arrhythmia, hypotension) from the usage of $MgSO_4$ by IV or inhalation routes and all mean serum magnesium levels were within normal range after treatment.

Multiple studies including patients with bronchial asthma and bronchiolitis showed significant improvement after addition of nebulized $MgSO_4$ to standard treatment, we showed the same improvement on patients with different causes of wheezy chest not asthma only [12,15,16].

In our study, we assessed arterial/inspired oxygen ratio, as in critically ill patients, the PaO2/FiO2 ratio is an indicator of oxygenation status [18]. A low PaO2/FiO2 value has been associated with increased mortality and hospital stay in patients admitted to the ICU [19]. This ratio is widely used in ICUs because it quickly and easily provides data on the oxygenation status of critically ill patients and its values are included in ICU prognostic scores [20].

Also it has been used to quantify the degree of abnormalities in pulmonary gas exchange and to quantify pulmonary gas exchange before and after therapeutic intervention [19].

There was significant improvement of arterial inspired oxygen ratio in group A after treatment (p= 0.0056). This indicates that patients received inhaled $MgSO_4$ showed better prognosis, improvement in ventilation perfusion mismatching, oxygenation state and pulmonary gaseous exchange.

Inhaled and IV $MgSO_4$ had beneficial effects in treating critically ill infants and children with wheezy chest other than asthma. $MgSO_4$ helped in the improvement of CRS, arterial/inspired oxygen ratio and reduction of ventilator rate after treatment.

References

1. Barclay L, Lie D (2008) Diagnosis of wheezing in Infants and Children. https://www.medscape.org/viewarticle/573491.
2. Brand P, Baraldi E, Bisgaard H, Boner AL, Castro-Rodriguez JA, et al. (2008) Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. Eur Respir J 32: 1096-1110.
3. Mahajan P, Haritos D, Rosenberg N, Thomas R (2004) Comparison of nebulized magnesium sulphate plus albuterol to nebulized albuterol plus saline in children with acute exacerbations of mild to moderate asthma. The journal of emergency medicine 27: 21-25.
4. Blitz M, Blitz S, Hughes R, Hughes R, Diner B, et al. (2005) Aerosolized magnesium sulfate for acute asthma: a systematic review. Chest 128: 337-344.
5. Asthma/recurrent wheezing management clinical guideline (2008) https://www.bcm . edu /web/pediatrics'/ documents/ rp_ archive _20.
6. Jones AE, Trzeciak S, Kline JA (2009) The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med 37: 1649-1654.
7. Øymar K and Halverson T (2009) Emergency presentation and management of acute severe asthma in children. Scandinavian

Journal of Trauma, Resuscitation and Emergency Medicine 17: 40.
8. Carroll W, Lenney W (2007) Drug therapy in the management of acute asthma. Arch Dis Child - Education and practice edition 92: 82-86.
9. Sellers W (2013) Inhaled and intravenous treatment in acute severe and life-threatening asthma. BJA: British Journal of Anaesthesia 110: 183-190.
10. Tschudy MM, Arcara KM (2012) The Harriet Lane Handbook: A Manual for Pediatric House Officers. Philadelphia, PA: Mosby Elsevier.
11. Mohammed S, Goodacre S (2007) Intravenous and nebulised magnesium sulphate for acute asthma: systematic review and meta-analyses. Emerg Med J 24: 823-830.
12. Powell CVE, Kolamunnage-Dona R, Lowe J, Boland A, Petrou S, et al. (2013) On behalf of the MAGNETIC study group MAGNEsium Trial in Children (MAGNETIC). A randomized, placebo-controlled trial and economic evaluation of nebulised magnesium sulphate in acute severe asthma in children. Health Technology Assessment 17: 45.
13. Singhi S, Grover S, Bansal A, Chopra K (2014) Randomized comparison of intravenous magnesium sulphate, terbutaline and aminophylline for children with acute severe asthma. ActaPaediatr 103:1301-1306.
14. Wang H, Xiong Y, Gong C, Yin L, Yan L, et al. (2015) Effect of Inhaled Magnesium Sulfate on Bronchial Hyperresponsiveness. The Indian Journal of Pediatrics 82: 321-327.
15. Modaresi M, Faghihinia J, Kelishadi R, Reisi M, Mirlohi S, et al. (2015) Nebulized Magnesium Sulfate in Acute Bronchiolitis: A Randomized Controlled Trial 82: 794-798.
16. Kose M, Ozturk M, Poyrazoğlu H, Elmas T, Ekinci D, et al. (2014) The efficacy of nebulized salbutamol, magnesium sulfate, and salbutamol/magnesium sulfate combination in moderate bronchiolitis. European Journal of Pediatrics 173: 1157-1160.
17. Abdelnabi E, Kamel M, Ali A (2012) Nebulized magnesium sulphate versus nebulized salbutamol in acute bronchial asthma. Egyptian Journal of Chest Diseases and Tuberculosis 61: 29-34.
18. Karbing D, Kjærgaard S, Smith B, Espersen K, Allerød C, et al. (2007) Variation in the PaO2/FiO2 ratio with FiO2: mathematical and experimental description, and clinical relevance. Critical Care 11: R118.
19. Kramer AA, Zimmerman JE (2010) A predictive model for the early identification of patients at risk for a prolonged intensive care unit length of stay. BMC Med Inform Decis Mak 10: 27.
20. Schneider AG, Lipcsey M, Bailey M, Pilcher DV, Bellomo R (2013) Simple translational equations to compare illness severity scores in intensive care trials. J Crit Care 28: 885.