

THE EFFECT OF INTRAVENOUS MAGNESIUM SULFATE ON CHILDREN ADMITTED WITH ACUTE BRONCHIOLITIS IN A TERTIARY CARE HOSPITAL

Andaleeb Ara, Farooq Ikram*, Hidayat Ullah**, Shakila Asmat***, Nadia Tareen***

Armed Forces Institute of Cardiology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Pak Emirates Military Hospital Multan/National University of Medical Sciences (NUMS) Pakistan, **Frontier Medical College, Abbottabad Pakistan, ***Sandeman Provincial Hospital, Quetta Pakistan

ABSTRACT

Objective: To assess the efficacy of using intravenous Magnesium Sulfate along with the conventional treatment in the management of acute bronchiolitis

Study Design: Quasi-experimental study.

Place and Duration of Study: Pediatrics department in Sandeman Provincial Hospital, Quetta, from Jan to Jul 2019.

Methodology: The study was approved by institutional ethical committee of Combined Military Hospital, Peshawar. Children, 2 months to 2 years of age, with acute bronchiolitis having clinical severity score of ≥ 5 , presenting to the OPD and emergency department were enrolled in the study after getting informed consent from the guardian. They were randomly assigned group A receiving intravenous Magnesium Sulfate and group B receiving placebo along with the conventional treatment for both. Data was analysed with SPSS-21.

Results: Total 108 patients were included in the study with 54 (50%) in group A and 54 (50%) in group B. Mean age in the study was 12.02 ± 6.421 months. Mean age in group A and B was 11.17 ± 6.40 and 12.87 ± 6.38 months respectively. Out of 108 patients 50 (46.3%) were males while 58 (53.7%) were females. There was statistically significant difference in the efficacy of treatment between two groups with values being 48 (88.9%) and 37 (68.5%) for Magnesium Sulfate and control groups respectively ($p=0.01$).

Conclusion: From a clinical point of view, intravenous Magnesium Sulfate combined with conventional treatment is more effective than conventional treatment alone in the management of acute bronchiolitis.

Keywords: Acute bronchiolitis, Bronchiolitis, Magnesium sulfate.

How to Cite This Article: Ara A, Ikram F, Ullah H, Asmat S, Tareen N. The Effect of Intravenous Magnesium Sulfate on Children Admitted with Acute Bronchiolitis in A Tertiary Care Hospital. *Pak Armed Forces Med J* 2021; 71(6): 2148-2151. Doi: <https://doi.org/10.51253/pafmj.v71i6.6247>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Acute bronchiolitis, an acute inflammatory respiratory illness, is one of the major causes of hospitalization in children who are under 2 years in age. It is marked by acute inflammatory changes in small airways leading to excessive production of mucus accompanied by bronchospasm. The resultant partial obstruction causes early collapsibility of the airways leading to air trapping which, if complete, results in atelectasis due to absorption of the distally trapped air.¹ The clinical picture comprises of rhinitis, cough, increased respiratory rate, wheeze, crackles and increased respiratory effort. In 72.4% of the cases, Respiratory Syncytial Virus (RSV) is responsible followed by rhinovirus which causes about 29% of the cases.² Winter is the peak season with the highest incidence of acute bronchiolitis. Factors, such as prematurity, low birth weight, tobacco smoke exposure, poverty, lack of breastfeeding

and multiple gestation also play an important role.³ Chronic lung disease and congenital heart disease also increase the susceptibility to severe acute bronchiolitis.

In United States approximately 31.2 per 1000 children of age less than 1 year are hospitalized annually with RSV bronchiolitis.⁴ In United Kingdom 30.8 per 1000 children are admitted with acute bronchiolitis.⁵ As per the World Health Organisation (WHO) reports that the approximate prevalence of RSV all across the globe is 64 million cases and 1,60,000 deaths every year.⁵ To date, no national studies have reported the disease burden at a population level in Pakistan.

Unfortunately, acute bronchiolitis does not have an effective drug treatment apart from supportive care (Oxygen inhalation, hydration). Nebulized albuterol and epinephrine have been used around the world but with variable effects.⁶ Many other treatment options including hypertonic saline in its nebulized form, parenteral, nebulized and oral corticosteroids, antiviral drugs like ribavirin in its aerosolized form and palivizumab, a monoclonal antibody against RSV infection have all been tried with similar results with some

Correspondence: Dr Andaleeb Ara, Department of Cardiology, Armed Forces Institute of Cardiology, Rawalpindi Pakistan
Received: 02 Feb 2021; revision received: 05 May 2021; accepted: 07 May 2021

having issue of being less cost effective and others not routinely recommended.⁷

Magnesium sulfate, being a smooth muscle relaxant with anti-inflammatory effects, offers good results in relieving symptoms in acute exacerbation of asthma and many studies have shown parenteral Magnesium Sulfate to show beneficial results in children and adults.⁸ In one study more patients with acute exacerbation of asthma who received intravenous Magnesium Sulfate in emergency department were allowed to go home instead of being admitted in hospital as compared to those who did not receive it (8/16 vs 0/14; $p=0.002$).⁹ The easy availability, affordability and safe side effect profile of Magnesium Sulfate are attractive attributes for its application in acute bronchiolitis also though some studies have shown it to be ineffective in treating acute bronchiolitis thus warranting further studies to elaborate the issue.¹⁰

Keeping in view the already mentioned high prevalence of acute bronchiolitis with many children requiring admission in hospitals along with a lack of consensus over the treatment options, it appears appropriate to test intravenous Magnesium Sulfate for any positive role through a placebo-controlled randomized control trial. The findings of this study are expected to help in getting insight in to the issue and thus play role in improving management of these children.

METHODOLOGY

It was a quasi-experimental study, carried out at the Pediatrics Department of Sandeman Provincial Hospital, Quetta from January to July 2019 in which 108 children of both genders were randomly assigned to two equal groups of 54 children each. Sample size was calculated by providing 80% power based on a decrease in Clinical Severity (CS) score to 13% of the initial value for the group receiving Magnesium Sulfate and epinephrine and to 33% of the initial value the group receiving only epinephrine.¹¹ The study was approved by Ethical Review Committee for medical and biomedical research of Combined Military Hospital, Peshawar in Dec 2017 (ltr no. 23/21). Non probability consecutive sampling technique was used. For clinical assessment of patients CS score used by Wang *et al* was utilized.¹² The total score considering all four variables was 12. The lesser the score the better was the clinical condition (Table-I).

Inclusion Criteria: Children admitted with acute bronchiolitis, having age between 2 months and 2 years and a CS score ≥ 5 were included in the study.

Exclusion Criteria: Patients who had congenital cardiac disease, chronic respiratory disease, a clinical picture and/or a chest radiograph showing the presence of pneumonia, a personal or family history of atopy or wheezing suggestive of early onset asthma were excluded. Patients with known Magnesium Sulfate hypersensitivity and seriously ill were also excluded from the study.

All the enrolled patients were given the conventional treatment of Oxygen therapy (titrated with oxygen saturation measured by pulse oximeter), nebulized Ipratropium bromide (250 μg 8 hourly) and nebulized steroids (Beclomethasone 200 μg 12 hourly). Group A, in addition to the conventional treatment, received intravenous Magnesium Sulfate 75 mg/kg (maximum dose 2 gram) given as a single dose infusion over 30 minutes along with the conventional treatment. Magnesium Sulfate was given in the maintenance fluid (5% Dextrose 1/2 NaCl or 5% Dextrose 1/5 NaCl depending on the fluid requirement according to age) at a dilution of maximum concentration of 20 mg/ml. Group B was given the same volume of placebo (0.9% saline) instead of Magnesium Sulfate along with the conventional combined treatment. Clinical severity score of the patients was recorded at the time of admission before administering treatment, at 24 hours and 48 hours after Magnesium Sulfate administration. During the intravenous administration of magnesium sulfate, the child was closely monitored to look for any side effects.

Clinical severity score findings were recorded and filled out in a proforma. Efficacy of treatment was decided on the basis of CS score. A score of < 5 at 48 hours, after administration of magnesium sulfate, was considered as effective. The criteria for declaring patients fit for discharge from hospital were no need for Oxygen therapy or IV fluids with the child feeding well and having no wheeze, crackles and chest retractions along with a CS score < 5 . The primary study outcome was the difference in the reduction of CS scores between the two groups in the form of a difference in efficacy of treatment. Statistical Package for the Social Sciences (SPSS) version 21 was used for data entry and analysis. Mean \pm SD was calculated for quantitative variables (age and respiratory rate at 48 hours after Magnesium Sulfate injection). Frequency and percentage were calculated for qualitative variables (gender and efficacy) in both groups. Comparison of efficacy was done by applying chi-square test keeping p -value ≤ 0.05 .

RESULTS

A total of 108 patients were included in study of which 26 (25.85%) and 24 (24.07%) presented in the months of February and March respectively.

Out of 108 patients 54 were kept in group A and received intravenous Magnesium Sulfate along with the conventional treatment while 54 were kept in group B who received placebo along with the conventional treatment.

The mean age of study population was 12.02 ± 6.42 months. Mean age for group A was 11.17 ± 6.40 months while for group B the mean age was 12.87 ± 6.38 months.

Out of 108 patients 50 (46.3%) were males while 58 (53.7%) were females. Group distribution of male patients was 23 (42.6%) and 27 (50%) for group A and B respectively. Similarly, group distribution of female patients was 31 (57.4%) and 27 (50%) for group A and B respectively.

Comparing the outcome of treatment in two groups, there was statistically significant difference in the efficacy in two groups with the frequency of efficacy of treatment observed in 48 (88.9%) and 37 (68.5%) patients for group A and B respectively ($p=0.01$) (Table-II).

treatment in patients aged >12 months was seen in 17 (81%) and 18 (64.3%) patients for group A and B respectively.

Among male patients, the efficacy was noted in 20 (87%) and 20 (74.1%) patients for group A and B respectively. For female patients, the efficacy was seen in 28 (90.3%) and 17 (63%) patients for group A and B respectively.

DISCUSSION

This study found that administration of intravenous Magnesium Sulfate to children having acute bronchiolitis results in clinical improvement. There was significant difference demonstrated between the Magnesium Sulfate and placebo groups with respect to improvement in CS score.^{12,13} In developing countries, acute bronchiolitis remains one of the important causes of lower respiratory tract infection and the resultant mortality in infants. In more than half of the cases RSV has been mentioned to be the cause of acute bronchiolitis in children less than 2 years of age with the majority being affected between 3 and 6 months of age.¹⁴ Clinically the disease exhibits fever, cough, wheezing, tachypnea, retraction and nasal flaring.

Generally, the management of acute bronchiolitis is supportive. No single medical treatment has exhibited improved clinical outcomes. Maintaining hydration, antipyretics, use of Oxygen, Inhaled saline, bronchodilator inhalation and steroids have all been advocated.¹⁵ A systematic review by Kellner *et al.* has reported only modest short term improvement in clinical scores with no reduction in the rate and duration of hospitalization after using inhaled short acting β-2 agonists or nebulized epinephrine.¹⁶ Another review mentions use of nebulized hypertonic saline leading to modest reduction of length of hospital stay in infants with acute bronchiolitis and also improvement of CS score.¹⁷ Multiple studies have been published on the management of bronchiolitis but the evidence to support different medications is not very strong and their role is controversial.¹⁸ Magnesium Sulfate can act as a bronchodilator by its effect on calcium translocation across cell membranes. Initially Magnesium Sulfate was used in treating asthmatic patients where studies showed significant improvement in the asthmatic children resistant to β-agonist treatments.¹⁹ Keeping in view clinical and pathophysiological similarities between bronchiolitis and acute asthmatic attack, Magnesium Sulfate is often considered as an alternative therapy for acute bronchiolitis. In this study we intended to explore the efficacy of intravenous Magnesium

Table-I: Clinical severity (CS) score*.

Variables	Score			
	0	1	2	3
Respiratory rate, breaths /min	<30	31-45	46-60	>60
Wheezing	None	Terminal expiratory or only with stethoscope	Entire expiration or audible on expiration without stethoscope	Inspiration and expiration without stethoscope
Retraction	None	Intercostal only	Tracheosternal	Severe with nasal flaring
General condition	Normal	-	-	Irritable, lethargic, poor feeding

* From Wang *et al*¹²

Table-II: Comparison of efficacy in both the groups.

Efficacy	Group A	Group B	p-value
	Frequency (%)		
Yes	48 (88.9)	37 (68.5)	0.010
No	6 (11.1)	17 (31.5)	

In patients of ≤12 months of age, the efficacy of treatment was noted in 31(93.9%) and 19 (73.1%) patients for group A and B respectively. The efficacy of

Sulfate in the management of acute bronchiolitis as compared to just the conventional treatment.

Mean age in our study for group A and B was 11.17 ± 6.401 and 12.87 ± 6.387 months respectively while in a study conducted by Modaresi *et al.*, mean age in years was 1.31 ± 0.41 and 1.39 ± 0.44 respectively.¹¹ Hervas *et al.*, during their study having 2384 patients found that most of the hospital admissions were in the months of January (27.3%, 652), February (18.6%, 443), and December (20.8%, 496).²⁰ In our study maximum admissions were in the month of February (25.85%, 26). Hervas *et al.*, showed that 58% of patients in their study were of male gender.²⁰ In our study patients of male gender were 46.29% (n=50). A study by Modaresi *et al.*, respiratory rate in terms of mean and standard deviation was 66 ± 5 while in our study, mean respiratory rate was 31.85 ± 5.46 .¹¹

In Kose *et al* study, nebulized Magnesium Sulfate plus salbutamol was found to have additive effects for improving the short-term CS score.²¹ This study, 88.9% of patients getting intravenous Magnesium Sulfate showed efficacy of treatment as compared to 68.5% cases of efficacy in patients getting placebo treatment along with the conventional treatment in the management of acute bronchiolitis. For wider applicability larger studies are recommended to assess the effectiveness of intravenous Magnesium Sulfate in the management of acute bronchiolitis in general population.²²

LIMITATION OF STUDY

Our study was limited by a relatively smaller study population of 108 patients from a particular socioeconomic background.

CONCLUSION

Intravenous Magnesium Sulfate along with the conventional treatment is more effective from a clinical point of view than the conventional treatment alone in the management of acute bronchiolitis. However, larger studies are recommended to assess the effectiveness of intravenous Magnesium Sulfate in the management of acute bronchiolitis in general population.

Conflict of Interest: None.

Authors' Contribution

AA: Concept, design, data collection, analysis/interpretation of data, discussion, FI: Analysis/interpretation of data, discussion, HU: Analysis/interpretation of data, discussion, manuscript writing, SA & NT: Data collection.

REFERENCES

1. St Geme JW, Blum NJ, Shah SS, Tasker RC, Wilson KM. Nelson textbook of pediatrics. 2020, [Internet] Available at: <https://www.uselsevierhealth.com/nelson-textbook-of-pediatrics-2-volume-set-9780323529501.html>

2. Papadopoulos NG, Moustaki M, Tsoia M, Bossios A, Astra E, Prezerakou A, et al. Association of rhinovirus infection with increased disease severity in acute bronchiolitis. *Am J Respir Crit Care Med* 2002; 165(9): 1285-1289.
3. Florin TA, Plint AC, Zorc JJ. Viral bronchiolitis. *Lancet* 2017; 389(10065): 211-224.
4. Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980-1996. *JAMA* 1999; 282(15): 1440-1446.
5. Bhandary R, Bolor R. Detection of respiratory syncytial virus using direct fluorescent antibody assay in paediatric patients with acute respiratory tract infection. *J Clin Diagn Res* 2016; 10(6): DC10.
6. Adhikari S, Thapa P, Rao K, Bk G. Comparison of initial response of nebulized salbutamol and adrenaline in infants and young children admitted with acute bronchiolitis. *Kathmandu Univ Med J.* 2016; 53(1): 31-35.
7. Angoulvant F, Bellêtre X, Milcent K, Teglas JP, Claudet I, Le Guen CG. Effect of nebulized hypertonic saline treatment in emergency departments on the hospitalization rate for acute bronchiolitis: a randomized clinical trial. *JAMA Pediatr* 2017; 171(8): e171333.
8. Alansari K, Sayyed R, Davidson BL, Al Jawala S, Ghadier M. IV Magnesium Sulfate for bronchiolitis: a randomized trial. *Chest* 2017; 152(1): 113-119.
9. Ciarallo L, Brousseau D, Reinert S. Higher-dose intravenous magnesium therapy for children with moderate to severe acute asthma. *Arch Pediatr Adolesc Med* 2000; 154(10): 979-983.
10. Pruikkonen H, Tapiainen T, Kallio M, Dunder T, Pokka T. Intravenous magnesium sulfate for acute wheezing in young children: a randomised double-blind trial. *Eur Respir J* 2018; 51(2): 1701579.
11. Modaresi MR, Faghini J, Kelishadi R, Reisi M, Mirlohi S, Pajhang F, et al. Nebulized magnesium sulfate in acute bronchiolitis: a randomized controlled trial. *Ind J Pediatr* 2015; 82(9): 794-798.
12. Wang EE, Milner RA, Navas L. Observer agreement for respiratory signs and oximetry in infants hospitalized with lower respiratory infections. *Am J Respir Crit Care Med* 1992; 145(1): 106-109.
13. Lieberthal AS, Bauchner H, Hall CB, Johnson DW, Kotagal U, Light MJ, et al. Diagnosis and management of bronchiolitis. *Pediatr* 2006; 118(4): 1774-1793.
14. Smith DK, Seales SM, Budzik C. Respiratory syncytial virus bronchiolitis in children. *Am Fam Phys* 2017; 95(2): 94-99.
15. Ghazaly M, Nadel S. Overview of prevention and management of acute bronchiolitis due to respiratory syncytial virus. *Expert Rev Anti Infect Ther* 2018; 16(12): 913-928.
16. Kellner JD, Ohlsson A, Gadomski AM, Wang EE. Efficacy of bronchodilator therapy in bronchiolitis: a meta-analysis. *Arch Pediatr Adolesc Med* 1996; 150(11): 1166-1172.
17. Zhang L, Mendoza-Sassi RA, Wainwright C, Klassen TP. Nebulised hypertonic saline solution for acute bronchiolitis in infants. *Cochrane Database Syst Rev* 2017; 12(12): CD006458.
18. Cavaye D, Roberts DP, Saravanos GL, Hsu ZY, Miyajima R, Randall LE. Evaluation of national guidelines for bronchiolitis: AGREements and controversies. *J Paediatr Child Health* 2019; 55(1): 25-31.
19. Silverman RA, Osborn H, Runge J, Gallagher EJ, Chiang W, Feldman J. IV Magnesium Sulfate in the treatment of acute severe asthma: a multicenter randomized controlled trial. *Chest* 2002; 122(2): 489-497.
20. Hervas D, Reina J, Yañez A, Del Valle J, Figuerola J, Hervas J. Epidemiology of hospitalization for acute bronchiolitis in children: differences between RSV and non-RSV bronchiolitis. *Eur J Clin Microbiol Infect Dis* 2012; 31(8): 1975-1981.
21. Kose M, Ozturk MA, Poyrazoğlu H, Elmas T, Ekinçi D, Tubas F, et al. The efficacy of nebulized salbutamol, magnesium sulfate, and salbutamol/Magnesium Sulfate combination in moderate bronchiolitis. *Eur J Pediatr* 2014; 173(9): 1157-1160.
22. Zeilstra D, Younes JA, Brummer RJ, Kleerebezem M. Perspective: fundamental limitations of the randomized controlled trial method in nutritional research: the example of probiotics. *Adv Nutr* 2018; 9(5): 561-571.