Research Article

Intravenous Magnesium Sulphate: An Effective Therapy for Acute Severe Attack of Bronchial Asthma

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Abstract | Asthma is a global public health problem of 21st century and occurs due to complex interaction between genetic, behavioral and environmental factors. There are many drugs available for asthma and magnesium sulphate is given intravenously as an important adjunct therapy during the acute severe attack of asthma

Objective: This study was panned to determine the effect of intravenous $MgSO_4$ on pulmonary function test in acute severe attack of asthma.

Methodology: A double blind placebo control study was conduced on about 132 asthmatics, which were aged between 18-60 years at Mayo Hospital Emergency with FEV_1 ≤ 30% of the predicted value. Spirometry of all asthmatics (study and placebo groups) in the emergency department was performed by Spirolab III. Detailed history, general physical and systemic examination was conducted and all parameters were recorded. Modified Borg scale was used to determine the grade of dyspnea from 0-10. A total of 2ml of venous blood was taken to determine the serum magnesium levels. All patients were given Salbutamol inhalation and intravenous (I/V) Hydrocortisone. The study group was given 2gm of $MgS0_4$ intravenously in 20 minutes in a burette and Placebo group was given placebo (0.9% normal saline). Salbutamol inhalation was given at regular intervals and Spirometry was performed to determine lung functions.

Results: The two groups (study group and placebo-treated group) were compared for FEV_1, FEV_1% predicted, PEFR and PEFR % predicted. There was 1.06 L increase in FEV_1 in study group compared to 0.8 L in placebo group ($p<0.05$). The mean FEV_1 in the study group was 47.75 % predicted as compared to 43.52% predicted in the placebo group. Similarly, PEFR also improved to 59.87% predicted in study group as compared to 48.7% predicted in the placebo treated patient ($p= < 0.01$).

Conclusion: Intravenous $MgSO_4$ causes improvement in lung functions during asthmatic attack.

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Introduction

Bronchial asthma is chronic inflammatory conditions of respiratory tract, which inflames and narrows the airway passages. It is associated with recurrent attacks of wheezing and cough, which may vary from person to person [(1)]. National Heart, Lung and Blood Institute (NHLBI) states "Bronchial asthma is

a chronic inflammatory condition of the air passages in which a number of cells play an important role, especially eosinophils, neutrophils, T-lymphocytes, macrophages, mast cells and epithelial cells" [2].
There is a persistent increase in asthma patients among children around the world in last decade [3]. According to the Center for Disease Control and Prevention (CDC), 9.5% of children and 8.2% adults had asthma in 2011 in the United States [4].

According to Global Initiative for Asthma (GINA), 250,000 patients succumbed due to asthma every year throughout the world [5]. In Singapore, about 140,000 peoples are the sufferers of the disease and death toll is 100 per annum [6]. The prevalence of asthma in Pakistan and central Asia is 4-5% [7].

The interaction between environmental and genetic components plays an important role in the pathogenesis of asthma [8,9,10]. It has been observed that genetics of the person play a big role in development of asthma however it is effective only when environmental factors are helpful otherwise risk of disease is minimized [11].

The gold standard treatment is Salbutamol inhalation along with oxygen therapy aided by anticholinergic drugs and I/V steroids. It was observed that in some asthmatics, the effects of standard drugs were not up to the mark. In such patients, there was a need of different agents and in this search $MgSO_4$ attracted the attention of researchers and practitioners. Magnesium (Mg^{++}) is an important intracellular inorganic element and paly important roles in the body. The serum concentrations of Mg^{++}may not precisely reflect the total body Mg^{++}[12]. It is involved in a number of metabolic reactions in the body by acting as a cofactor [13].

Materials and Methods

A total of 132 asthmatic subjects between 18-60 ages with $FEV_1 \leq 30\%$ predicted presented with acute attack in the Emergency Department (ED) of Mayo Hospital, Lahore. The study was approved by the Advance Study and Research Board of King Edward Medical University Lahore along with ethical permission and provision of funds. Patients with emphysema, chronic bronchitis, congestive cardiac failure chronic renal insufficiency, and pneumonia were excluded from the study.

It was a placebo-controlled, randomized, double blinded study.

Written informed consent to participate in the study was obtained from each subject. Patients with the $FEV_1 \leq 30\%$ predicted by Spirometry in the ED by Spirolab III were selected for study. A careful history of disease was taken covering present and past history along with family history of the illness. Complete general physical examination (GPE) was done, body weight (BW), height, body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressures were determined according to the standard procedures [14]. Intensity and severity of breathlessness was measured by modified Borg scale [15].

The study population was divided into two groups:

- Study group given I/V $MgSO_4$ (n=66)
- Control group given placebo (n=66)

After spirometry, both groups received Salbutamol (2.5 mg) inhalation through nebulizer and followed by intravenous injection of 250 mg of IV hydrocortisone. The study group was given 2 gm of $MgSO_4$ in 50 ml of 0.9% normal saline solution I/V slowly over 20 min and a placebo (50ml of 0.9% normal saline) was given to control group. This time was taken as 0 min. Spirometry was performed on emergency department arrival, at 30min and 180 min after giving I/V $MgSO_4$ or placebo to check the response in two groups.

A total of 0.5 mL of 0.5% salbutamol (2.5 mg) via wet nebulizer with 100% oxygen inhalation was given again after 30 min. Clinical assessment of respiratory system was made and spirometry was performed prior to each treatment and again at 180 min and the results were recorded. The aim of spirometry was to determine the effects $MgSO_4$ or placebo in the two groups. Any complaint of the patients was noted.

After treatment of 180 min, hospitalization or discharge the patients depended upon their condition. The criterion of hospitalization was if the patient's $FEV_1 < 50\%$ predicted, respiratory rate ≥ 22 breaths/min and there was no positive change in the condition of patient without any improvement in shortness of breath or wheezing.

The data collected was analyzed by SPSS version 17.0

(SPSS, Inc. Chicago, IL, USA). All the variables, which were quantitative, expressed as mean ± standard deviation (SD). General Linear Model test, one way Anova to compare different variables and finally Student's t-test was applied to observe the differences between study and control groups. A p-value of < 0.05 was taken as significant statistically.

Results

A total of 132 patients were screened during this study. In the study group (I/V $MgSO_4$) out of 66 patients, five were unable to complete the study protocol up to 180min. In the control group, 66 patients were included and three among those were unable to complete the protocol.

Mean respiratory rate was 22/min on arrival in ED in both groups. There was no significant difference (p>0.05, Table 1) in the respiratory rate between magnesium (study) group and placebo (control) group on arrival in ED (0 min). There was no significant decrease in respiratory rate after 30min in both groups. After 180 min, there was significant (p<0.05) decrease in the respiratory rate in the study group as compared to control group (Table 2 and 3). When magnesium group was compared at 0 min and 180 min, there was significant decrease in the respiratory rate 180 min after I/V Mg SO_4 was given.

Borg scale was 7.5 on arrival in ED in both groups. There was no significant difference in the Borg scale at 0 min in ED arrival between study and control group (P>0.05, Table 3). There was significant decrease (p<0.05) in Borg scale after 30min and 180 min of treatment in magnesium treated group as compared to placebo (Table 2 and 3). There was significant decrease in the Borg scale at 0 min in ED and 180 min after magnesium treatment.

There was no statistically significant (p 0.54) difference in the FEV_1 of both study and control groups at 0 min in ED arrival (Table 3 and 4). There was non-significant increase in FEV_1 in magnesium treated group as compared to placebo after 30 min (p 0.72, Table 3). There was significant (p 0.004) improvement in FEV_1 in magnesium treated group compared to placebo group as after 180 min (Table 4). There was 1.06 L increase in FEV_1 in magnesium treated group after 180 min compared to 0.8 L in placebo group.

There was no significant (p>0.05) difference in the FEV_1 % predicted of both study and control group at 0 min in ED arrival (Table 3 and 4). There was non-

Table 1: *Clinical Parameters in two groups on ED arrival (0min), 30 min and 180 min after treatment*

Variables	0 min		30 min		180min		
	Placebo	Magnesium	Placebo	Magnesium	Placebo	Magnesium	P value
Respiratory rate/min	22.06±2.29	22.33±2.38	21.43±2.84	21.77±2.38	20.9±2.25	17.85±2.69*	<0.001*
Pulse rate/min	95.46±4.9	95.5±5.23	98.95±4.39	98.18±3.08	99.9±3.59	99.82±2.86	0.821
Systolic BP (mm Hg)	137.6±7.44	137±5.29	136.9±6.9	136.01±4.4	136.14±0.5	137±3.5	0.74
Diastolic BP (mm Hg)	85.05±3.33	84.74±3.44	84.90±3.93	85.03±4.21	84.43±4.38	83.93±5.09	0.563
Borg scale	7.60±0.79	7.59±0.99	5.65±0.73	5.20±0.92*	3.45±0.90	2.53±0.45*	<0.001*

Data are presented as mean ± SD. Placebo and magnesium groups were compared at 0 min, 30 min and 180 minby't' test. P value <0.05 was statistically significant.*

Table 2: *Clinical Parameters in two groups on ED arrival (0 min) and 180 min after treatment*

Variables	0 min			180min		
	Placebo	Magnesium	P value	Placebo	Magnesium	P value
Respiratory rate/min	22.06±2.29	22.33±2.38	0.53	20.9±2.25	17.85±2.69	<0.001*
Pulse rate/min	95.46±4.9	95.5±5.23	0.887	99.9±3.59	99.82±2.86	0.821
Systolic BP (mm Hg)	137.6±7.44	137±5.29	0.955	136.14±0.5	137±3.5	0.74
Diastolic BP (mm Hg)	85.05±3.33	84.74±3.44	0.611	84.43±4.38	83.93±5.09	0.563
Borg scale	7.60±0.79	7.59±0.99	0.975	3.45±0.90	2.53±0.45	<0.001*

Data are presented as mean ± SD. Placebo and magnesium groups were compared at 0 min and 180 min by 't' test. P value <0.05 was considered statistically significant.*

significant increase in FEV_1 % predicted in study group as compared to placebo after 30 min (p 0.72, Table 3). The mean FEV_1 at 180 min in the study group was 47.75 % predicted compared to 43.52% of predicted as in the placebo-treated group, which was statistically (p 0.004) significant (Table 4). There was 26.03% increase in FEV_1 % predicted in magnesium treated group (from 21.72 % to 47.75%) after 180 min compared to 22 % (from 21.50% to 43.5%)in placebo group.

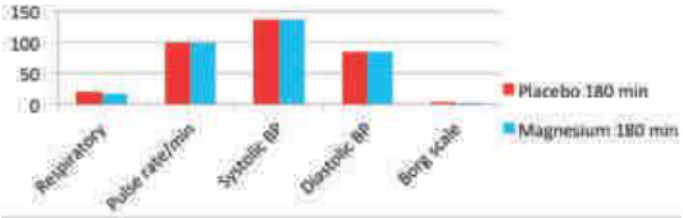

Figure 1: *Clinical parameters of Placebo and control groups 180 min after treatment protocol*

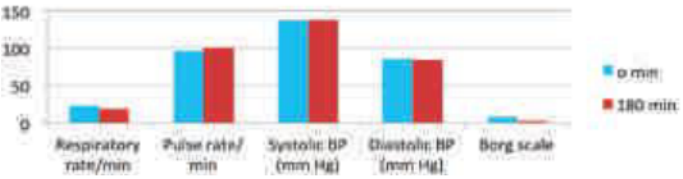

Figure 2: *Clinical parameters of magnesium treated group on ed arrival (0min) and 180 min after treatment*

PEFR of both study and control group at 0 min in ED arrival was not significantly (p 0.58) different (Table 3 and 4). There was significant improvement in PEFR (160L/min) in magnesium treated group as compared to placebo (157L/min) at 30 min (p<0.05, Table 3 and 4). PEFR showed significant improvement in magnesium treated group (263L/min) as compared to placebo (227L/min) group at180 min (p 0.004), Table 4). There was improvement in PEFR of 124 L/min (from 139 L/min to 263L/min) after180 min in the magnesium treated group compared to the placebo group in which mean improvement in PEFR was 87L/min (from 140L/min to 227L/min)

PEFR % predicted of both study and control group at 0 min in ED arrival was not significantly (p 0.73) different (Table 3 and 4). There was significant increase in PEFR % predicted in magnesium treated group as compared to placebo at 30 min (p<0.05, Table 3 and 4). There was significant improvement in PEFR % predicted of magnesium treated group as compared to placebo group at 180 min (p 0.001, Table 4 and Figure 3).

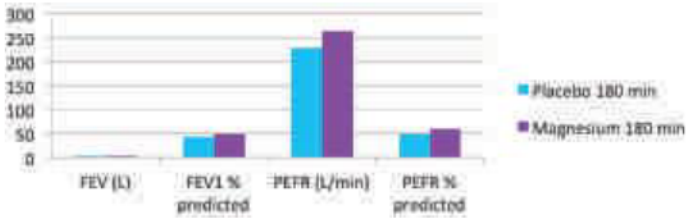

Figure 3: *Pulmonary Function Test of Placebo and magnesium treated groups 180 min after treatment protocol.*

Table 3: *Pulmonary Function Test in two groups on ED arrival (0min), 30 min and 180 min after treatment.*

Variables	0 min		30 min		180min	
	Placebo	Magnesium	Placebo	Magnesium	Placebo	Magnesium
FEV_1 (L)	0.78±0.08	0.77±0.06	0.98±0.15	1.01±0.19	1.58±0.55	1.83±0.38*
FEV_1% predicted	21.50±3.97	21.72±2.80	29.43±4.15	29.98±4.19	43.5±4.2	47.75±3.20*
PEFR (L/min)	140±6.07	139±4.36	157±6.22	160±12.11*	227±24.4	263±32.23*
PEFR % predicted	30.64±2.34	30.49±2.80	35.94±2.69	37.49±4.08*	48.78±8.01	59.87±7.45*

Data are presented as mean ± SD. Placebo and magnesium groups were compared at 30 min and 180 min by 't' test. P value <0.05 was statistically significant.*

Table 4: *Pulmonary Function Test in two groups on ED arrival (0min) and 180 min after treatment.*

Variables	0 min			180 min		
	Placebo	Magnesium	p- value	Placebo	Magnesium	P-value
FEV_1(L)	0.78±0.08	0.77±0.06	0.54	1.58±0.55	1.83±0.38*	0.004*
FEV_1 % predicted	21.50±3.97	21.72±2.80	0.72	43.5±4.2	47.75±3.20*	<0.001*
PEFR (L/min)	140±6.07	139±4.36	0.58	227±24.4	263±32.23*	<0.001*
PEFR % predicted	30.64±2.34	30.49±2.80	0.73	48.78±8.01	59.87±7.45*	<0.001

Data are presented as mean ± SD. Placebo and magnesium groups were compared at 0 min and 180 min by 't' test. P value <0.05 was considered statistically significant.*

There was improvement in PEFR % predicted of 29.38% (from 30.49% to 59.87%) after180 min in the magnesium treated group compared to the placebo group in which mean improvement in PEFR% predicted was 18.14% (from 30.64% to 48.78%). When GLM model was applied, it further confirmed that independent of age and sex,the effect of I/V magnesium on pulmonary function (FEV_1, FEV % predicted, PEFR, PEFR% predicted) and compared to placebo was significantly greater (p 0.004 ,0.001 .0.001 & 0.001, respectively) in patients at 180 min of the study protocol.

The overall hospital admission rate at 180 min was not significantly different in patients receiving magnesium (18 of 61 patients) or placebo (20 of 63 patients) group.

Discussion

In the present study, a total of 132 adult subjects with acute severe asthma were analyzed to determine the role of I/V Mg SO_4 when given as an adjunct to standard asthma treatment on pulmonary function test. There was no statistically significant difference in the age, body weight, height, BMI, respiratory rate, pulse rate, SBP, DBP and Borg dyspnea scale on ED arrival between the magnesium treated group and placebo group in the present study.

It was found in the present study, that 2 g of IV $MgSO_4$ when given as an adjunct to standard asthma treatment significantly improves pulmonary functions in adults. The results of previous studies investigating the role of IV $MgSO_4$ in severe asthma have reported controversial results; data is available suggesting the use of magnesium in treating acute severe asthma (16.17). It has been reported in many studies to be useful in children [18,19,20], whereas available data in adults have revealed controversial results [21,22,23,24]. There was no decrease in SBP and DBP in both groups in the present study; however respiratory rate and Borg dyspnea scale showed significant decrease in the present study in magnesium treated group at 180 min. There was increase in the pulse rate at 180 min as compared to the time in ED arrival in both groups, the increase in pulse rate might be due to repeated salbutamol nebulization at 0 min, 30min, 60 min, and 120 min in the present study.

A previous study has reported that when 2gm of I/V $MgSO_4$ was given along with salbutamol nebulization, there was no significant improvement in PEFR and hospital admission rates in patients with acute asthma[22]. Later on in another study, Tiffany et al [21] have reported that there was no significant improvement in PEFR and FEV_1 when I/V $MgSO_4$ was given in moderate to severe asthma, but surprisingly when given in severely ill patients there was a remarkable improvement in lung functions as compared to placebo.

The current study revealed significant improvement in PEFR after I/V $MgSO_4$ was given along with salbutamol but no significant improvement was observed in placebo group. Similar results have been reported in a previous study, when 1.2 g of magnesium or placebo was given in patients with moderate-to-severe airway obstruction, significant improvement occurred in PEFR. Whereas Aggrawal et al [23] have reported significant rise in PEFR in both groups i.e. magnesium treated group and placebo group with no significant difference in PEFR between these groups when magnesium was given along with conventional asthma treatment Another study reported that when 1.2 gm I/V $MgSO_4$ was given it resulted in no improvement in % predicted PEF at 60 min and decrease in hospital admission rates in acute asthma [23]. These differences in the results might be due to different doses of $MgSO_4$ used in different studies.

In the present study, there was 1.06 L increase (from 0.78 to 1.83) in FEV_1 in magnesium treated group at 180 min as compared to 0.8 L (from 0.7 to 1.58) in placebo group. Overall, patients receiving IV $MgSO_4$ had a final FEV_1 of 47% predicted (from 22% to 47.5%) compared to 43.5% (from 21.50% to 43.5%) predicted for patients receiving placebo. In the present study there was 26.03% increase in FEV_1 % predicted in magnesium treated group at 180 min as compared to 22 % in placebo group (mean difference= 4.03%). Likewise, Singh et al [24] reported increase in percentage of FEV_1 predicted (40.7+/-9.2% in magnesium groups 34.77+7.3% in placebo group) at 120 minutes in adults (mean difference= 6.07%).

The modified Borg scale for rating dyspnea decreased from 7.59±0.99 to 2.53±0.45 in the magnesium group after 180 min in the present study whereas the peak flow increased significantly. This finding indicated that there was a significant correlation between the change in modified Borg scale for rating dyspnea

scores and the change in PEFR in the magnesium treated group. There was a significant improvement in PEFR from 139 + 4.36 to 263+ 32.23 a previous study has reported similar results with significant correlation between modified Borg scale for rating dyspnea and PEFR [25].

The finding of the present study that IV $MgSO_4$ did not decrease hospital admission rates is in accordance with the previous report by Silverman et al [26], whereas Singh et al [24] have reported that IV $MgSO_4$ decreased the hospital admission rates.

The present study reported definite role of I/V $MgSO_4$ in asthmatic patients whereas Green and Rothrock have reported no improvement in the patients who received 2gm of I/V $MgSO_4$ as adjunct in addition to conventional treatment. There was no decrease in SBP and DBP in both groups in the present study; however respiratory rate and Borg dyspnea scale showed significant decrease in the present study in magnesium treated group at 180 min. There was increase in the pulse rate at 180 min as compared to the time in ED arrival in both groups, the increase in pulse rate might be due to repeated salbutamol nebulization at 0 min, 30min, and 180 min, in the present study.

A previous study has reported that when 2gm of I/V $MgSO_4$ was given along with salbutamol nebulization, there was no significant improvement in PEFR and hospital admission rates in patients with acute asthma. Later on in another study, Tiffany et al [21] reported that there was no significant improvement in PEFR and FEV_1 when I/V $MgSO_4$ was given in moderate to severe asthma, but surprisingly when given in severely ill patients there was a remarkable improvement in lung functions as compared to placebo.

The beneficial effects of I/V $MgSo_4$ observed during attack of asthma proves the importance of the adjunct and effects are mediated by inhibition of Ca entry in the smooth muscles of bronchi. As far as level of $MgSO_4$ in serum is concerned it does not match with true level inside the cells. Sometimes serum level is normal but still deficiency at cellular level. It is not confirmed that effects of $MgSO_4$ are either due to replenish of deficiency or due to its known mechanisms of actions. In short it is proved by the study that there is a definite and confirmed role of $MgSO_4$ in the treatment of asthma and it shows it's effects through the improvement in lung functions.

Conclusion

Upon studying variables specially the pulmonary function test, a tremendous improvement in the study group as compared to the control was observed. Moreover the qualitative parameters such as breathlessness improved more in study group as compared to control group. On this basis, it can be concluded that use of intravenous $MgSO_4$ along with conventional treatment may prove beneficial to the asthmatics.

Reference

1. World Health Organization: Asthma , 2013. Available from http://www.who.int/mediacentre/factsheets [Accessed in August, 2013].
2. National, Heart, Lung and Blood Institute. Definition, Pathophysiology and Pathogenesis of Asthma and Natural History of Asthma. 2007. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm
3. Ding G, Ji R, Bao Y. Risk and Protective Factors for the Development of Childhood Asthma. Paediatr Respir Rev. 2014; 1. pii: S1526-0542(14)00082-7.
4. Center for Disease Control and Prevention (CDC); 2011, Retrieved from www.cdc.gov/asthma/asthmadata [Accessed on June, 2012]
5. Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma (GINA), 2006. Available from June, 2013].
6. Chew FT, Goh DY and Lee BW. The economic cost of asthma in Singapore. Aust NZ J Med 1999;29(2): 228-33. https://doi.org/10.1111/j.1445-5994.1999.tb00688.x
7. Masoli M, Fabian D, Holt S, Beasley R.Global Initiative for Asthma (GINA) Program.The global burden of asthma: Executive summary of the GINA Dissemination Committee report. Allergy 2004;59(5): 469-78. https://doi.org/10.1111/j.1398-9995.2004.00526.x
8. Martinez FD. Genes, environments, development and asthma: A reappraisal. Eur Respir J 2007; 29(1): 179-84. https://doi.org/10.1183/09031936.00087906
9. Wennergren G, Ekerljung L, Alm B, Bjerg A, Lötvall J, Lundbäck B. Alarmingly high prevalence of smoking and symptoms of bronchitis in young women in Sweden: A population-based questionnaire study. Prim Care Respir J. 2013;22(2):214-20. https://doi.org/10.4104/pcrj.2013.00043

10. Holgate ST. Genetic and environmental interaction in allergy and asthma. J Allergy Clin Immunol 1999; 104(6): 1139–46. https://doi.org/10.1016/S0091-6749(99)70005-9
11. Guerrero-Romero F, Rodríguez-Morán M. Hypomagnesemia is linked to low serum HDL-cholesterol irrespective of serum glucose values. J Diabetes Complications 2000; 14(5):272-276. https://doi.org/10.1016/S1056-8727(00)00127-6
12. Elin RJ. Magnesium: the fifth but forgotten electrolyte. Am J Clin Patho 1994; 102(5):616-22. https://doi.org/10.1093/ajcp/102.5.616
13. World Health Organization. WHO 1989.Measuring obesity classification and description of anthropometric data. Report on a WHO consultation of the epidemiology of obesity. Warsaw 21-23 Oct 1987 Copenhagen.
14. Kendrick KR, Baxi SC, Smith RM. Usefulness of the modified 0-10 Borg scale in assessing the degree of dyspnea in patients with COPD and asthma. J EmergNurs, 2000; 26(3):216-22. https://doi.org/10.1016/S0099-1767(00)90093-X https://doi.org/10.1067/men.2000.107012
15. Rolla G, Bucca C, Caria E, Arossa W, Bugiani M, Cesano L, Caropreso A. Acute effect of intravenous magnesium sulfate on airway obstruction of asthmatic patients.Ann Allergy 1988; 61(5): 388-91.
16. Noppen M, Vanmaele L, Impens N, Schandevyl W. Bronchodilating effect of intravenous magnesium sulfate in acute severe bronchial asthma. Chest, 1990; 97(2): 373-6. https://doi.org/10.1378/chest.97.2.373
17. Ciarallo L, Sauer A, Shannon MW. Intravenous magnesium therapy for moderate to severe pediatric asthma: results of a randomized, placebo-controlled trial. J Pediatr 1996; 129: 809-814. https://doi.org/10.1016/S0022-3476(96)70023-9
18. Shan Z, RongY, Yang W, Wang D, Yao P, Xie J, LiuL. Intravenous and nebulized magnesium sulfate for treating acute asthma in adults and children: A systematic review and meta-analysis. Respir Med 2013; 107(3):321-30. https://doi.org/10.1016/j.rmed.2012.12.001
19. Bradshaw TA, Matusiewicz SP, Crompton GK, Innes JA, Greening AP. Intravenous magnesium sulphate provides no additive benefit to standard management in acute asthma. Respir Med 2008; 102(1):143-9. https://doi.org/10.1016/j.rmed.2007.07.022
20. Tiffany BR, Berk WA, Todd IK, White SR. Magnesium bolus or infusion fails to improve expiratory flow in acute asthma exacerbations. Chest 1993; 104(3): 831-4. https://doi.org/10.1378/chest.104.3.831
21. Devi PR, Kumar L, Singhi SC, Prasad R, Singh M.Intravenous magnesium sulfate in acute severe asthma not responding to conventional therapy. Indian Pediatr 1997; 34(5):389-97.
22. Aggarwal P, SharadS, Handa R, DwiwediSN,Irshad M. Comparison of nebulised magnesium sulphate and salbutamol combined with salbutamol alone in the treatment of acute bronchial asthma: a randomised study. Emerg Med J 2006;23(5): 358-62. https://doi.org/10.1136/emj.2005.026203
23. Singh AK, Gaur S, Kumar R. A randomized controlled trial of intravenous magnesium sulphate as an adjunct to standard therapy in acute severe asthma. Iran J Allergy AsthmaImmunol, 2008; 7(4): 221-9
24. Silverman RA, Osborn H, Runge J, Gallagher EJ, Chiang W, Feldman J, Gaeta T, Freeman K, Levin B, Mancherje N, ScharfS. Acute Asthma/Magnesium Study Group. IV magnesium sulfate in the treatment of acute severe asthma: a multicenter randomized controlled trial. Chest 2002, 122(2): 489-97.
25. Green SM, Rothrock SG. Intravenous magnesium for acute asthma: Failure to decrease emergency treatment duration or need for hospitalization.Ann Emerg Med 1992; 21(3): 260-5.
26. Reinhart RA. Magnesiummetabolism: A review with special reference to the relationship between intracellular content and serum levels. Arch Intern Med 1998; 148(11): 2415.