**Hemodynamic Effects of Magnesium Sulphate therapy in critically ill infants and children with wheezy chest**

**Abstract**

Intravenous and inhaled magnesium sulphate (Mgso4) had been recently used as an adjuvant therapy in cases suffering from wheezy chest. **Objective**: We aimed to determine possible change in the hemodynamic state in cases received Intravenous or inhaled Mgso4 in comparison to cases received standard treatment in critically ill infants and children with wheezy chest. **Methods:** A randomized controlled trial comprised 81 patients suffering from wheezy chest divided into 3 groups. In addition to bronchodilators and systemic steroids, MgSo4 was given by inhalation in group A, intravenously in group B, and group C didn't receive MgSo4. Hemodynamic state was determined by assessment of blood pressure, heart rate, capillary refill time and the need of shock therapy or inotropic support just before and 24 hours after receiving treatment in 3 groups. **Results:** There was no significant difference in the hemodynamic state at the studied groups before and after treatment. Means of blood pressure were 102.2/63.2, 105.1/64.8 before and after inhaled MgSo4; respectively. Means of blood pressure were 105.5/64.2, 104.1/64.9 before and after Intravenous MgSo4; respectively. Means of blood pressure were 107.4/62.8, 104.4/62.1before and after standard treatment; respectively. There was statistically insignificantreduction of the means of the heart rate in group A and group B after treatment rather than group C. There was no associated prolongation in capillary refill time and/or the need for inotropic support or shock therapy after treatment in the studied groups. **Conclusion:** Mgso4 is a safe adjuvant therapy and not associated with significant alteration in the hemodynamic state in critically ill infants and children with wheezy chest.

**Key Words:** 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 wheezing, increasing to 40% at 3 years and more than 50% at 6 years. ***(1)***

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. ***(3)*** The use of IV Mgso4 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 beta2 receptors**. *(3) (4***)

However hypotension and circulatory collapse were from the estimated possible side effects of IV administration of Mgso4. Possible mechanism of blood pressure lowering is by acting like a natural calcium channel blocker. Also Magnesium competes with sodium for binding sites on vascular smooth muscle cells, increases prostaglandin E, binds to potassium in a cooperative manner, induces endothelial-dependent vasodilatation, decreases intracellular calcium and sodium, and reduce blood pressure (BP).***(5)***

So we aimed to assess the hemodynamic state of critically ill infants with wheezy chest who received inhaled or IV Mgso4 versus standard treatment.

**Patients and methods**

The present study is a prospective cohort study conducted at PICU of the Cairo University, Children Hospital, between August 2013 and August 2015.The study included 81 patients were suffering from wheezy chest with various diagnoses.

The included cases were critically ill infants and children between 2 months and 15 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 Mgso4 or whom Mso4 is contraindicated. Eighty one eligible patients were subjected to clinical assessment on admission including full history, examination and blood pressure assessment. The patients were divided into three groups using sealed envelopes for randomized allocation, Group A: Inhaled Mgso4**,** Group B: IV Mgso4**,** Group C: control group.

The three groups received respiratory support according to the patients’ condition. Nebulized drugs were given by Atom ultrasonic nebulizer 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. *(****6)*** IV hydrocortisone in a dose 4mg/kg/dose every 6 hours ***(7)*** and IV bronchodilators as salbutamol (5 μg/kg/dose) every 6 hours.

In severe cases (resistant cases or whom developed respiratory failure); IV methyl prednisolone in a dose of 10mg/kg once can be used. ***(8)***

In addition to the above, **Group A** received inhaled Mgso4 in a dose of 100mg MgSO4 every 6 hours for 24 hours ***(9)***, **Group B** received IV Mgso4 at a dose of 25mg/kg every 6 hours for 24 hours ***(9)*** and **Group C (**control group) only received the standard treatment.

In all groups follow up within 24 hours after starting treatment by assessment of the clinical state including blood pressure, Heart rate, capillary refill time and the need for addition of shock therapy or inotropic drugs after treatment.

The protocol was approved by Paediatric department at children Hospital of Cairo University and informed parental consents were taken and the data were documented on Excel spreadsheet.

**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**

We assessed the hemodynamic state before and after treatment in patients received MgSo4 (inhaled or IV route) versus standard treatment in critically ill infants and children with wheezy chest with median age 11 months, mean weight 9.3kg and median SOFA score 1.

Eighty one patients were enrolled in our study, their age ranged from 2 months to 12 years, 52% male, and 48% female. Group A (25 patients) received inhaled Mgso4, Group B (29 patients) received IV MgSo4 and Group C (27 patients) received placebo.

**Table 1: Distribution of included patients and their percent**

|  |  |  |
| --- | --- | --- |
| **Group** | **Frequency** | **Percent** |
| **A** | 25 | 30.9 |
| **B** | 29 | 35.8 |
| **C** | 27 | 33.3 |
| **Total** | 81 | 100.0 |

Group A: inhaled MgSo4, group B: IV MgSo4, group C: control

**Table 2: Characteristics of studied groups**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Groups** | **A** | | **B** | | **C** | |
| **Median (IQ)** | | | | | |
| **Age (months)** | 18(6-36) | | 12(7-29) | | 9(4-18) | |
| **Weight (Kg)** | **Mean** | **S.D.** | **Mean** | **S.D.** | **Mean** | **S.D.** |
| 8.75 | 4.306 | 11.79 | 9.722 | 7.07 | 3.168 |
| **p value** | **A/B** | | **A/C** | | **B/C** | |
| **Age (months)** | 0.544 | | 0.058 | | 0.056 | |
| **Weight (Kg)** | 0.161 | | 0.121 | | **0.022** | |

Most of the cases presented with primary diagnosis of pneumonia 67.9 % followed by bronchiolitis 16.1 %, bronchial asthma 12.3 % and foreign body inhalation 2.5 %.

**Table 3: Blood pressure in 3 groups before and after treatment**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Groups** | **A** | | **B** | | **C** | | **p value** | | |
|  | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **A/B** | **A/C** | **B/C** |
| **SBP before** | 102.2 | 14.8 | 105.5 | 14.3 | 107.4 | 14.5 | 0.41 | 0.22 | 0.63 |
| **DBP before** | 63.2 | 11 | 64.2 | 15 | 62.8 | 8.1 | 0.78 | 0.88 | 0.67 |
| **MBP before** | 76.2 | 10.3 | 78 | 13.9 | 77.7 | 8.6 | 0.6 | 0.59 | 0.92 |
| **SBP after** | 105.1 | 18.7 | 104.1 | 12.9 | 104.4 | 14.6 | 0.81 | 0.89 | 0.92 |
| **DBP after** | 64.8 | 14.1 | 64.9 | 12.5 | 62.1 | 11.6 | 0.97 | 0.48 | 0.4 |
| **MBP after** | 78.2 | 14.6 | 78 | 10.8 | 76.2 | 10.8 | 0.94 | 0.59 | 0.56 |

SBP: systolic blood pressure, DBP: diastolic blood pressure, MBP: mean blood pressure, SD: standard deviation.

There was no significant difference in the blood pressure at the studied groups before and after treatment.

**Table 4: Heart rate before and after treatment**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Groups** | **A** | | **B** | | **C** | | **Total** | | **p value** | | |
| **HR** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **Mean** | **SD** | **A/B** | **A/C** | **B/C** |
| **Before** | 134.4 | 17.8 | 136.3 | 21.2 | 139.4 | 22.4 | 136.7 | 20.5 | 0.73 | 0.39 | 0.59 |
| **After** | 127.2 | 18.1 | 127 | 21.7 | 136.3 | 18.4 | 130.1 | 19.8 | 0.98 | 0.09 | 0.10 |

There was reduction of the mean heart rate in group A and group B after treatment rather than group C but this was statistically insignificant.

There was no prolongation in capillary refill and/or need for inotropic support or shock therapy after treatment in the studied groups.

**Discussion**

We studied the hemodynamic state in patients receiving MgSo4 (inhaled or IV route) versus standard treatment in critically ill infants and children with wheezy chest. Eighty one patients were enrolled in our study. There was no statistically significant change in blood pressure before and after administration of IV or inhaled Mgso4 in critically ill infants and children with wheezy chest.

The study by Kokotajlo and his colleagues showed that one patient experienced hypotension as an adverse drug reaction related to the rapid infusion of IV MgSo4, which resolved after decreasing the infusion rate. ***(10)***

In our study, MgSO4 was given very slowly IV, so we did not face this complication. Also the study by Sarhan and his colleagues showed mild transient drop in blood pressure in one patient after inhaled Mgso4. ***(11)*** Magnesium reduces BP more when administered as multiple minerals in a natural form and as a combination with potassium, and calcium than when given alone, which is not the condition in our cases. So we did not face significant decline in the blood pressure of our cases after Mg so4 administration.

There was lowering in the mean of heart rate in group B and group A after treatment rather than group C, although it was not significant. Also the study by Goodacre and his colleagues on adults showed insignificant decline of the main heart rate in both IV and inhaled MgSo4 (IV˃ inhaled) groups, rather than placebo and this was in accordance with our study. **(12)**

The study by Abdelnabi and his colleagues showed that there was a statistically significant reduction in the mean HR in the patients received inhaled MgSo4, if compared to the patients received nebulised salbutamol. These findings illustrate the fact that nebulised MgSo4 can be used safely without possible increase in the heart rate if compared with salbutamol. ***(13)***

**Conclusion:** There was no statistically significant change in the hemodynamic state before and after administration of IV or inhaled MgSO4 in critically ill infants and children with wheezy chest.

**الملخص العربى**

**متابعة حالة الدورة الدموية اثناء العلاج بسلفات المغنيسيوم في الرضع و الاطفال ذوى الحالات الحرجة المصابين بضيق في الشعب الهوائية**

**قد استخدمت مؤخرا سلفات المغنيسيوم عن طريق الوريد اوالاستنشاق كعلاج مساعد في الحالات التي تعاني من الصدر الصافر و ضيق في الشعب الهوائية. الهدف: هدفنا إلى تحديد التغيير المحتمل في حالة الدورة الدموية في الحالات التى تلقت سلفات الماغنيسيوم عن طريق الاستنشاق او الحقن الوريدى بالمقارنة مع الحالات التي تلقت العلاج القياسي في الرضع و الاطفال ذوى الحالات الحرجة المصابين بضيق في الشعب الهوائية. الطريقة: شملت التجربة العشوائية 81 مريضا يعانون من الصدر الصافر نتيجة ضيق في الشعب الهوائية و تم تقسيمهم إلى 3 مجموعات, بالإضافة إلى موسعات الشعب الهوائية وعقار الكورتيزون بالوريد و الاستنشاق ، تم اعطاء سلفات الماغنيسيوم عن طريق الاستنشاق في المجموعة (أ) ، عن طريق الوريد في المجموعة (ب) ، ومجموعة (ج) لم تتلق سلفات الماغنيسيوم. تم متابعة حالة الدورة الدموية عن طريق تقييم ضغط الدم ومعدل ضربات القلب، زمن اعادة ملء الشعيرات الدموية والحاجة إلى العلاج بالمحاليل نتيجة صدمة أو عقارت منشطة للقلب قبل وبعد 24 ساعة من تلقي العلاج في الثلاث مجموعات. النتائج: لم يكن هناك تغيير في حالة الدورة الدموية في المجموعات المدروسة قبل وبعد العلاج. وكان متوسط ضغط الدم 102.2 / 63.2، 105.1 / 64.8 قبل وبعد استنشاق سلفات المغنيسيوم على التوالي. وكان متوسط ضغط الدم 105.5 / 64.2، 104.1 / 64.9 قبل وبعد سلفات المغنيسيوم في الوريد. على التوالي. وكان متوسط ضغط الدم 107.4 / 62.8، 104.4 / 62.1 قبل وبعد العلاج القياسي على التوالي. و قد لوحظ انخفاض في معدل ضربات القلب في المجموعة (أ) و (ب) بعد العلاج بالمقارنة بالمجموعة (ج) ولكن ذلك الانخفاض لا يعتد به احصائيا . لم يكن هناك إطالة في زمن إعادة ملء الشعيرات الدموية و / أو الحاجة إلى العلاج بالمحاليل نتيجة صدمة أو عقارت منشطة للقلب بعد العلاج في الثلاث مجموعات. الخلاصة : سلفات الماغنيسيوم هو العلاج مساعد آمن و لا يصحبه تغير ملحوظ في حالة الدورة الدموية في الاطفال ذوى الحالات الحرجة المصابين بضيق في الشعب الهوائية**

**الكلمات الرئيسية: الرضع والأطفال ذوى الحالات الحرجة ، سلفات الماغنيسيوم بالاستنشاق ، سلفات الماغنيسيوم بالوريد ، ضيق الشعب الهوائية**

**References:**

1. Barclay L and Lie D. (2008). Diagnosis of Wheezing in Infants and Children. Retrieved 04/25/2008, from [http://www.medscape.org/view article/573491](http://www.medscape.org/view%20article/573491).
2. Brand P, Baraldi E, Bisgaard H et al. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. Eur Respir J. 2008;32:1096–1110.
3. Mahajan P, Haritos D, Rosenberg N and Thomas R. 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. 2004;27:21-25.
4. Blitz M, Blitz S, Hughes R, et al., Aerosolized magnesium sulfate for acute asthma: a systematic review. Chest. 2005;128:337–344.
5. Houston, M. (2011), the Role of Magnesium in Hypertension and Cardiovascular Disease. The Journal of Clinical Hypertension, 13: 843–847. doi:10.1111/j.1751-7176.2011.00538.x
6. Øymar K and Halverson T. Emergency presentation and management of acute severe asthma in children. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine. 2009;17:40.
7. Carroll W, Lenney W. Drug therapy in the management of acute asthma. Arch Dis Child - Education and practice edition. 2007;92(3), ep82-86.
8. Tschudy MM, Arcara KM. Eds. The Harriet Lane Handbook :A Manual for Pediatric House Officers. Philadelphia, PA: Mosby Elsevier; 2012.
9. Mohammed S, Goodacre S. Intravenous and nebulised magnesium sulphate for acute asthma: systematic review and meta-analyses. Emerg Med J. 2007;24:823-30.
10. Kokotajlo S, Degnan L, Meyers R, Siu A, and Robinson C. Use of Intravenous Magnesium Sulfate for the Treatment of an Acute Asthma Exacerbation in Pediatric Patients. J Pediatr Pharmacol Ther. 2014;19(2):91-97.
11. Sarhan HA, EL-Garhy OH, Ali MA, Youssef NA. The efficacy of nebulized magnesium sulfate alone and in combination with salbutamol in acute asthma.Drug Design, Development and Therapy. 2016;10:1927-1933. doi:10.2147/DDDT.S103147.
12. [Goodacre S](http://www.ncbi.nlm.nih.gov/pubmed/?term=Goodacre%20S%5BAuthor%5D&cauthor=true&cauthor_uid=24731521)1, [Cohen J](http://www.ncbi.nlm.nih.gov/pubmed/?term=Cohen%20J%5BAuthor%5D&cauthor=true&cauthor_uid=24731521)1, [Bradburn M](http://www.ncbi.nlm.nih.gov/pubmed/?term=Bradburn%20M%5BAuthor%5D&cauthor=true&cauthor_uid=24731521)1, [Stevens J](http://www.ncbi.nlm.nih.gov/pubmed/?term=Stevens%20J%5BAuthor%5D&cauthor=true&cauthor_uid=24731521)1, [Gray A](http://www.ncbi.nlm.nih.gov/pubmed/?term=Gray%20A%5BAuthor%5D&cauthor=true&cauthor_uid=24731521)2, [Benger J](http://www.ncbi.nlm.nih.gov/pubmed/?term=Benger%20J%5BAuthor%5D&cauthor=true&cauthor_uid=24731521)3, [Coats T](http://www.ncbi.nlm.nih.gov/pubmed/?term=Coats%20T%5BAuthor%5D&cauthor=true&cauthor_uid=24731521)4; [3Mg Research Team](http://www.ncbi.nlm.nih.gov/pubmed/?term=3Mg%20Research%20Team%5BCorporate%20Author%5D). The 3Mg trial: a randomised controlled trial of intravenous or nebulised magnesium sulphate versus placebo in adults with acute severe asthma. 2014 Apr;18(22):1-168.
13. Abdelnabi E, Kamel M, Ali A. Nebulized magnesium sulphate versus nebulized salbutamol in acute bronchial asthma. Egyptian Journal of Chest Diseases and Tuberculosis. 2012;61:29–34.

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