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INHALATION THERAPY WITH MAGNESIUM SULFATE AND SALBUTAMOL SULFATE IN BRONCHIAL ASTHMA*

*Adalet Meral MD***, *Mahmut Çoker MD***, *Remziye Tanaç MD****

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Inhalation therapy with magnesium sulfate and salbutamol sulfate was applied to two groups, each consisting of 20 patients with acute asthma. The effects of inhaled magnesium sulfate and salbutamol sulfate were compared. The evaluation of patients was done using respiratory score, peak expiratory flow rate with a Wright peak flow meter, respiration rate, heart rate and blood pressure. Although magnesium sulfate's bronchodilating effect continued for approximately one hour, treatment of acute asthma using salbutamol sulfate inhalation was found to be more successful and its effect continued for six hours. *Key words: childhood asthma, magnesium sulfate, inhalation therapy.*

Asthma is one of the most common chronic diseases of childhood. new treatment protocols have been developed due to improvement of our knowledge of asthma pathogenesis. Recent studies have proved that the magnesium (Mg^{+2}) ion inhibitis contraction of smooth muscle, acetylcholine release from cholinergic nerve terminals and histamine release from mast cells[1-4]. Thus, magnesium sulfate ($MgSO_4$) administration has become one of the treatment modalities for symptomatic asthmatic patients.

This study was designed to evaluate the effect of $MgSO_4$ inhalation on bronchoconstriction in bronchial asthma and compare its possible usefulness as a bronchodilating agent with salbutamol sulfate inhalation.

Material and Methods

Forty patients who had previously been diagnosed according to the American Thoracic Society's definitions[5] of asthma at the Department of Pediatric Allergy of Ege University Hospital, İzmir, Turkey were randomly selected for the study. All patients gave voluntary consent. Patients were divided into two groups; the first group received $MgSO_4$ inhalation and the second received salbutamol sulfate during asthma attacks. All patients had received maintenance therapy consisting

* From the Allergy and Chest Disease Unit, Department of Pediatrics, Ege University Faculty of Medicine, İzmir.

** Pediatrician, Ege University Faculty of Medicine.

*** Professor of Pediatrics, Ege University Faculty of Medicine.

of beta-2 adrenoreceptor stimulants and/or theophylline derivatives, but none of them had taken medication within 12 hours before the attack. They had neither cardiac nor renal dysfunctions.

The mean age was 10 years (10.55 ± 2.37) for the first group receiving $MgSO_4$ inhalation, and 11 years (10.95 ± 2.45) for the second group receiving salbutamol sulfate inhalation. They were all evaluated and found to be in the normal range according to Neyzi et al's[6] Growth and Development Chart for Turkish Children.

In each subject, a respiratory distress score according to Davis-Leffert-Dabbous' scoring system[7-9] (Table I), heart rate, respiratory rate, blood pressure and peak expiratory flow rate (PEFR) were measured before $MgSO_4$ or salbutamol sulfate inhalations. PEFRs were measured by using the Wright peak flow meter[10], and the increase observed in PEFR values was compared with the height-adjusted predicted PEFR values of normal children as determined by Süren et al.[11] The patients whose PEFR values had decreased 25 percent or more were considered to have acute asthma. Salbutamol sulfate solution (commercially available as Ventolin Nebules 2.5 mg in 2.5 ml) or $MgSO_4$ solution 2 ml (280 mmol/L, 258 mOsm, pH: 6.7) was inhaled by an ultrasonic inhaler in 10 to 15 minutes. The same parameters were again determined after 5, 15, 30, 60, 180, 240, and 360 minutes of $MgSO_4$ or salbutamol sulfate inhalations. The subjects were also evaluated for possible adverse effects of the drugs.

Table I: Respiratory Score Standardization was Accomplished by Taking 5 Points or More Into Consideration

Nasal flaring	0	Absent
	1	Present
Cyanosis	0	Absent
	1	Present
Retractions	0	Absent
	1	Mild (Subcostal + inferior costal)
	2	Moderate (1 + supraciavicular)
	3	Severe (2 + superior intercostal)
Wheezing	0	Absent
	1	Sibilation with stethoscope
	2	1 + mild wheezing
	3	2 + severe wheezing
	4	3 + prolongation of expirium
	5	Decreased or absent breath sounds

The paired t test, student's t test and correlation analysis were used to analyze differences between the two groups. Statistical significance was considered to be at $p < 0.05$.

Results

The parameters measured in each group before the treatment had no statistical differences (Table II). PEFR began to increase five minutes after $MgSO_4$ inhalation,

Table II: Physical Examination Signs at the Beginning of the Therapy

	MgSO4	Salbutamol Sulfate
Respiratory score	5.50 ± 0.60	6.40 ± 0.90
Decrease in PEFR	40.23 ± 13.27	45.94 ± 12.95
Respiration rate	29.40 ± 5.62	33.40 ± 8.80
Heart rate	107.60 ± 20.60	11.80 ± 17.95
Systolic blood pressure	105.00 ± 10.50	103.20 ± 9.65
Diestolic blood pressure	66.00 ± 8.20	68.75 ± 10.49

reaching its maximum value at the end of one hour. By six hours, it decreased to a value which was not statistically different from the PEFR measured before $MgSO_4$ inhalation. In the second group receiving salbutamol sulfate inhalation, PEFR values were found to be significantly higher at five minutes, at the time of maximal response, and at six hours than the values of the $MgSO_4$-inhaling group (Table III, Fig. 1).

Table III: PEFR Values with $MgSO_4$ and Salbutamol Sulfate Inhalation Ratio of Increase in PEFR (%)

	$MgSO_4$ Increase (I)	Salbutamol Sulfate Increase (II)	Statistical Analysis
5^{th} min. (a)	16.31 ± 6.43	42.19 ± 23.18	I-II: $p < 0.01$
Maximum response (1^{st} hour) (b)	42.63 ± 20.21	79.40 ± 52.09	I-II: $p < 0.05$
6^{th} hour (c)	14.54 ± 23.42	75.10 ± 56.72	I-II: $p < 0.01$
Statistical analysis	a-b: $p < 0.01$	a-b $p < 0.01$	
	a-c: $p > 0.05$	a-c: $p < 0.05$	
	b-c: $p < 0.01$	b-c: $p < 0.01$	

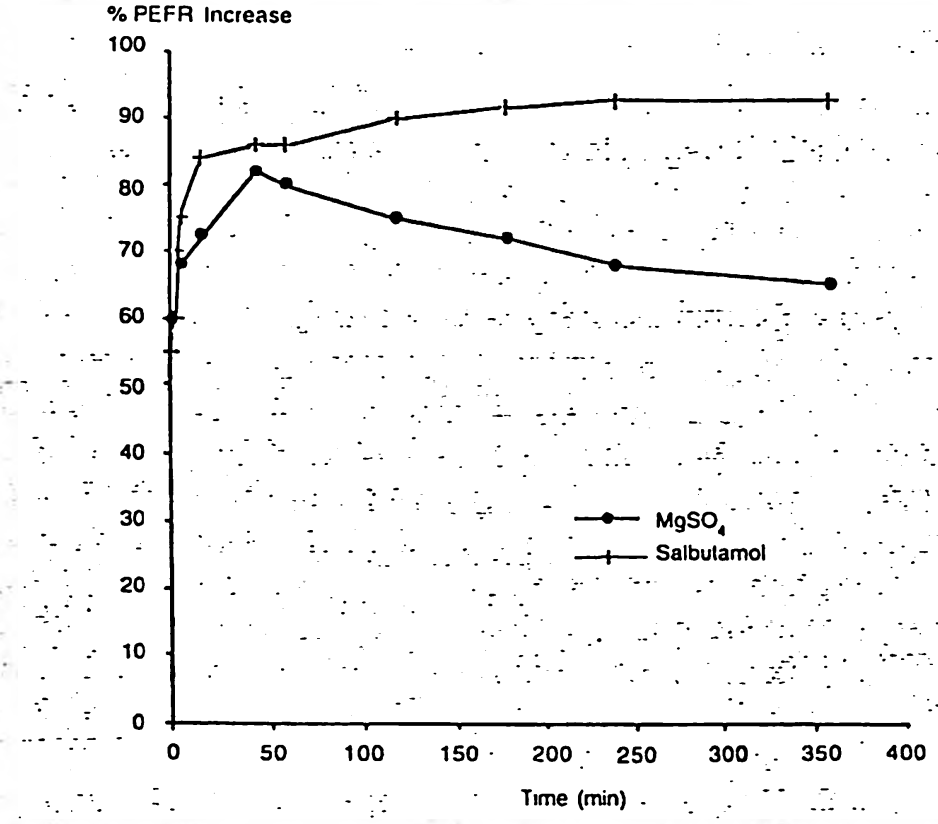

Fig. 1: Ratio of increase in PEFR (%)

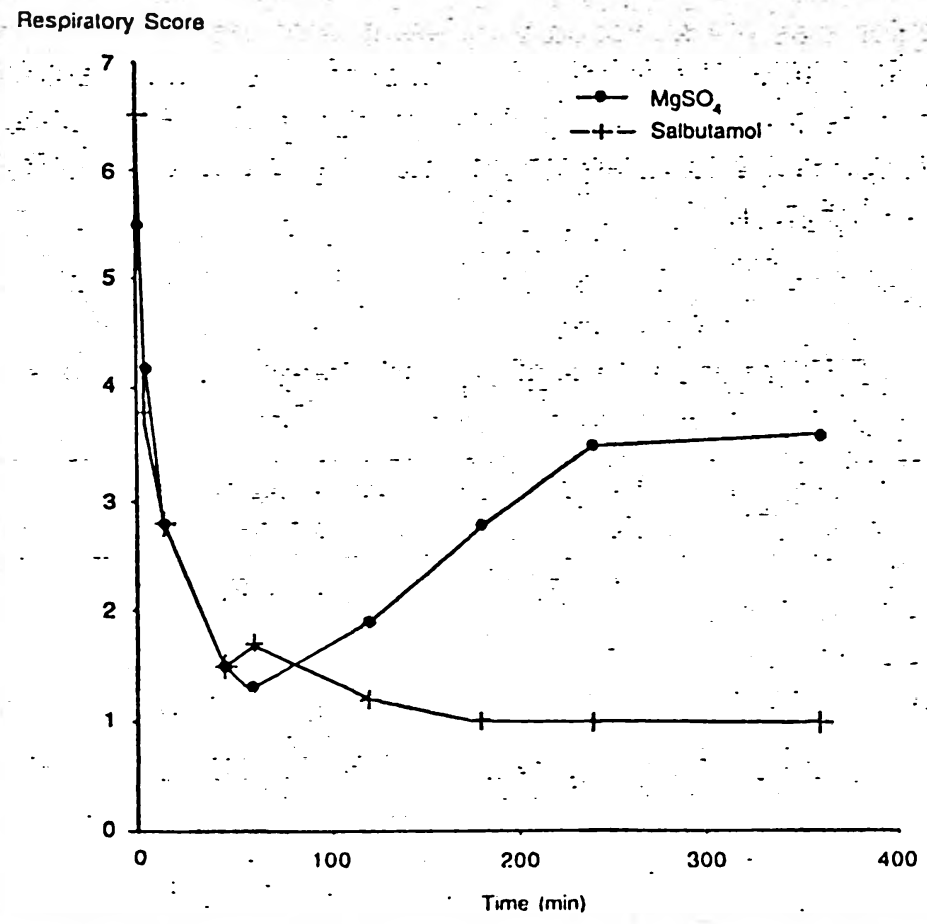

Fig. 2: Ratio of decrease in respiratory score (%)

Although the respiratory distress score improved in both groups, the most significant decrease in the fifth minute and the sixth hour were found in the second group ($p < 0.01$). There was no statistically significant difference in the decrease in respiratory distress scores between the two groups. The respiratory distress score was increased at six hours in the first group parallel to the decrease of PEFR values in the same group ($r = 0.5$, $p < 0.05$). The respiratory distress score decreased and was maintained until the end of the sixth hour only in the salbutamol sulfate inhaling group (Table IV, Fig. 2).

Table IV: The Improvement of Respiratory Scores with $MgSO_4$ and Salbutamol Sulfate Inhalation

	Ratio of Decrease in Respiratory Score (%)		
	$MgSO_4$ Inhalation (I)	Salbutamol Sulfate Inhalation (II)	Statistical Analysis
5th min. (a)	23.33 ± 17.70	43.14 ± 22.12	I-II: $p < 0.01$
Maximum response (1st hour) (b)	79.97 ± 19.18	83.17 ± 26.73	I-II: $p > 0.05$
6th hour (c)	30.80 ± 34.79	80.41 ± 30.32	I-II: $p < 0.01$
Statistical analysis	a-b: $p < 0.01$ a-c: $p > 0.05$ b-c: $p < 0.01$	a-b $p < 0.01$ a-c: $p < 0.01$ b-c: $p > 0.05$	

Respiratory rate, heart rate and blood pressures were in the normal range in both groups, and no statistical differences in the parameters were found between the two groups ($p > 0.05$).

Discussion

There have been new approaches related to the pathogenesis of asthma in recent years. Mg^{+2} itself as a physiologic antagonist of calcium (Ca^{+2}) induces an inhibitory action on smooth muscle contraction by blocking the intracellular influx of Ca^{+2} [12-15].

In this study, we investigated the bronchodilating effect of Mg^{+2} in acute asthma crisis and compared it with a beta-2 adrenoreceptor agonist, salbutamol sulfate. In both groups, PEFR increased at five minutes. However, the increase in the salbutamol sulfate-inhaling group was more significant ($p < 0.01$). The maximum effect of $MgSO_4$ was reached by one hour. However, its effect was short-term compared to that with salbutamol sulfate inhalation, since the PEFR values were still high by six hours in the salbutamol sulfate-inhaling group and was decreased

to the beginning values by six hours in the $MgSO_4$-inhaling group. Similar results were obtained in the respiratory distress scores.

There was no adverse reaction in either group, as the blood pressure and heart rate did not change ($p > 0.01$). Hypotension and tachycardia noted in the literature during intravenous $MgSO_4$ administration were also not observed in our study[16, 18].

Hiroshi et al.[19] showed that intravenous $MgSO_4$ had a fast but short-term bronchodilating effect; its effect started in two minutes but declined after 10 minutes of administration. In several studies, it has been suggested that $MgSO_4$ can be used in mild or severe acute asthma attacks either with a beta-2 adrenoreceptor agonist or alone in non-responders to beta-2 agonists[3, 16, 18].

In our study, we found that the inhalable form of $MgSO_4$ takes effect as quickly as the intravenous forms but lasts longer. Its effect continued for one hour and then started to decline in our study. Salbutamol sulfate inhalation was found to be more effective, and its effect continued for six hours.

In conclusion, the results indicate that $MgSO_4$ inhalation produces statistically significant but shot-term bronchodilatation in asthmatics. Therefore, it should not be the first agent used in acute asthmatic attacks but may be used as an adjuvant agent with a beta-2 agonist. Further investigations are needed to provide more data on this subject.

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