

# Comparison of the efficacy of nebulized budesonide and systemic steroids in children admitted to the emergency service with acute asthma attacks

 Bilge Sahin Akkelle<sup>1</sup>,  Metin Aydogan<sup>2</sup>,  Rengin Siraneci<sup>3</sup>

<sup>1</sup>Department of Pediatric Gastroenterology, Faculty of Medicine, Marmara University, Istanbul, Turkey

<sup>2</sup>Department of Pediatric Allergy, Faculty of Medicine, Kocaeli University, Izmit, Turkey

<sup>3</sup>Department of Pediatrics, University of Health Science Kanuni Sultan Suleyman Research and Training Hospital, Istanbul, Turkey

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## Abstract

**Aim:** Systemic steroids are used when necessary in the treatment of acute asthma attacks, but they have a high potential for side effects. The role of nebulized steroids in acute asthma attacks is controversial and there are few studies on the subject. In our study, it was aimed to evaluate the efficacy of nebulized budesonide treatment in children presenting with acute asthma attack.

**Materials and Methods:** In this study, patients aged 5-18 years who presented to emergency service with a mild acute asthma attack were evaluated. Patients with mild acute asthma attack who did not respond to nebulized salbutamol treatment at 3 doses (0.15 mg/kg/dose) administered within the first hour, were included in the study. The patients were randomly divided into two groups. Group A received single-dose systemic steroid (1mg/kg) while Group B received single-dose nebulized budesonide (500µg). The groups were compared in terms of demographics, % O<sub>2</sub> saturation, pulmonary index score (PIS), and duration of hospital stay.

**Results:** A total of 61 cases were enrolled to the study (Group A n=33, Group B n=28). There was no statistically significant difference between groups in terms of mean age and gender (P>0.05). In both groups, % O<sub>2</sub> saturation values at 4<sup>th</sup> hour of treatment increased and PIS regressed significantly compared to the baseline values (P<0.001). It was also found that the % O<sub>2</sub> saturation values at 4<sup>th</sup> hour were higher in patients treated with nebulized budesonide compared to patients treated with systemic steroids (p:0.02). There was no statistically significant difference between the groups in terms of duration of hospital stay (P>0.05).

**Conclusion:** Based on the results of our study, a single dose (500µg) of nebulized budesonide was shown to be as effective as systemic steroid therapy in the treatment of mild acute asthma attacks.

**Keywords:** Asthma; budesonide; child; steroid

## INTRODUCTION

Asthma is characterized by respiratory inflammation, bronchial hyperreactivity, and reversible airway obstruction. It is a chronic disorder that is common in childhood and has negative socio-economic effects (1). In asthma the drugs that aim to control airway inflammation, reduce asthma attacks and hospitalizations are the basis of long-term treatment. Inhaled steroids that are used to control inflammation are the first choice of maintenance treatment due to their high concentration by directly reaching the respiratory tract at low doses and low potential for side effects. Systemic steroids are mostly used in acute asthma attacks and are very effective in rapidly eliminating asthma exacerbations and preventing relapse (2-4). In contrast, they have very serious potential

side effects (2). Potential side effects and administration difficulties of systemic steroids in pediatric age group in acute asthma attacks have raised the question of the alternative feasibility of inhaled steroids which are still used effectively in maintenance therapy.

There are few studies on the use of nebulized steroids in acute asthma attacks in the pediatric age group (5-22). The effectiveness of nebulized steroids in treatment of acute asthma attacks is still controversial and data are insufficient (23).

In our study, it was aimed to compare nebulized steroid (budesonide) and systemic steroid (methyl prednisolone) treatment in terms of efficacy and duration of hospital stay in children who were admitted to our emergency department with acute mild asthma attacks.

**Received:** 04.01.2021 **Accepted:** 25.02.2021 **Available online:** 26.05.2021

**Corresponding Author:** Bilge Sahin Akkelle, Department of Pediatric Gastroenterology, Faculty of Medicine, Marmara University, Istanbul, Turkey **E-mail:** [bilgesahin9@hotmail.com](mailto:bilgesahin9@hotmail.com)

## MATERIALS and METHODS

Patients aged 5-18 years who presented to the Pediatric Emergency Outpatient Clinic of the Republic of Turkey Ministry of Health Bakirkoy Obstetrics and Paediatrics Training and Research Hospital with mild acute asthma attacks between September 1, 2007 and October 31, 2007 were evaluated in the study. Patients with lung disease or systemic disease other than asthma and patients who had used medication for asthma attack in the last 24 hours were excluded from the study.

### Study Design and Treatment Protocol

The study was conducted in a randomized single-blind manner. Asthma attack severity was determined based on GINA (Global Initiative for Asthma) at the time of admission and by evaluating consciousness, position, shortness of breath, speech style, respiratory rate, pulse, retraction, inspiration-expiration ratio, saturation and wheezing status of the patients (1), and pulmonary index scoring was applied (24). Oxygen saturation was measured with Nellcor® pediatric saturation probe. Patients received nebulized salbutamol (Ventolin®, Glaxo Wellcome) 0.15 mg/kg/dose 3 times with a maximum of 5 mg/dose and an interval of 20 minutes within the first hour. Attack severity assessment was repeated at the first hour. The study was continued in patients with mild attacks who did not respond rapidly to bronchodilator therapy in the first hour. A random list was generated and participants allocated to the next treatment on the list when they arrive. In the next stage, one of the randomized study groups (Group A) was administered systemic steroids (1 mg/kg, max 40 mg) orally (Prednol tablets 4 mg, 16 mg) and intramuscularly (Prednol ampoule 20 mg, 40 mg) for patients who couldn't tolerate oral treatment. In the other group (Group B), a single dose of nebulized budesonide (Pulmicort®, Astra Zeneca) with a dose of 500 µg / dose was administered by nebulization (Omron® C29 compressor nebulizer) through a mask. Afterwards nebulization of salbutamol (0.15 mg/kg/dose) was continued at 60 min intervals with close monitoring in both patient groups. The follow-up of the patients included in the study was planned for at least 4 hours. Evaluation of attack severity and pulmonary index scoring was repeated at the fourth hour. Patients who responded well to the treatment were discharged with recommendations when their physical examinations were normal. Those with inadequate response were monitored in the emergency department with the continuation of the treatment, so that their findings were evaluated intermittently until they met the discharge criteria. The duration of hospital stay was recorded for each patient (Figure 1).

The study was approved by the ethics committee of the Republic of Turkey Ministry of Health Bakirkoy Obstetrics and Pediatrics Training and Research Hospital. Informed consent was obtained from the parents of the patients.

### Statistical Analysis

The data in our study were evaluated using SPSS for Windows 16.0 package software. In addition to descriptive statistical methods, Fisher Exact Test was used to compare

the categorical data of the two groups. In comparison of numerical (quantitative) data, Independent Samples T Test was used in normally distributed (parametric) and independent groups, and Paired Samples T Test was used in dependent repeat measurements. Mann-Whitney U Test was used in non-normally distributed (non-parametric) and independent groups, and Wilcoxon analysis was used in dependent repeat measurements. Results were shown as mean ± standard deviation. If  $P < 0.05$ , the difference between the means was considered significant.

## RESULTS

Of the 61 patients included in the study, the mean age of 33 patients in Group A, in which 11 were female (33.4%) and 22 were male (66.6%), was  $8.21 \pm 2.21$  years. Of the 28 patients in Group B, 16 were female (57.1%) and 12 were male (42.8%), and the mean age was  $8.57 \pm 2.33$  years. There was no statistically significant difference between the two groups in terms of mean age and gender ( $P > 0.05$ ) (Table 1).

**Table 1. Comparison of the groups according to the parameters evaluated**

	Group A (n=33)	Group B (n=28)	P
Age (year) (mean±SD)	8.21±2.21	8.57±2.33	0.54
Gender (M/F)	22/11	12/16	0.06
<sup>1</sup> SaO <sub>2</sub> (%) (baseline)	97.2±0.59	97.07±0.76	0.42
SaO <sub>2</sub> (%) (4 <sup>th</sup> hour)	99.2±0.50	99.5±0.57	<b>0.02</b>
<sup>2</sup> PIS (baseline)	4.15±0.56	4.21±0.91	0.74
PIS (4th hour)	0.18±0.46	0.25±0.51	0.59
Duration of hospital stay (hour)	5.23	4.81	0.14

The mean %O<sub>2</sub> saturation value at the end of first hour in Group A was comparable with Group B ( $97.2 \pm 0.59$ ;  $97.07 \pm 0.76$ ,  $p > 0.05$ ). In patients who received systemic steroids (Group A), the % O<sub>2</sub> saturation values at the 4th hour were significantly increased compared to the baseline values ( $97.2 \pm 0.59$ ,  $99.2 \pm 0.50$ ) ( $P < 0.001$ ). Likewise, it was found that the O<sub>2</sub>% saturation values at the 4th hour significantly increased compared to the baseline values ( $97.07 \pm 0.76$ ,  $99.5 \pm 0.57$ ;  $P < 0.001$ ) in patients that received nebulized steroid (Group B). The fourth hour mean saturation values of the patients with mild attacks who received nebulized steroid were higher than those who received systemic steroids, and the difference was statistically significant ( $99.2 \pm 0.50$ ,  $99.5 \pm 0.57$ ) ( $P < 0.02$ ) (Table 1) (Figure 2).

When the pre-treatment and post-treatment pulmonary index scores of the patients who received systemic steroids and the patients received nebulized steroid were evaluated separately, it was found that there was a significant improvement in both groups [(PIS Group A pre-treatment:  $4.15 \pm 0.56$ ; post-treatment:  $0.18 \pm 0.46$ ) ( $p < 0.001$ ), (PIS Group B: pre-treatment:  $4.21 \pm 0.91$ ; post-

treatment:  $0.25 \pm 0.51$ ) ( $p < 0.001$ ) (Table 1). There was no statistically significant difference between the groups in terms of duration of hospital stay (5.23 hours in Group A, 4.81 hours in Group B;  $P > 0.05$ ) (Table 1).



Figure 1. Flow chart of the study

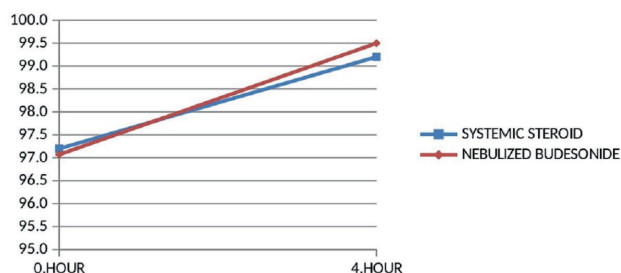


Figure 2. The mean O<sub>2</sub>% saturation values at baseline and at 4<sup>th</sup> hours

## DISCUSSION

Asthma attacks are characterized by acute exacerbation of airway inflammation and bronchospasm, and bronchodilators and anti-inflammatory agents form the basis of the treatment. Systemic steroids, which are indisputably the most effective drugs on bronchial inflammation, have the potential for side effects and administration difficulty. The question is still up to date as to whether inhaled steroids can be an alternative in acute attack treatment due to their high local activity, low systemic effect, high clearance, and short half-life. In the literature, pediatric studies comparing the efficacy of inhaled steroid / placebo alone (6,13,17-19), inhaled steroid / systemic steroid alone (5,7-12,14-16)

and evaluating the efficacy of combined therapy in the treatment of acute asthma attacks have been reported. In a recent meta-analysis, the positive effects of high-dose inhaled steroid therapy combined with systemic steroid therapy have been reported in moderate-severe asthma attacks (25).

It is striking that studies comparing the efficacy of inhaled budesonide and systemic steroids have generally been conducted with high or repeated doses of budesonide on patients admitted to the emergency room with moderate and / or severe attacks (5-15,17,19). Two randomized and placebo-controlled studies have been conducted comparing the efficacy of inhaled budesonide 800µg/dose (3 doses) and systemic steroid 2mg/kg in children presenting with moderate-severe asthma attacks (7,8). In both studies, at the end of the 2-hour follow-up period, there was a more significant improvement in symptoms and findings in the group receiving nebulized budesonide compared to the group receiving oral prednisolone and the rate of discharge from hospital was higher in the group receiving budesonide. In another study comparing the efficacy of nebulized budesonide 800µg/dose (3 doses) and systemic steroid 2mg/kg with a similar method, a more significant improvement was obtained in early period in the group treated with nebulized budesonide, while no difference was detected between the groups in symptoms and signs at the end of the 12-hour follow-up period (9). Matthews EE et al. evaluated systemic steroid efficacy with a higher dose of nebulized budesonide (2 mg/dose every 8 hours) in acute asthma attacks in the pediatric age group and found that respiratory functions improved more significantly in the group receiving nebulized budesonide at the end of a longer follow-up period (24 hours) (10). In another study conducted in the pediatric age group comparing the efficacy of systemic steroids (2mg/kg) and nebulized budesonide (1500µg), no difference was found between treatment groups in terms of pulmonary index scores, O<sub>2</sub> saturation and pulmonary function tests at the end of the 2-hour follow-up period (8). There are pediatric studies comparing the two treatment modalities with longer follow-up and showing that nebulized steroids are as effective as systemic prednisolone (12,13).

In general, studies comparing inhaled steroid and systemic steroid efficacy have heterogeneity in terms of attack severity, active substance used, dose, dose range, route of treatment, additional therapies used (O<sub>2</sub> support, salbutamol) and duration of treatment. This is considered to have caused variable results in the studies. Our study showed that low dose (500 µg) nebulized budesonide had similar efficacy to systemic steroids in mild asthma attacks. In a study comparing budesonide 3000 µg and placebo in patients with mild to moderate asthma attacks in the literature, there was no difference between the groups in terms of FEV<sub>1</sub>, β<sub>2</sub> agonist use and hospitalization rates, but less systemic steroid requirement was observed in the group receiving budesonide (13).



## LIMITATIONS

The limitation of our study is that pulmonary function tests could not be used in the evaluation of patients in this age group due to application difficulties in emergency room. In many studies investigating the efficacy of inhaled steroids in the treatment of acute attacks, the parameters of pulmonary function tests have been evaluated because they were well correlated with the clinical severity and provide objective data. In our study, attack severity scoring was performed for clinical evaluation, % O<sub>2</sub> saturation value and pulmonary index scores were used as objective data. Non monitoring of patients after 4 hours is another restriction for our study. The results of this single center study cannot be generalized as the study was conducted with a small number of patients.

## CONCLUSION

The data obtained in our study show that low-dose nebulized budesonide treatment is as effective as systemic steroids in the treatment of mild asthma attacks in pediatric age group in terms of efficacy and duration of hospital stay.

*Acknowledgments: We respectfully commemorate Dr. Suat Bicer, who contributed to the realization of the study.*

*Competing interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Ethical approval: Republic of Turkey Ministry of Health Bakirkoy Obstetrics and Paediatrics Training and Research Hospital; Ethics committee.*

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