

Comparison of Nebulized vs Systemic Corticosteroids for Management of Children Presenting with Acute Exacerbation of Asthma

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ABSTRACT

Objective: The aim of current study is to determine the outcomes of nebulized vs systemic corticosteroids for the treatment of children presenting with acute exacerbation asthma.

Study Design: Simple blind/parallel study

Place and Duration: Children Medical Center (CMC) / Dr Habib un Nabi Children Hospital Airport Road Mingora Swat and Pediatrics department of Ayub Medical College and Teaching Hospital, Abbottabad for the duration 06 months from April 2021 to September 2021.

Methods: There were 60 cases of both genders presented with ages <10 years. Included patients had acute exacerbation of asthma. After obtaining written agreement, the demographics of all registered patients were recorded. Patients were split into 2-groups. Group I received nebulized corticosteroids and group II received systemic corticosteroids. Post treatment after 2 weeks of follow up outcomes among both groups were assessed by using oscillometric resistances. SPSS 21.0 version was used to analyze complete data.

Results: There were 40 males (20 in each group) and 20 females (10 in each group). Mean age of the patients in group I was 5.8±7.45 years and group II had mean age 6.4±4.35 years. In group I 19 (63.3%) cases had family history of allergy and in group II 18 (60%) cases had history. Mean duration of asthma in group I was 3.4±6.15 years and in group II mean duration was 4.1±4.19 years. Mean hospitalization was lower in group I 1.5±3.14 days as compared to group II 2.8±9.31 days. By using oscillometric resistances reduction in disease severity was found higher in group I 4.1±5.14 as compared to group II 5.1±5.12 from 8.3±6.31.

Conclusion: We concluded in this study that the use of nebulized steroids were effective and useful as compared to systemic steroid in the treatment of acute exacerbation asthma in terms of reduction of severity of disease and hospital stay.

INTRODUCTION

In children, bronchial asthma is the most common long-term illness. Inflammation of the airways might lead to permanent structural changes if it is not well treated [2-3]. For children under the age of four, bronchial asthma is poorly-diagnosed and under-treated [4]. Recent years have seen a dramatic rise, and the symptoms may be severe enough to need immediate hospitalisation [5]. [5] Acute asthma exacerbations are best treated with systemic corticosteroids and beta2-agonists, although repeated rounds of therapy may raise the risk of systemic adverse effects in children [5]. For long-term treatment of bronchial inflammation and asthmatic symptoms, inhaled corticosteroids (ICSs) are used instead [5].

52 percent of patients with asthma had at least one exacerbation that necessitated a visit to an emergency room, according to an American study. An asthma quality of life score dropped from 6.2 to 4.2 for children who were hospitalised in one research.[6]In the treatment of acute asthma exacerbations, systemic corticosteroids (SCs) are beneficial.[7] Treatment with SC within one hour of an exacerbation decreased admission rates by 60% (95 percent CI: 0.21–0.78) compared to those who did not receive corticosteroid therapy. [8]

Asthma exacerbations are often treated with inhaled corticosteroids (ICS), however the effectiveness of these medications in preventing flare-ups is still debated. The reported advantages of utilising ICS over oral prednisolone include a larger chance of being discharged from the ER within 2 hrs (23 percent vs. 7 percent), a bigger percentage of patients without respiratory distress (34 percent vs. 15 percent), and less vomiting (0 percent vs. 15 percent). [9,10] Another research found that children with asthma exacerbations were more likely to be admitted to the hospital when given inhaled fluticasone rather than oral prednisone (31 percent vs. 10 percent). [11]

The 2018 Global Initiative for Asthma Report said that ICS may be used for asthma exacerbation in children;[12] in contrast,

the Japanese recommendations for paediatric asthma do not include ICS for asthma exacerbation. [13] A meta-analysis evaluating ICS usage in the emergency department found that admission rates might be reduced by 56% (95 percent confidence interval: 0.31–0.62). [14,15] Acute asthma exacerbations in children treated with inhaled corticosteroids (ICS) are still debatable.

The purpose of this research was to update the meta-analysis on the usefulness of ICS and systemic steroids in the therapy of acute asthma exacerbation in children who were hospitalized.

MATERIAL AND METHODS

This parallel single blind study was conducted at Children Medical Center (CMC) / Dr Habib un Nabi Children Hospital Airport Road Mingora Swat and Pediatrics department of Ayub Medical College and Teaching Hospital, Abbottabad for the duration 06 months from April 2021 to September 2021. The study was comprised of 60 children with acute exacerbation of asthma. After obtaining written agreement, the demographics of all registered patients were recorded. We eliminated children who had taken ICSs daily for the past three months, cromons, theophylline, antileukotrienes, antihistamine drugs, and systemic corticosteroids in the preceding month from the research.

On the basis of three factors, the existence and severity of an asthma exacerbation were determined. Sleep disruption, wheezing, usage of axillary muscle and/or suprasternal retraction were all included in a single score that was produced by summing the scores from the following scale: Only those patients who had at least mild symptoms in the 24 hours before to enrollment were included in this study; those who had at least moderate symptoms were not. There were three criteria used to classify mild exacerbation: a total symptom score between 4 and 8; an arterial oxygen saturation (SaO₂) while the patient was breathing room air of 91-95 percent; and a decrease in oscillometric resistances

greater than 35 percent from baseline following inhalation of 200 ug salbutamol delivered via metered dose inhaler and spacer.

First, flunisolide was administered twice daily for seven days, and then every other day for the next 7 days at a dosage of 20 ug/kg. Systemic budesonide at a 0.5 mg twice daily for 7 days and then 0.25 mg twice daily for the next 7 days was administered to Group 2. Aerochamber plus, Markos Mefar SpA) at a dose of 200 ug 4 times daily for the first 3 days of the research and thereafter when needed was given to both groups as inhaled salbutamol.

An air-jet nebulizer (Nuovo Nebula/MB5, Markos Mefar SpA) was used to give the medication and the parents were taught on how to use it. The medications were diluted in 3 ml of sterile saline before being nebulized using a spacer mouth mask and a spacer mouthpiece. After each nebulization, patients were asked to clean their mouth and cheeks. Post treatment after 2 weeks of follow up outcomes among both groups were assessed by using oscillometric resistances. SPSS 21.0 version was used to analyze complete data.

RESULTS

There were 40 males (20 in each group) and 20 females (10 in each group). Mean age of the patients in group I was 5.8±7.45 years and group II had mean age 6.4±4.35 years. Mean duration of asthma in group I was 3.4±6.15 years and in group II mean duration was 4.1±4.19 years (table 1)

Table 1: Characteristics on presented children

Variables	Group I	Group II
Gender		
Male	20 (66.7%)	20 (66.7%)
Female	10 (33.3%)	10 (33.3%)
Mean age (years)	5.8±7.45	5.8±7.45
Mean Duration of Asthma (years)	3.4±6.15	4.1±4.19

In group I 19 (63.3%) cases had family history of allergy and in group II 18 (60%) cases had history.(fig 1)

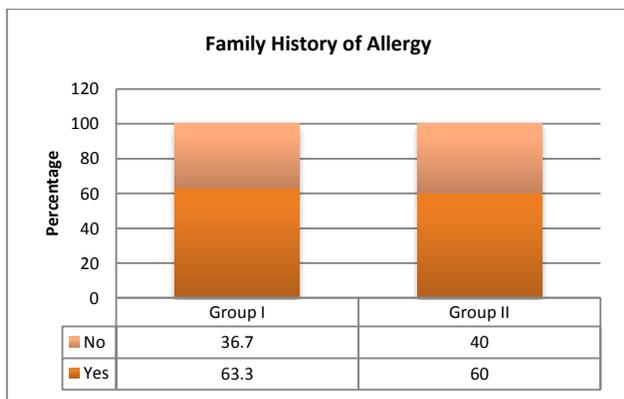


Figure 1: Family history of allergy among cases

By using oscillometric resistances reduction in disease severity was found higher in group I 4.1±5.14 as compared to group II 5.1±5.12 from 8.3±6.31.(table 2)

Table 2: Post-treatment comparison of diseases reduction in both groups

Variables	Group I	Group II
Oscillometric Resistances		
First day (cmH20/LIs)	8.3±6.31	8.3±6.31
7 days (cmH20/LIs)	6.16±4.15	7.0±3.11
14 days (cmH20/LIs)	4.1±5.14	5.1±5.12

Mean hospitalization was lower in group I 1.5±3.14 days as compared to group II 2.8±9.31 days. Satisfaction rate among mothers of group I was greater found among 27 (90%) as compared to group II found in 24 (80%) cases.(table 3)

Table 3: Comparison of hospital stay and satisfaction among both groups

Variables	Group I	Group II
Mean Hospitalization (days)	1.5±3.14	2.8±9.31
Satisfaction		
Yes	27 (90%)	24 (80%)
No	3 (10%)	6 (20%)

DISCUSSION

Even at large dosages, budesonide has long been recognized as being safe and effective.[16] According to de Benedictis et al. [17], when nebulized Fluticasone is given to bronchodilator treatment in children with moderate asthma, a short course of the medicine has the same effects as a double dosage of the drug when nebulized Budesonide is added.

In our study 60 children with acute asthma were presented. There were 40 males (20 in each group) and 20 females (10 in each group). Mean age of the patients in group I was 5.8±7.45 years and group II had mean age 6.4±4.35 years. In group I 19 (63.3%) cases had family history of allergy and in group II 18 (60%) cases had history. Results of our study were comparable to the previous studies.[18,19] By using oscillometric resistances reduction in disease severity was found higher in group I 4.1±5.14 as compared to group II 5.1±5.12 from 8.3±6.31.We found that nebulized flunisolide improved acute asthma symptoms more quickly than budesonide used as systemic steroid. In fact, in the first seven days of therapy, oscillometric resistances and symptom ratings decreased more quickly in group 1 (FLU) than in group 2. (BUD). The therapeutic impact of the two medications remained even after the dosage was reduced by half as advised by the GINA recommendations [20], with no increase in airway resistance.

As a result of FLU's high water solubility, the drug is dispersed throughout the nebulizer chamber in a more homogeneous solution than is the case with other ICSs, making for more consistent drug concentrations throughout the aerosol droplet (budesonide, beclometasone dipropionate, fluticasone propionate). [21] Mean hospitalization was lower in group I 1.5±3.14 days as compared to group II 2.8±9.31 days. Satisfaction rate among mothers of group I was greater found among 27 (90%) as compared to group II found in 24 (80%) cases. These results were comparable to the previous studies.[22,23] In addition to decreasing the number of asthma hospitalizations, multiple studies have shown that ICS improves clinical scores[24] and lung function tests, notably FEV115; decreases the usage of bronchodilators; and shortens hospital stays[25]. [26] Even though one research revealed a nonsignificant 1.29-fold increase in the probability of tremor (95 percent CI: 0.58–2.88), no major side events were recorded in any trial. [27] Additionally, intravenous methylprednisolone may be more intrusive than intravenous corticosteroid injections. ICS higher costs, limited availability in underdeveloped countries, and decreased efficacy in patients with a high respiratory rate are some of the drawbacks of using ICS. The risks associated with using ICS are quite minimal. Pituitary-adrenal axis suppression was less in comparison to that caused by SC. [24]

Asthma exacerbations may benefit from the use of large dosages of inhaled corticosteroids, which may be clinically active within seconds or minutes because to their non-genomic methods of action. [28] The quicker impact of flunisolide found in our research might be attributed to its larger non-genomic action than budesonide, which has a longer half-life.

CONCLUSION

We concluded in this study that the use of nebulized steroids were effective and useful as compared to systemic steroid in the treatment of acute exacerbation asthma in terms of reduction of severity of disease and hospital stay.

REFERENCES

1 American Lung Association Data and Statistic. Trend in asthma morbidity and mortality. New York: American Lung Association 2001.

- 2 Barbato A, Turato G, Baraldo S, et al. Epithelial damage and angiogenesis in the airways of children with asthma. *Am J Respir Crit Care Med* 2006; 174:
- 3 Saglani S, Payne DN, Zhu J, Wang Z, Nicholson AG, Bush A, Jeffery PK. Early detection of airway wall remodeling and eosinophilic inflammation in preschool wheezers. *Am J Respir Crit Care Med* 2007; 176:858-64.
- 4 Cane RS, Ranganathan SC, McKenzie SA. What do parents of wheezy children understand by "wheeze" ? *Arch Dis Childhood* 2000; 82:327-32.
- 5 National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program. Guidelines for the Diagnosis and Management of Asthma. Full Report 2007. www.nhlbi.nih.gov/guidelines
- 6 Akinbami LJ, Moorman JE, Liu X. Asthma prevalence, health care use, and mortality: United States, 2005-2009. *Natl Health Stat Report*. 2011;32:1-4
- 7 Chipps BE, Haselkorn T, Rosén K, Mink DR, Trzaskoma BL, Luskin AT. Asthma Exacerbations and Triggers in Children in TENOR: Impact on Quality of Life. *J Allergy Clin Immunol Pract*. 2018;6:169-7600
- 8 Rowe BH, Spooner C, Ducharme FM, Bretzlaff JA, Bota GW. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev*. 2001 CD002178.
- 9 Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. [Last accessed on 2018 May 16]. Available from: <https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention>
- 10 Devidayal, Singhi S, Kumar L, Jayshree M. Efficacy of nebulized budesonide compared to oral prednisolone in acute bronchial asthma. *Acta Paediatr*. 1999;88:835-40
- 11 Scarfone RJ, Loiselle JM, Wiley JF, 2nd, Decker JM, Henretig FM, Joffe MD. Nebulized dexamethasone versus oral prednisone in the emergency treatment of asthmatic children. *Ann Emerg Med*. 1995;26:480-6
- 12 Schuh S, Reisman J, Alshehri M, Dupuis A, Coren M, Arseneault R, et al. A comparison of inhaled fluticasone and oral prednisone for children with severe acute asthma. *N Engl J Med*. 2000;343:689-94
- 13 Arakawa H, Hamasaki Y, Kohno Y, Ebisawa M, Kondo N, Nishima S, et al. Japanese guidelines for childhood asthma 2017. *Allergol Int*. 2017;66:190-204
- 14 Edmonds ML, Milan SJ, Camargo CA, Jr, Pollack CV, Rowe BH. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. *Cochrane Database Syst Rev*. 2012;12:CD002308
- 15 Su XM, Yu N, Kong LF, Kang J. Effectiveness of inhaled corticosteroids in the treatment of acute asthma in children in the emergency department: A meta-analysis. *Ann Med*. 2014;46:24-30
- 16 Sano F, Cortez GK, Sol D, Naspitz CK. Inhaled budesonide for the treatment of acute wheezing and dyspnea in children up to 24 months old receiving intravenous hydrocortisone. *J Allergy Clin Immunol* 2000; 105:699-703.
- 17 De Benedictis FM, Miraglia Del Giudice M, Vetrilla M, Tressanti F, Tronci A, Testi R, Dasic G: Flicl2 Study Group. Nebulized fluticasone propionate vs. budesonide as adjunctive treatment in children with asthma exacerbation. *J Asthma* 2005; 42:331-6
- 18 Duse, M., Santamaria, F., Verga, M.C. et al. Inter-society consensus for the use of inhaled corticosteroids in infants, children and adolescents with airway diseases. *Ital J Pediatr* 47, 97 (2021).
- 19 Tavey Dorofaeff, Kevin Plumpton. 2014. Acute respiratory failure in children. *Oh's Intensive Care Manual*, pages 1085-1095.e2.
- 20 Global initiative for asthma (GINA). Global Strategy for Asthma Management and Prevention. Revised Nov. 2006.
- 21 Kantar A, Mroueh S, Fiocchi A. A reappraisal of the clinical safety of nebulized flunisolide in pediatric asthma: The Italian experience. *Allergy Asthma Proc* 2007; 28:1-17
- 22 Alangari AA. Corticosteroids in the treatment of acute asthma. *Ann Thorac Med*. 2014;9(4):187-192. doi:10.4103/1817-1737.140120
- 23 Sawanyawisuth K, Chattakul P, Khamsai S, et al. Role of Inhaled Corticosteroids for Asthma Exacerbation in Children: An Updated Meta-Analysis. *J Emerg Trauma Shock*. 2020;13(2):161-166.
- 24 Sharma S, Harish R, Dutt N, Digra KK. To evaluate the efficacy of nebulized budesonide compared to oral prednisolone in the management of moderate exacerbation of acute asthma. *Int J Contemp Pediatr*. 2017;4:1278-83
- 25 Yanagida N, Tomikawa M, Shukuya A, Iguchi M, Ebisawa M. Budesonide inhalation suspension versus methylprednisolone for treatment of moderate bronchial asthma attacks. *World Allergy Organ J*. 2015;8:14
- 26 Razi CH, Akelma AZ, Harmanci K, Kocak M, Kuras Can Y. The Addition of Inhaled Budesonide to Standard Therapy Shortens the Length of Stay in Hospital for Asthmatic Preschool Children: A Randomized, Double-Blind, Placebo-Controlled Trial. *Int Arch Allergy Immunol*. 2015;166:297-303.
- 27 Estrada-Reyes E, Del Río-Navarro BE, Rosas-Vargas MA, Nava-Ocampo AA. Co-administration of salbutamol and fluticasone for emergency treatment of children with moderate acute asthma. *Pediatr Allergy Immunol*. 2005;16:609-14
- 28 Wanner A, Horvath G, Brieva JL, Kumar SD, Mendes ES. Non-genomic actions of glucocorticosteroids on the airway vasculature in asthma. *Proc Am Thorac Soc* 2004; 1:235-8