

EFFICACY OF VERY LOW DOSE INHALED CORTICOSTEROID AND REDUCTION OF MISUSE OF ANTIBIOTICS AND HOSPITAL ADMISSION IN INFANTS AND TODDLERS WITH RECURRENT WHEEZY CHEST

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Abstract

Background: Wheeze in infants and toddlers are a common symptom and sign. Inhaled Corticosteroids are considered the most effective treatment available for long-term control of asthma or recurrent wheezing of children. The aim of the present study was to see the efficacy of very low dose inhaled Beclomethasone in reducing the misuse of antibiotics and hospital admission among the infants and toddlers with recurrent wheezing. **Materials and methods:** This was a prospective study done among 70 infants and toddlers of 4 months to 3 years of age having a recurrent wheeze. Open-ended questionnaires were used. All patients were studied with Beclomethasone Dipropionate HFA inhaler 1 puff (50 micrograms) twice daily and Salbutamol inhaler 1-2 puffs (Each puff contain 100 micrograms) 3 to 4 times daily when needed via small volume spacer with a mask. Sixty patients completed the study for total 3 months and were included in the analysis. Patients were followed up every 4 weeks interval and symptoms, use of antibiotics and need for hospital admission all were calculated. Data were analyzed by SPSS 20. **Results:** Among the 70 patients, persistent wheezing was present in 7.1% cases, recurrent cough was present in 21.4% cases and recurrent wheezing was present in 71.4% cases. 14.2% cases had a family history of asthma and 85.8% had no such family history. Among 60 patients those completed

the study, day cough and day wheezing were reduced to 30(50%) and 5(8.3%) respectively following the first month of low dose ICS therapy. Day cough and day wheezing were reduced to 10(16.6%) and 1(1.6%) after 2 months and after 3 months these were reduced to 1(1.6%) and 0% respectively. Night cough and night wheeze were reduced to 40(66.6%) and 20(33.3%) respectively after the first month of ICS therapy. After 2nd month these were reduced to 15(25%) and 5(8.3%) and after 3rd month these were 2(3.3%) and 0% respectively. Antibiotics received before initiation of ICS therapy 100% (n=70) and after initiation of ICS therapy was 16.6% (n=60). Hospital admission rate before initiation of ICS therapy was 66.66% (n=70) and after ICS therapy was 8.33% (n=60). Both hospital admission and need of antibiotics were reduced after the initiation of low dose ICS therapy which was statistically significant ($p < 0.01$). **Conclusion:** Our study has shown the improvement in symptoms and also decreases the use of antibiotics and reduces the frequency of hospitalization following treatment with low dose Inhaled Corticosteroid.

Key words

Wheeze; Bronchial asthma; Infant and Toddlers; Corticosteroid.

Introduction

Asthma is a disorder defined by clinical, physiological and pathological characteristics as follows. "Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment¹.

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Worldwide, an estimated 300 million people are affected by asthma². Based on the application of standardized methods to the measurement of the prevalence of asthma and wheezing illness in children and adults. It appears that the global prevalence of asthma ranges 1–18% of the population in different countries³. Its prevalence has been increasing in some countries but has stabilized or even begun to decline in others⁴⁻⁷. The WHO has estimated that 15 million disability-adjusted life are lost annually due to asthma, representing 1% of the total global disease burden⁸. The differences in the prevalence of asthma are more within developing countries than in developed countries⁹. Asthma is the second leading cause of death in Bangladesh according to Bangladesh Bureau of Statistics¹⁰. According to second National Asthma Prevalence Study (NAPS) during 2010 in Bangladesh it was estimated that out of 150 million people about 10.5 million (7%) have been suffering from bronchial asthma¹¹.

Material and methods

This was a prospective study done in the OPD of BGC Trust Medical College and Ibrahim Iqbal Memorial Hospital, Chandaniash, Chittagong and OPD of Child Care Center, Chawkbazar, Chittagong. Patients were enrolled from the rural and urban residential areas of different places of Chittagong. A total number of patients were enrolled 70. Study period was 3 months. Inclusion criteria were age between 4 months to 3 years, H/O recurrent wheeze (Occurring on at least 3 or more occasions in a month) documented wheeze at first consultation, children received previous oral bronchodilator, oral steroid and antibiotics, irrespective of personal or family history of atopy (Eczema, bronchial asthma, seasonal rhinitis). Children those were already using regularly Inhaled Corticosteroid, and had major congenital malformations were excluded from the study. All patients were studied with Beclomethasone Dipropionate HFA inhaler one puff (50 microgram) twice daily and Salbutamol inhaler 1-2 puffs (Each puff contain 100 micrograms) 3 to 4 times daily in conjunction with ICS when required. Equipment used for medication was a small volume spacer with mask. Bronchochamber or Respochamber with mask (Child). Open ended questionnaires were used to interview the Parents waiting in OPDs. Study was explained to parents

and they were given written consent. At first visit, thorough history, physical examination and weight, length/height was recorded from each subject. Parents were taught and given written instruction on the optimum use of Bronchochamber. Adverse effects of drugs were also explained to the parents. Parents were instructed to record symptoms of wheeze and cough in a diary. The number of puffs of Salbutamol and Beclomethasone Dipropionate HFA inhaler administered each day was also recorded in the diary. Each child was re-examined every 4 weeks interval throughout the study (3 visits within 3 months and emergency visit when required) and each visit symptoms analysis, inhaler techniques, weight, length/height and adverse effects of drugs were recorded. 60 patients had completed the study for the total 3 months and were included in analysis, 10 were lost during follow up. After the completion of whole study, data from diaries were analyzed for symptoms free days, exacerbations days, dose of salbutamol inhaler and inhaled Beclomethasone Dipropionate HFA, usage of antibiotics and frequency hospital admission were analyzed. Spirometry was not done in this age group to perform pulmonary functions. X-ray was done for each child to exclude other pathology. Data was analyzed by SPSS (Statistical Package for Social Sciences) 20.

Results

Table I: Patients' database (n=70)

Parameters	No	%
Age		
4 mo – 1 yr	39	55.72%
1 – 2 yr	20	28.57%
2 – 3 yr	11	16.29%
Mean age 19.5 months		
Sex		
Male	40	57.15%
Female	30	42.85%
Male to female ratio was 1.25:1		
Investigations		
Chest X-ray		
Normal	66	94.2%
Bronchopneumonia	4	5.8%

Table II : Distribution of presenting symptoms (n=70)

Parameters	No (%)
Recurrent wheeze	50 (71.4%)
Recurrent cough	15 (21.4%)
Persistent wheeze	5 (7.1%)

Table III : Diary analysis of symptoms for 3 months following ICS (n= 60)*

Parameters	First month (n, %)	2nd month (n, %)	3rd month (n, %)
Day cough	30(50%)	10(16.6%)	1(1.6%)
Day wheeze	5(8.3%)	1(1.6%)	0
Night cough	40(66.6%)	15(25%)	2(3.3%)
Night wheeze	20(33.3%)	5(8.3%)	0
Symptom free days	20 days	25 days	28 days
Exacerbation days	4 days	0	0

*10 patients were unable to maintain asthma diary so excluded from the analysis.

Table IV : Usage of Antibiotics in relation with ICS

Need of antibiotics	Number	Percentages	p value
Antibiotics received before initiation of ICS therapy	70	100%	<0.01
Antibiotics given after initiation of ICS therapy (n=60)	10	16.6%	

Table V : Frequency of hospital admission before and after ICS therapy

Need of hospital admission	Number	Percentages	p value
Hospital admission before initiation of ICS therapy (n= 70)	40	66.66%	<0.01
Hospital admission after initiation of ICS therapy (n= 60)	5	8.33%	

Table I showing age group distribution where 4 month to 1 year was 39(55.72%), 1- 2 years age was 20(28.57%) and 2- 3 years was 11(16.29%) and mean age was 19.5 months. Sex distribution of study patients where male was 40(57.15%) and female was 30(42.85%). Male to female ratio was 1.25:1. Normal chest X-ray was found in 66(94.2%) cases and bronchopneumonia was found in 4(5.8%) cases.

Table II showing the distribution of respondents by symptoms where persistent wheezing was present in 5(7.1%) cases, recurrent cough was present in 15(21.4%) cases and recurrent wheezing was present in 71.4% cases.

Table III showing analysis of symptoms for 3 months following ICS where at the first month day cough was present in 30(50%) cases and day wheezing was present in 5(8.3%) cases whereas it reduced to 10(16.6%) and 1(1.6%) after second months and after third months it reduced to 1(1.6%) and 0 respectively. Regarding night cough and night wheeze after first month it was 40(66.6%) and 20(33.3%) after 2nd month it was 15(25%) and 5(8.3%), after 3rd month it reduced to 2(3.3%) and 0 respectively. Symptoms free days were 20 days, 25 days and 28 days after first, second and third months respectively. Exacerbation days were 4 days in first month but it was 0 in second and third month.

Table IV showing antibiotics received before initiation of ICS therapy 100% (n=70) and after initiation of ICS therapy was 16.6% (n=60) which was statistically significant (p<0.01).

Table V showing hospital admission rate before initiation of ICS therapy was 66.66% (n=70) and after ICS therapy was 8.33% (n=60) which was statistically significant (p<0.01).

Discussion

In our study, 70 children of age 4 months to 36 months were enrolled. Mean age of our study was 19.5 months. The study showed that recurrent wheeze was more common in males than female (Male: female: 1.2:1). 60 patients completed the study for 3 months. Daily diary analysis of symptoms, we found a significant fall in daily symptoms associated with the rise in the number of symptoms free days with very low dose inhaled Beclomethasone inhaler (50 micrograms twice daily). A study by Kraemer and colleagues in Twenty-nine of initially 42 infants with recurrent wheeze (20 male and 9 female) with an age range of 2.1-25.2 months were randomly assigned to receive 100 micrograms Beclomethasone Dipropionate (BDP) twice daily combined with 200 micrograms salbutamol 3 times daily for a 6 weeks' treatment period¹². They had shown that use of low dose beclomethasone dipropionate improved the clinical status and lung function when given in combination with salbutamol by a

baby-adapted spacer device in wheezy infants. Cecil Vella also shown that ICS improves symptoms and reduce the number of exacerbations in infants and pre-school children with persistent wheezing¹³. Craig Mellis also found that reasonable trial period of ICS for 4-6 weeks in infant and toddlers reduction in symptoms and reduced the need for bronchodilators¹⁴. Stick and colleagues could not measure a response to Beclomethasone either by pulmonary function testing or symptom score, their only positive finding being a potentially beneficial effect on bronchial responsiveness¹⁵. Barrueto and colleagues conducted a double-blind, parallel, and placebo-controlled study in 31 children under age 2 years with recurrent wheezing with Beclomethasone Dipropionate (BDP) for 8 weeks¹⁶. At the end of the study, patients in both groups had significantly decreased symptoms. No significant difference was found between BDP and placebo groups regarding clinical score, the number of salbutamol doses, sleep disturbances, the number of symptom-free days. Castro-Rodriguez and Rodrigo also shown that Infants and preschoolers with recurrent wheezing or asthma had less wheezing/asthma exacerbations and improve their symptoms and lung function during treatment with inhaled corticosteroids¹⁷. Bisgaard and colleague found that intermittent inhaled corticosteroid therapy had no effect on the progression from episodic to persistent wheezing and no short-term benefit during episodes of wheezing in the first three years of life¹⁸. We used very low dose Beclomethasone inhaler (50 microgram twice daily) because there are few studies with beclomethasone inhaler and all of the studies used beclomethasone 100 -200 micrograms twice daily^{12,15,16,19}. Some studies have shown that use of large dose of ICS in young children whose wheezing persists should be discouraged.^{13,20} Many studies have shown an improvement in symptoms but all of them used fluticasone inhaler 100 – 150 micrograms twice daily^{13,14,17,18,21-25}. In our study, only 10 patients needed antibiotics and 5 patients required hospital admission due to bronchopneumonia and acute exacerbation respectively. We found that need of antibiotic and hospital admission rate are also reduced significantly ($p<0.01$). Boyer and colleagues showed unnecessary use of antibiotics

with use of ICS in infants with recurrent wheezing²⁶. Mutasim and Miles also shown that inhaled corticosteroid therapy reduces the use of antibiotics and hospital admission²⁷.

Conclusion

Management of recurrent wheezing in the infants and toddlers remain a challenging clinical problem. In our study, We have shown an improvement in symptoms and increase in symptoms free days, decreases the usage of antibiotics and hospitalization of infant and toddlers with recurrent wheezing following treatment with very low dose inhaled Corticosteroid. But our above findings do not reach significance because of relatively small size of the study and study duration. This needs to be re-examined in larger study for a longer period.

Disclosure

All the authors declared no competing interest.

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