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Original Research Article

Comparing the efficacy of Budesonide and Montelukast in children with asthma: a prospective interventional open label controlled clinical study

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ABSTRACT

Background: Bronchial asthma is a chronic inflammatory airway disease and is more prevalent in children. Inhaled corticosteroids (Budesonide) and leukotriene receptor antagonist (Montelukast) are the drugs of choice for asthma in children. The present study was aimed to compare the efficacy of these drugs in childhood asthma at tertiary care center.
Methods: This is a prospective interventional open label controlled clinical study carried out from January 2012 to December 2014. Children recently diagnosed with mild persistent asthma that attended Asthma clinic or admitted in ward of department of paediatrics LTMMC and Hospital, Sion, Mumbai was participated in the study. A total of 70 patients were selected for the study and are categorized into two groups consisting of 35 in each group. Group A patients were given metered dose inhaler (MDI) Budesonide 200 mcg 1 puff twice a day (with MDI spacer and mask for children <5 years and without mask for children >5 years. Group B patients were given Montelukast 4 mg (<5 years) and 5 mg (>5 years) tablet as once a daily in the evening for 1 year. Primary and secondary outcome measures were calculated and analysed.
Results: No significant difference on the basis of age and gender was observed among both groups. The complaints of cough, wheeze and breathlessness, lesser emergency department visits, nebulization and lesser number of systemic steroids (days/year) was significantly lesser in patients of group A ($p<0.05$) compared to group B. Group A subjects had lesser number of acute exacerbations, required lesser number of systemic steroids courses and the frequency of hospitalization. Statistically significant ($p<0.05$) difference was observed in episode free days in a year among both groups.
Conclusions: The findings of the study prove that Budesonide had better efficacy over Montelukast in control of asthma.

Keywords: Asthma, Budesonide, Efficacy, Montelukast

INTRODUCTION

Asthma is a chronic inflammatory disease of the airways that causes serious illness in childhood.[1] It causes respiratory symptoms that are interposed with serious attacks, which needs immediate health care and may be fatal.[2] The burden of asthma is immense, with more than 300 million individuals currently suffering from asthma worldwide, about 1/10th of those living in India.[3] The prevalence of asthma has been estimated to range 3-38% in children, being the commonest chronic disorder among children. Incidence of asthma is increasing worldwide and greatest prevalence is increasing in children. Even with the advances in the asthma management the incidence of asthma is still remains same.[4] All recent guidelines now advocate aggressive treatment of airway

inflammation. But clinical utility of asthma therapy for paediatric age group is limited by a narrow therapeutic Index, long term tolerability, frequency and difficulty of administration of drugs.[5] Inhaled corticosteroids (Budesonide) and leukotriene receptor antagonist (Montelukast) are the drugs of choice for mild persistent asthma in children. Inhaled corticosteroids are most commonly used therapy while Montelukast has the ease of administering once daily tab/granules. Also, it seems to lack the adverse effect on growth, bone mineralization and on the adrenal axis, associated with long term steroid therapy.[6]

Multiple expert panel including National Asthma Education and prevention program (NAEPP) and Global Initiative for Asthma (GINA) have published goals of asthma management along with guidelines regarding assessment of asthma severity and suitable pharmacotherapy.[7] Although most of the studies concentrate on the improvement in the lung function (PEF, FEV1, FEV1/FVC ratio), requirement of use of beta agonist, day/night time symptomatic relief following treatment of asthma, all these measures are short term measures to assess control of asthma. Long term measures to assess control of asthma are number of acute exacerbations, need for systemic corticosteroids, school/work absenteeism (limitation of daily activities), hospital/emergency department visits and quality of life of the patient.

Our primary outcome measure was episode free days (EFDs) over 1 year. Episode free day was defined as a day during which the child was free from - cough, wheeze, breathlessness, limitation of daily activity, sleep disturbance, ED visit or hospitalization for acute exacerbation. It reflects multiple components of asthma disease burden. It is also more informative in comparing the effects of long term controller medications for asthma in patients with chronic symptoms. So, we decided to compare the long-term efficacy of Budesonide vs. Montelukast in children with mild persistent asthma at tertiary care center using EFDs as primary outcome.

METHODS

This prospective interventional open label controlled clinical study was carried out from January 2012 to December 2014. Children recently diagnosed with mild persistent asthma that attended Asthma clinic or admitted in ward of Department of Paediatrics, LTMMC and Hospital, Sion, Mumbai was participated in the study. An informed written consent was taken from the parents. Institutional ethics committee approval was taken.

Detailed history (including perinatal history, family history and allergen history) of the patients were collected. On the day of enrollment, general examination and baseline investigations like complete blood count with absolute eosinophilic count, chest X-ray, pulmonary function test (whenever feasible mostly children >6 years of age) were done.

Children's of both sexes of age between 2-12 years and with symptoms suggestive of recurrent airflow obstruction like recurrent wheeze, recurrent isolated cough, recurrent breathlessness, nocturnal cough, tightness of chest, with signs of generalized air flow obstruction and patients having more than 3 episodes of airflow obstruction were included in the study.

Those patients with age <2 years, recurrent respiratory tract infections, chronic respiratory diseases (e.g. cystic fibrosis, tuberculosis), congenital anomalies of respiratory tract (e.g. laryngomalacia), congenital heart disease, chronic asthmatics who are on prior controller medications, any patient requiring step up or addition of new drug for control of asthma, patient having adverse drug reaction (ADR) requiring change of medication were excluded from study.

Patients were randomized by using computer generated random number sequence into two groups of 35 each and accordingly medications were given.

Group A: patients were given metered dose inhaler (MDI) Budesonide 200 mcg 1 puff twice a day (with MDI spacer and mask for children <5 years and without mask for children >5 years.

Group B: patients were given Montelukast 4 mg (<5 years) or 5 mg (>5 years) tablet as once a daily in the evening for 1 year.

Parents were taught how to use MDI Budesonide with spacer and also about the dose frequency and route of administration of medication. Patients were followed over 1 year after starting medication. Follow-up was done monthly and as and when patient is symptomatic. During course of study, exacerabations were treated with standard protocol of asthma management (GINA guidelines).

Parents were advised to keep diary in which columns were made including cough, wheeze, breathlessness, limitation of daily activities, sleep disturbance, emergency department visit, hospitalization for acute exacerabation and the treatment received for these exacerabations (number of oral steroid doses/course, number of days nebulization required). Daily records of these days were maintained by parents in diary and were noted monthly in our follow up record sheet.

Our primary outcome variable was proportion of episode free days (EFDs) in each group. An episode free day is defined as a day during which the child was free from-cough, wheeze, breathlessness, limitation of daily activity, sleep disturbance due to emergency department (ED) visit or hospitalization for acute exacerbation.

Secondary outcome measures were number of systemic (oral/intravenous) corticosteroids courses, number of days of systemic (oral/intravenous) corticosteroids used, number of episodes of rhinitis, number of days of treatment for rhinitis, number of visits to emergency department (ED), number of days nebulization required, number of days of hospital admission for acute exacerbation.

Statistical analysis

The statistical analysis was done using SPSS Software Ver. 17. Qualitative data (sex) were described with frequency and Percentages and were compared using Chi-Square test. The Quantitative data (age, mean episodes) were described as mean and standard deviation and were compared using Student's t-test. The ordinal data (mean episodes, mean visits) were compared using Man-Whitney's test. The p-value of <0.05 was considered as significant.

RESULTS

Total 100 asthmatic patients were screened and 70 patients with mild persistent asthma were enrolled in our study according to inclusion criteria. These patients were randomised by using computer generated random number sequence into two groups of 35 each and accordingly medications were given. Group A (n=35) received MDI Budesonide (200 mcg/puff) 1 puff twice a day and group B (n=35) received tablet Montelukast 4 or 5 mg once a day. Group A had four dropouts and group B had three dropouts (Figure 1).

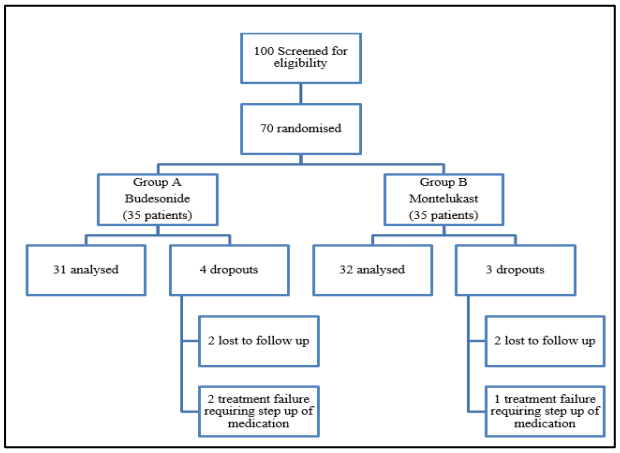

Figure 1: Flow chart of the study.

As shown in Table 1, most of the patients in group A (16) were more than 5 years of age whereas in group B most of them (19) were ≤5 years. As per age wise distribution both groups were comparable as the statistical difference was insignificant (p=0.38).

No significant difference on the basis of gender was observed among both groups. Though the females patients were more in group A (67.7% vs. 50%), this difference was statistically insignificant (p=0.24).

Table 1: Demographic data of the patients.

Variables	Group		P-value
	A	B	
Age (years)			
≤5 years	15	19	0.38
>5 years	16	13	
Sex			
Male	10	16	0.24
Female	21	16	

The mean age of study subjects in group A and B was 5.7 and 5.5 years respectively. The age difference was statistically not significant (unpaired t-test; p=0.78). Similarly, the age of onset of asthma in both groups was statistically insignificant (2.6 vs. 3.9 years; p=0.08) as given in Table 2.

Table 2: Distribution of patients on the basis of mean age and age at onset.

Variable	Group	Mean	SD	P-value
Age (years)	A	5.7	3.3	0.78
	B	5.5	3.0	
Age at onset (years)	A	2.6	2.5	0.08
	B	3.9	3.2	

Table 3: Comparison of baseline parameters between group A and group B.

Parameters	Mean duration in a year (days) in mean±SD		t value	P value
	Group A	Group B		
Cough	12.6±6.0	18.3±8.0	-3.19	0.002
Wheeze	3.0±2.9	5.8±5.3	-2.64	0.011
Breathlessness	2.5±2.7	5.3±4.7	-2.87	0.006
Limitation of daily activity	2.3±2.4	5.5±5.1	-3.19	0.002
Sleep disturbance	2.7±2.7	6.3±5.2	-3.41	0.001
School absenteeism	2.8±3.3	4.9±5.2	-1.96	0.05
Nebulization	3.6±3.5	7.1±6.3	-2.75	0.008
Systemic corticosteroids	4.0±3.8	8.0±6.9	-2.87	0.006
Rhinitis	9.5±6.8	12.8±8.8	-1.68	0.098
Emergency department visits	1.1±1.0	2.2±1.8	-2.9	0.005

On the basis of various parameters, it was found that subjects of group A had significantly lesser limitation of daily activities, sleep disturbance and school absenteeism. Group A subjects also required significantly lesser

emergency department visits, nebulization and lesser number of systemic steroids (days/year) than group B.

Table 4: Comparison mean episodes in a year between group A vs. group B.

Variables	Mean duration in a year (days) in mean±SD		t-value	P value
	Group A	Group B		
Acute exacerbations	1.2±1.0	2.2±1.9	-2.70	0.009
Frequency of hospitalization	0.4±0.7	1.2±1.0	-3.62	0.001
No. of corticosteroid courses	0.9±0.9	1.9±1.5	-3.03	0.004
Rhinitis	2.4±1.6	2.9±1.8	-1.05	0.298

As shown in Table 4, group A subjects had lesser number of acute exacerbations and required lesser number of systemic steroids courses.

The frequency of hospitalization was also significantly lower in group A patients (p< 0.05). However, in case of number of episode of rhinitis difference was statistically insignificant.

On comparing the episode free days in a year among both groups, we found that patients of group A had 352.4 days without any symptoms across a year as compared to 347.0 days in patients of group B. The difference was statistically significant (p<0.05) with t value 2.88 as shown in Figure 2.

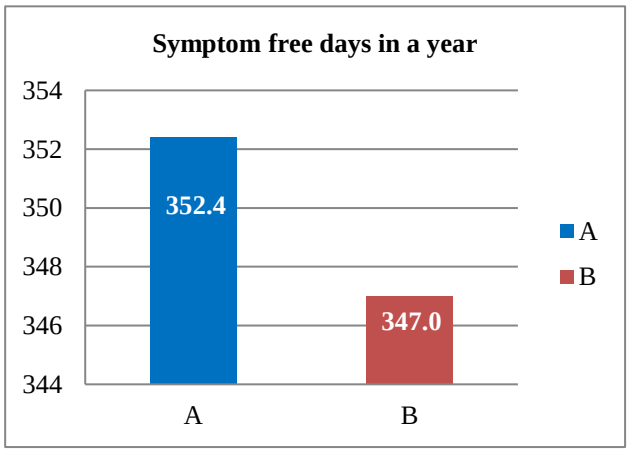

Figure 2: Distribution of patients on the basis of episode free days.

DISCUSSION

This study includes 100 patients with physician diagnosed asthma in the age group less than 12 years were screened for the study, of these, seventy patients who fulfilled our study criteria were enrolled in our open label, randomized control study and were randomized in to two groups by lottery method, group A (n=35) were started on inhaled Budesonide (200 mcg/puff, 1 puff BD) and group B (n=35) were started on Montelukast (4/5 mg OD). From Budesonide group four were excluded (2 lost to follow up and 2 treatment failure) and from Montelukast group three (2 lost to follow up and 1 treatment failure) were excluded so from group A total 31 patient and group B total 32 patient completed study.

Similar study done by Szefler et al in 52 weeks trial, open-label, randomized, active-controlled, multicenter study; 328 Children with mild asthma between 2 to 4 years were screened. Out of these 202 children were randomized and received either Budesonide (n=105) 0.5 mg or Montelukast (n=97) 4 to 5 mg once daily.[9]

In present study, we found that the mean age of study subjects in Budesonide group and Montelukast group was 5.7 (SD=3.3) and 5.5 (SD=3) years respectively. The mean age of onset of asthma in Budesonide group was 2.6 (SD=2.5) and in Montelukast group was 3.9 (SD=3.2 years), so both groups were comparable and found to be was statistically insignificant. These observations are similar with the results of Szefler et al.[9] In another study of Raghava et al, the mean age of the children in Budenoside group was 12.7±3.51 years and in group Montelukast group was 14.07±3.36 years.[10] The mean age of onset of symptoms was not mentioned in this study.

In present study, female preponderance was observed in both groups; group A had 21/31 females and group B had 16/32 females. Similar female preponderance was observed by Karaman et al.[11]

In our study, mean days of cough/year was 12.6 (SD=6) in Budesonide group and 18.3 (SD=8) in Montelukast group. Also mean days of wheezing/year in Budesonide group was 3.0 (SD=2.9) and on Montelukast group was 5.8 (SD=5.3). Mean days of breathlessness/year was 2.5 (SD=2.7), 5.3 (SD=4.7) with Budesonide and Montelukast respectively. These symptoms were significantly less in Budesonide group. But in case of number of days of rhinitis/year both groups were comparable 9.5 (SD=6.8) vs. 12.8 (SD=8.8) and difference was not significant (p=0.098). Our study also found that budesonide group had significantly lower limitation of daily activities (number of days/year) 2.3 (SD=24) vs. 5.5 (SD=51) and sleep disturbance (number of days of sleep disturbance/year) 2.7 (SD=2.7) vs. 6.3 (SD=5.2). They also had less school absenteeism (number of days of school absenteeism/year) 2.8 (SD=3.3) vs. 4.9 (SD=5.2). Similar favourable response with Budenoside in the treatment of asthma was observed in the studies of Szefler et al.[9]

We also found that patient on Budesonide group had lesser acute exacerbation of asthma 1.2 (SD=1.0) vs. 2.2 (SD=1.9), required lesser hospitalization 0.4 (SD=0.7) vs. 1.2 (SD=1.0) and lesser number of systemic

corticosteroid courses 0.9 (SD=0.9) vs. 1.9 (SD=1.5) with p values being 0.009, 0.001, 0.004 respectively. These findings were statistically very significant. Present findings are consistent with the studies of Szefler et al.[12]

The primary outcome in present study was number of episode free days in both group, which was 352.4 days in Budesonide group and 347.0 days in Montelukast group. This showed better efficacy of Budesonide over Montelukast (p=0.005) in control of asthma. Similar observations were also made by Biswas et al on 100 patients and stated that metered dose inhaled corticosteroids are superior than oral Montelukast in mild persistent childhood asthma.[13] Similarly Vidal et al, compared Montelukast vs. Budesonide in the treatment of exercise-induced bronchoconstriction. Budesonide showed significantly better response over montelukast.[14]

CONCLUSION

Our study concludes that Budesonide group showed better symptomatic control in case of cough, wheezing and breathlessness also they had lesser limitation of daily activities, sleep disturbance and school absenteeism. Budesonide group had better outcome in terms of lesser acute exacerbations, lesser emergency department visits, lesser nebulization and systemic steroid requirement. Both drugs had similar efficacy in controlling rhinitis. Budesonide group had shown significantly more episode free days than Montelukast which proves better efficacy of Budesonide over Montelukast in control of asthma.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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