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Comparison of montelukast versus montelukast plus inhaled corticosteroid (Budesonide) in children with mild persistent asthma.

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ABSTRACT… Objective: To compare therapeutic response between Montelukast versus Montelukast plus inhaled corticosteroid (Budesonide) in children having mild persistent asthma. **Study Design:** Randomized Controlled Trial. **Setting:** Department of Pediatrics Medicine, National Institute of Child Health, Karachi. **Period:** 1st April 2016 to 30th September 2016. **Material & Methods:** Children aged 2 years to 14 years having mild persistent asthma for more than 6 months were included. After treatment Good response was considered when, forced expiratory volume in first second (FEV1) became >7.5% from baseline. Group A was given montelukast as monotherapy once daily and Group B was given Montelukast along with inhaled corticosteroid (Budesonide. At 6 weeks followup change in FEV1 was recorded. **Result:** Mean age of the patients in montelukast alone (Group A) was 6.77+/-2.16 years while in montelukast with Inhaled Corticosteroid (Group B) was 6.97+/-2.17 years. Duration of disease in Group A was 18.32+/-6.12 months while in montelukast with ICS group was 18.50 +/-6.08 months. Baseline FEV1 in Group A was 81.83+/-0.85% while in Group B was 82.05 +/-0.63%. Males were higher with 131 (61.8%). Family history was positive in 82 (38.70%) patients. After 6 weeks mean FEV1 was 89.49 +/-0.87% in Group A while in Group B was 89.53+/-0.86%. Overall good responses were found in 21 (9.09%) patients. In Group A, good response was found in 5 (4.7%) patients while in Group B was in 16 (15.1%) with significant p-value. **Conclusion:** In our study montelukast along with inhaled steroids had better response than montelukast alone in mild persistent asthma.

Key words: Asthma, Chronic Airway Disease, Forced Expiratory Volume, Leukotriene Inhibitors.

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INTRODUCTION

Asthma is a chronic inflammatory airway disease with increased responsiveness to various stimuli, manifesting as peroxisomal difficulty in breathing, wheezing or cough. Airway obstruction is reversible either spontaneously or in response to medical treatment.[1] Asthma is categorised in mild intermittent, mild, moderate and severe persistant based on day and night time symptoms. Children with mild persistent asthma have respiratory symptoms > 2 days/week or night times awakenings >2/month. Asthma therapy is directed to control asthma so that the child can lead a normal life. There should be minimal asthma symptoms, maintain normal activity with good sleep, can grow normally, attend school regularly and participate in all school activities including sports without any asthma exacerbations.[2]

In mild persistent asthma, Montelukast may be used as a monotherapy or in addition to Inhaled Corticosteroids for improving clinical manifestations.[3] According to GINA guidelines for children 2015, the preferred controller therapy is low dose inhaled corticosteroid (ICS) on daily basis. For achieving good control, atleast 3 months of therapy is indicated. Leukotriene receptor antagonist (LTRA) may be considered as an alternate therapy.[4] Previous studies showed that at the end of 6 months therapy, 86.4% of children were well controlled and 13.6% were not well controlled on Montelukast monotherapy.[5]

Hypothesis of this study was that "Montelukast

along with inhaled corticosteroids is better than montelukast alone in mild persistent asthma". Previous studies showed variable results among montelukast alone verses inhaled corticosteroids used in children with mild persistent asthma but studies on montelukast alone and with inhaled corticosteroids in mild persistent asthma is scarce. Therefore the present study is designed to compare the response of orally administered montelukast alone versus inhaled steroids and montelukast.

MATERIAL & METHODS

This Randomized controlled trial was performed at Pediatrics Medicine Department, NICH, Karachi from 1st April 2015 to 30th September 2015. Sample size was 212 that is calculated with 5% Significance level (α), 17% population proportion and Power of the test= 80%. In each group there were 106 children, selected with Non-probability consecutive sampling technique. Children aged 2years to 14 years with mild persistent asthma for more than 6 months and belonging to either gender were included in the study.

Mild persistent asthma was categorized in patients having cough and/or difficulty in breathing at day time more than once a week or more than two night symptoms per month and FEV1 more than 80 % of the normal.

Response was considered good when at the end of 6 weeks treatment FEV1 increased to more than 7.5% from baseline and poor if FEV1 increased <7.5% from the baseline. Children with other chronic lung disorders, moderate asthma, sever asthma or if already on any controller therapy were not enrolled for study.

This study was undertaken after approval from RTMC, college of physicians and surgeons Pakistan. Study was carried out at out-door department of Pediatrics Medicine, NICH, Karachi. The patients who fulfilled the inclusion criteria were enrolled and informed consent was taken. Children were divided into 2 groups on the basis of choosing an sealed envelops having cards in it bearing either group A or group B. Envelop was picked by a person who was not involved in this research study, after that group allocation was done. Baseline FEV1 was recorded in all patients. Group A was given only montelukast (4 mg for 2–5 year olds children and 5mg for 6–14 year olds children). It was given at bedtime by parents for total 6 weeks duration. In Group B inhaled corticosteroid therapy was added (100 microgram budesonide in 2-<6years and 200 microg for 6-14yrs old children). After 6 weeks of therapy FEV1 was remeasured and considered good if response was more then 7.5% of the baseline.

Variables like gender, age, disease duration, history of asthma in family, baseline and 6 weeks FEV1 and response (poor or good) was recorded on predesigned proforma. SPSS version 22 used for data analysis. Qualitative variable like Sex of children, history of asthma in family were measured by using frequency and percentage. Quantitative variables like age of children, disease duration, baseline and 6 weeks FEV1 were computed for Mean ±SD. To compare the response between the two groups, Chi square test was used, Significant p value was <0.05. For analysing outcome effect stratification was done for age, sex and disease duration.

RESULT

Total number of patients included in this study was 212 (106 in each group). Age and gender distribution is shown in Table-I and distribution of mean age, mean duration of disease and baseline FEV1 in two groups with P-value are shown in Table-II. There was no significant difference in these parameters in both groups. Male preponderance was found to be higher with 131 (61.8%). Family history of asthma was present in 82 (38.70%) patients.

After 6 weeks FEV1 was 89.49 +/-0.87% in montelukast alone group while in montelukast with ICS group mean FEV1 after 6 weeks was 89.53+/-0.86% (Table-III). Overall good responses were found in 21 (9.09%) patients. In montelukast alone group, good response was found in 5 (4.7%) patients while in montelukast with ICS group good response was found in 16 (15.1%). Chi-square test was applied and p-value

was found <0.011. (Table-III). Stratification was done to see the effect of age, duration of diseases and gender on the outcome. (Table-III)

DISCUSSION

In this study we found that the montelukast alone group had good response in 5 (4.7%) patients while in montelukast with ICS group, good response was found in 16 (15.1%). Similar findings was found in a study in which there was good response in 17% children on inhaled steroids along with montelukast, while 23% children had good response on inhaled steroids alone and 5% on montelukast. 55% children did not responded to either medication.[6] An international meta-analysis study demonstrated that fluticasone was better than montelukast. 33% patients benefited more from fluticasone than montelukast.[7]

Another Indian study showed better response with inhaled Budesonide compared to Montelukast. There was improvement in PEFR, FEV1/FVC as well as day and night time symptoms.[8] While in another indian study at the end of 6 months, 89 children (86.4%) were found to be well controlled with montelukast alone.[9] In a international study subjects, who took inhaled corticosteroids had significantly lesser limitation of daily activities, sleep disturbance and school absenteeism as compared to children who took montelukast.[10] In

Variables	Group-A	Group-B	Total
	N (%)	N (%)	N (%)
Male	80 (38)	51 (24)	131 (62)
Female	26 (12)	55 (26)	81 (38)
Age Group			
2-8 years	23 (11)	26 (12)	49 (23)
8-14 years	83 (39)	80 (38)	163 (77)
Total	106 (50)	106 (50)	212 (100)

Table-I. Age and gender distribution (n=212)

Parameters	Group A (n=106) (Monteleukast Monotherapy)	Group B (n=106) (Monteleukast & ICS)	P-Value
Mean Age	6.77+/-2.16 years	6.97+/-2.17 years	0.5020
Mean Duration of Disease	18.32+/-6.12 months	18.50+/-6.08 months	0.8301
Baseline FEV1	81.83+/-0.85%	82.05+/-0.63%	0.0334

Table-II. Distribution of age, mean duration of disease and baseline FEV1 in two groups. (n=212)

		Montelukast (Group A) n=106			Montelukast + ICS (Group B) N=106			P-Value
		Mean	S.D	95% C.I	Mean	S.D	95% C.I	
		89.49	0.875	89.32-89.65	89.53	0.86	89.34-89.66	0.7375
Good Response		Yes	No	Total	Yes	No	Total	
		5 (4.7)	101 (95.3)	106 (100)	16 (15.1)	90 (84.9)	106 (100)	0.011 0.011
Response between groups with respect to age groups	<8yr	1 (4.3)	22 (95.7)	23 (100)	6 (23.1)	20 (76.9)	26 (100)	0.062
	>8yr	4 (4.8)	79 (95.2)	83 (100)	10 (12.5)	70 (87.5)	80 (100)	0.080
Response between groups with respect to gender	M	2 (2.5)	78 (97.2)	80 (100)	13 (25.5)	38 (74.5)	51 (100)	0.001
	F	3 (11.5)	23 (88.5)	26 (100)	3 (5.5)	52 (94.5)	55 (100)	0.329
Response between groups with respect to duration of diseases	≤ 20 months	1 (2)	48 (98	49 (100)	9 (17.6)	42 (82.4)	51 (100)	0.009
	> 20 months	4 (7)	53 (93)	57 (100)	7 (12.7)	48 (87.3)	55 (100)	0.310

Table-III. showing comparison in both groups for FEV1 after 6 weeks (n=212)

a study 28% children on montelukast controller therapy had acute exacerbations of asthma.[11] According to a study, combined steroid and montelukast therapy versus only montelukast had same results.[12] In an international study after 8-week treatment, patients who received combined montelukast and inhaled corticosteroid had better outcome in lung function, compared with patients who took only budesonide.[13] A study compared the efficacy of montelukast combined with inhaled corticosteroid versus only inhaled corticosteroid. After 12 weeks of therapy, there was no significance difference in the efficacy among both groups.[14] In a study inhaled corticosteroids plus montelukast was superior to inhaled corticosteroid plus theophylline therapy in improving FEV1 in asthmatic children.[15]

CONCLUSION

In our study the response of montelukast along with inhaled steroids was better than montelukast alone in children with mild persistent asthma.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Versha Rai	Concept design, Data research, Final approval.	
2	M. Nadeem Chohan	Data analysis, Drafting, Final approval.	
3	Nazimuddin	Data collection concept design, Final approval.	
4	Khuda Bux	Critical analysis, Final approval.	
5	Saadullah Chacher	Drafting, Final approval.	