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Research Article

Effect of montelukast as monotherapy in mild persistent asthma

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ABSTRACT

Background: Leukotriene Receptor Antagonists (LTRAs) have a role in moderate and severe persistent asthma as a steroid sparing agent. The role of these agents as monotherapy in mild persistent asthma still needs to be determined. Montelukast is FDA approved for use in children >1 year of age. This study was done to assess the effect of montelukast as monotherapy in children with mild persistent asthma.
Methods: A prospective interventional study was conducted in Department of Pediatrics in Chennai Medical College Hospital and Research centre, Trichy, India from June 2014 to August 2015. A 12 week interventional trial to compare the effect of montelukast with placebo in children with mild persistent asthma and 6 months follow up of cases and controls. The assessment was done by clinical scoring and peak expiratory flow rate (PEFR).
Results: At the end of 12 weeks therapy and at 3 months follow up symptom control was significant in the montelukast group. The difference in clinical assessment scoring and PEFR between the montelukast group and placebo group was statistically significant ($p<0.01$). However at 6 months follow up symptom control in the montelukast group was not significant and the difference between the two groups was not statistically significant ($p>0.05$).
Conclusions: Montelukast provides significant symptom control and improvement in PEFR in mild persistent asthma compared to placebo. It is effective as monotherapy in mild persistent asthma in children aged 2-12 years. Symptom control is good during therapy and until three months after discontinuation of drug.

Keywords: Montelukast, Clinical scoring, PEFR

INTRODUCTION

The cysteinyl leukotrienes cause bronchoconstriction, increased mucus production and airway inflammation, three major features of asthma. Several randomized controlled trials have shown the efficacy of leukotriene receptor antagonists for improving asthma outcomes.[1] The drug is favored for treating childhood asthma, where poor compliance with inhalation therapy is a therapeutic challenge. Placebo-controlled trials of montelukast once daily in preschoolers and in school-aged children with persistent asthma have demonstrated efficacy on clinical outcomes including increase in proportion of asthma-free days, reduction in daytime and night-time asthma symptoms, and reduction in requirement for SABA and oral corticosteroids. The onset of action of montelukast is rapid and sustained, with benefits observed within the first day of treatment. The greatest benefits have been observed in children with relatively mild asthma. This study was done to assess the effectiveness of Montelukast as monotherapy in children with mild persistent asthma, including a 6 months follow up of cases and controls.

METHODS

A prospective interventional study conducted in Chennai Medical College Hospital and Research centre, Irungalur, Trichy during the period of June 2014 to August 2015. All children aged 2 to12 yrs attending respiratory care unit with criteria fitting for mild persistent asthma (Symptoms-day >2/week but <1/day, night->2/month) and not on any prophylaxis were included in the study. The parents were informed of the study and written consent was obtained. Detailed history regarding age of

onset of symptoms, family history of atopy, frequency of symptoms and medications taken were recorded. Clinical assessment scoring (Table 1) based on common symptoms of asthma was done for all children. Peak expiratory flow rate (PEFR) was recorded using a peak expiratory flow meter for children aged above 5 years. The enrolled children were randomly allocated into two groups The first group were started on montelukast and the second group on placebo. Parents were instructed to get drugs every 15 days at the RCU clinic of our institution. The drugs were prescribed as a single dose to be taken in the evening. Clinical assessment scoring and PEFR were recorded at each visit. 12 weeks of therapy was given to both cases and controls. After completion of therapy parents were motivated for monthly follow up for 6 months. All children on inhaled corticosteroids and those with previous hypersensitivity to montelukast were excluded from the study.

Interpretation of scoring
Total score - 12
< 4 - Symptoms under control.
> 4 - Symptoms not under control.
Drug dosage regimen
Cases
2 - 4 yrs - 4 mg tab of montelukast od for 12 weeks.
> 4 yrs - 5 mg of montelukast od for 12 weeks.
Controls
Multi vitamin tablets -1 od for 12 weeks.

RESULTS

A total number of 155 children with mild persistent asthma who matched the inclusion criteria were enrolled in the study. The enrolled children were randomly allocated in two groups, cases and controls. Drug therapy was given for 12 weeks and subjects were followed up for 6 months. The information collected was recorded in a master chart. Data analysis was done with SPSS software, version 11.Using this software, percentages, means, standard deviation, paired t test, p values were calculated. Paired t test was used to test the statistical significance of the difference in the scoring pattern and peak expiratory flow rate before and after therapy. A 'p' value of less than 0.05 was taken to denote significant relationship.

The 155 enrolled children were randomly allocated into 78 cases and 77 controls. 10 cases did not complete therapy and 8 cases did not come for follow up. 12 controls did not complete therapy and 5 controls did not complete follow up. So, only 60 cases and 60 controls completed therapy and follow up (Table 2).

Of the 60 cases 25 were less than 5 years, 24 were 6 to 10 years, and 11 were more than 10 years. Of the 60 controls 23 were less than 5 years, 26 were 6 to 10 years, and 11 were more than 10 years (Table 3).

Of the 60 cases, 8 cases had clinical assessment scoring between 4 to 6, 43 cases had scores between 6 to 9 and 9 cases had scores between 9 to 12. Of the 60 controls, 1 case had clinical assessment scoring between 4 to 6, 50 cases had scores between 6 to 9 and 9 cases had scores between 9 to 12 (Table 4).

Table 1: Clinical assessment scoring.

Parameter	0	1	2	3
Cough	None	Occasional	Frequent	Continuous
Wheeze	None	Mild	Medium	Severe
Activity	Normal	Can run short distance	Can walk only	Missed school
Sleep	Fine	Slept well/slight cough or wheeze	Awake 2-3 times, wheeze and/or cough	Badnight, Awake all the night

Table 2: Base line data.

	Cases	Controls
Enrolled	78	77
Completed therapy and follow up	60	60
Drop outs during therapy	10	12
Drop outs during follow up	8	5

Table 3: Age distribution of cases and controls.

Age in Years	Cases		Controls	
	No. of patients	%	No. of patients	%
≤ 5 years	25	41.7	23	38.3
6 – 10 years	24	40.0	26	43.3
≥ 10 years	11	18.3	11	18.3
Total	60	100	60	100

Table 4: Classification of cases according to clinical scoring.

Clinical scoring	Cases	Controls
4 - 6	8	1
6 - 9	43	50
9 -12	9	9

Cases versus controls

In this study among the 60 cases the mean clinical assessment scoring before therapy was 8.20 (out of 12). At the end of 12 weeks of therapy, the mean clinical scoring decreased to 1.93 (out of 12). On follow up after completion of therapy, at 3 months the mean scoring increased to 4.05 (out of 12). After 6 months of completion of therapy the mean scoring increased to 6.30

(out of 12). Among the controls the mean clinical scoring before therapy was 8.48 (out of 12). At the end of 12 weeks of therapy, the mean clinical scoring was 8.02 (out of 12). On follow up after completion of therapy, at 3 months the mean scoring was 8.17 (out of 12). After 6 months of completion of therapy the mean scoring was 8.05(out of 12). At the end of therapy and at 3 months follow up the difference in clinical assessment scoring between cases and controls was statistically significant(p<0.01). However scoring at 6 months follow up did not show a significant difference between the two groups (p > 0.05) (Table 5).

Table 5: Clinical assessment scoring.

Clinical assessement scoring	Cases (n=60)		Controls (n=60)		'p' value
	Score (out of 12)	S.D	Score (out of 12)	S.D	
Before Therapy	8.20	1.35	8.48	1.07	
End of 12 weeks of Therapy	1.93	1.18	8.02	1.44	< 0.01 Significant
3 months follow up	4.05	1.32	8.17	1.33	< 0.01 Significant
6 months follow up	6.30	1.32	8.10	1.28	> 0.05 Not Significant

Table 6: Peak expiratory flow rate.

Pefr	Cases (n=34)		Controls (n=35)		'p' value
	Mean % (Expected > 80%)	S.D	Mean % (Expected > 80%)	S.D	
Before Therapy	82.65	1.64	83.15	2.02	
End of 12 weeks of Therapy	92.18	3.22	82.61	1.97	<0.01 Significant
3 months follow up	86.19	2.50	82.46	1.67	<0.01 Significant
6 months follow up	84.22	1.81	82.40	1.73	>0.05 Not Significant

Cases versus controls

PEFR was recorded in all children above 5 years. Of the 34 cases for whom PEFR was recorded, the mean recording before therapy was 82.65%. At the end of 12 weeks of therapy the mean recording increased to 92.18 %. After completion of therapy, at 3 months follow up mean recording was 86.19%. At 6 months follow up after therapy the mean recording decreased to 84.22 %.Among the 35 controls for whom PEFR was recorded, the mean recording before therapy was 83.13%. At the end of 12 weeks of therapy the mean recording decreased to 82.61 %. After completion of therapy, at 3 months follow up the mean recording was 82.46%. At 6 months follow up after therapy the mean recording was 82.40%. At the end of therapy and at 3 months follow up the difference in PEFR between cases and controls was statistically significant (p<0.01). However the PEFR recording at 6 months follow up did not show a significant difference between the two groups(p>0.05) (Table 6).

DISCUSSION

In our study out of the 155 enrolled children only 60 cases and 60 controls completed therapy and follow up. Of the 60 cases 33 had a positive family history of asthma and of the 60 controls 36 had a positive family history.

At the end of 12 weeks therapy and at 3 months follow up symptom control (score <4/12) was significant in the montelukast group. The difference in clinical assessment scoring between the montelukast group and placebo group was statistically significant (p <0.01). However at 6 months follow up symptom control in the montelukast group was not significant (>4/12) and the difference between the two groups was not statistically significant (p>0.05). Similarly at the end 12 weeks of therapy and at 3 months follow up the improvement in PEFR in the montelukast group when compared with the placebo group was statistically significant(p<0.01). However the PEFR recording at 6 months follow up did not show a significant difference between the two groups(p>0.05).

In the study done by Wei-Fong Wu CY, et al,[1] montelukast was given once daily for 12 consecutive weeks. By the end a significant improvement of the daytime asthma symptom score, night time asthma score, peak expiratory flow rate (PEFR) and mean score of the investigators global evaluation was noted (p<0.05). These results suggest that montelukast is an effective monotherapy controller in children with mild persistent asthma. The drug is favored for treating childhood asthma, where poor compliance with inhalation therapy is a therapeutic challenge.

Bisgaard H et al,[2] in their study, Montelukast significantly reduced the rate of asthma exacerbations by 31.9% compared with placebo. In our study no significant relation was found between age group, sex, age of onset of symptoms, family history and response to the drug. None of the previous studies have included long term follow up of patients after montelukast trial. This study shows that montelukast is an effective controller medication in mild persistent asthma as long as the drug is taken. Symptoms tend to recur about 3 months after the discontinuation of drug. However there is a decrease in the frequency of symptoms even at 6 months after completion of therapy.

Straub et al,[3] found that LTRAs are generally safe and well tolerated, with an overall incidence of adverse events that is similar to placebo. The side effects of

corticosteroids are well known and LTRAs, which have better safety profiles than ICS, can offer an alternative early intervention treatment in infants and young children with mild asthma. In our study also, except for the defaulters and those who lost follow up, regular compliance was noted in both groups. None of the subjects reported any side effects during therapy.

Global Initiative for Asthma (GINA)[4] and Expert Panel Report 35: Guideline for the Diagnosis and Management of Asthma (EPR3) suggest that LTRAs offer an alternative treatment for mild persistent asthma, whereas the Practicing Allergology (PRACTALL)[6] consensus report, which is more specialized for younger patients than GINA and EPR3, proposed that LTRAs offer an alternative first-line treatment for persistent asthma in children.

CONCLUSION

Montelukast provides significant symptom control and improvement in PEFR in mild persistent asthma compared to placebo. It is effective as monotherapy in mild persistent asthma in children aged 2-12 years. Symptom control is good during therapy and three months after discontinuation of drug. Montelukast is well tolerated and drug compliance is satisfactory and has no significant adverse effects.

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REFERENCES

1. Wei-Fong Wu, Jiunn-Ren Wu, Zen-Kong. Montelukast as monotherapy in children with mild persistent asthma. Asian Pac J Allergy Immunol. 2009;27(4):173-80.
2. Bisgaard H, Zielen S, Garcia-Garcia ML, Polos P. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. Am J Respir Crit Care Med. 2005;171(4):315–22.
3. Straub DA, Moeller A, Minocchieri S. The effect of montelukast on lung function and exhaled nitric oxide in infants with early childhood asthma. Eur Respir J. 2005;25(2):289–94.
4. Global Initiative for Asthma: GINA report-2015.
5. National Asthma Education and Prevention Program: Expert Panel Report 3 (EPR 3). Guidelines for the diagnosis and management of asthma, 2007.
6. Bacharier LB, Boner A, Carlsen KH, et al. Diagnosis and treatment of asthma in childhood: A Practall consensus report. Allergy. 2008;63:5-34.

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