

COMPARISON OF KETOTIFEN VS MONTELUKAST SODIUM IN CONTROLLING MILD TO MODERATE PERSISTENT ASTHMA IN CHILDREN AGED 5-15 YEARS OF AGE

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Abstract

Background: Asthma is a chronic inflammatory airway illness, which impacts about 399 million people globally, and a significant proportion is numbered among children in Pakistan. Majority of mild to moderate persistent asthma needs optimal control in order to avoid morbidity and enhance the quality of life. The most frequently used controller therapies include montelukast (antihistamine leukotriene receptor antagonist) and ketotifen (mast cell stabilizer with antihistaminic effects), but there is a paucity of comparative data in pediatric groups.

Objective: To compare outcome of ketotifen versus montelukast in mild to moderate persistent asthma in children 5-15 years of age.

Methodology: This was a randomized clinical trial carried out at the Department of pediatrics, Children Hospital and Institute of child health, Lahore during July 2024 and December 2024. Sixty children who fitted the inclusion criteria were recruited and randomly divided into two groups (n=30 each). Group A was given ketotifen syrup (0.2mg/mL, 5mL twice a day), and Group B was prescribed montelukast 5mg one time a day over a period of three months. At the baseline and monthly follow-ups, the Asthma Control Test (ACT) score was used to measure asthma control. The data were examined by the use of SPSS version 20 where post-stratification independent t-test was used. A p-value ≤ 0.05 was considered significant.

Results: The ACT score of the montelukast group was significantly greater than that of the ketotifen group (21.4 \pm 2.3 vs 18.6 \pm 2.9; $p=0.001$). A higher percentage of patients had well-controlled asthma in the montelukast (73.3) group as opposed to ketotifen (43.3) group.

Conclusion: Montelukast was more effective than ketotifen in asthma control of children with mild to moderate persistent asthma. It can be used as a first line adjunct control therapy in this group of people.

INTRODUCTION

Asthma is a widespread ailment, having a prevalence of about 399 million people worldwide; in Pakistan, it is estimated to be 15 million people, with 15 million being children (1). Asthma has a clinical manifestation between mild wheez and acute and acute airways constriction, which may be deadly. Childhood asthma has a negative impact on both the school performance and the physical, social and emotional health of the child which often results in frequent hospitalization (2).

Asthma is a multifactorial etiological disease that is affected by both genetic and environmental factors. There are a number of known triggers of asthma attacks, such as respiratory tract infections, smoking, chemical fumes, dust, obesity, insects, plants, pollen, and exercise (3,4). Airway inflammation in asthma takes place when exposed to these triggers. The pathological process is triggered when an irritant or allergen, e.g., pollen or cold air is inhaled. This causes airway inflammation and mucus production, causing bronchial hyperresponsiveness and airway resistance. Intrusion of inflammatory cells also leads to hypersecretion of mucus as well as airway blockage. With time, this can result in irreversible alterations as the basement membrane thickens, collagen is deposited and epithelial desquamation occurs (5,6).

The typical asthma management incorporates the reliever and controller treatment. Short-acting bronchodilators, ipratropium and systemic corticosteroids are used to provide immediate relief, whereas inhaled corticosteroids, long-acting bronchodilators, theophylline, and anti-leukotrienes like montelukast are used in the long term (7). Moreover, ketotifen, a first-generation H1-antihistamine, and mast-cell-stabilizing effect has also been found to be useful in childhood asthma (8).

Past researches comparing ketotifen and montelukast have revealed that both medications have similar effects in terms of reducing the severity of asthma compared to the baseline but montelukast is more effective. In one of the studies, the post-treatment scores of asthma severity were significantly lower using montelukast

than ketotifen (1.00 ± 0.40 vs 2.54 ± 1.02 , respectively) (9). Likewise, in another study, there were greater mean scores on the asthma severity scale in the ketotifen group than the montelukast group (3.60 ± 1.25 vs 2.10 ± 0.92 , respectively) (10).

Although these results were obtained, little information exists on the relative effectiveness of ketotifen and montelukast in children with mild to moderate persistent asthma, in particular. Optimal asthma management in this population is crucial in that frequent attacks and hospitalization result in a high level of morbidity and can even cause death. Even though literature tends to support the use of leukotrien receptor antagonists over mast cell stabilizers, the efficacy and safety profile of ketotifen is well proven (11). Thus, the given study is carried out to compare these two therapeutic agents and decide on the more effective one to control the severity of asthma in children. The results can contribute to evidence-based clinical practice and better the outcomes in managing asthma in children.

OBJECTIVE

To compare the effect of ketotifen and montelukast in mild to moderate persistent asthma in children aged 5-15 years of age.

METHODOLOGY

The trial was a randomized clinical trial that took place at Paediatric Medicine Department of The Children's Hospital, Lahore from July 2024 to December 2024. Non-probability consecutive sampling was used to enroll 60 children who fit the inclusion criteria. Two similar groups of participants were then selected randomly using the lottery technique. Group A was given ketotifen syrup (0.2mg/mL, 5 mL twice daily) and Group B was given montelukast 5 mg (1 time a day) over 3 months. Before the therapy, baseline demographic and clinical data was taken. Follow-up of the patients was done after every month and the Asthma Control Test (ACT) score was used to evaluate the control of asthma. All the data were entered on a structured proforma.

INCLUSION CRITERIA

The children who were 5-15 years of either gender and diagnosed with mild to moderate persistent asthma were included.

EXCLUSION CRITERIA

Patients with mild intermittent asthma, severe persistent asthma, or who used systemic corticosteroids within a 6-week period, used ketotifen or montelukast within 3 months, hypersensitive to study drugs, heart disease, immunodeficiency diseases, or chronic lung diseases (cystic fibrosis and tuberculosis) were excluded.

DATA COLLECTION PROCEDURE

All participants were informed using the informed consent form and their parents or guardians provided the informed consent after receiving the approval of the institutional ethical review committee. Patients that met the inclusion criteria were recruited into the study. The predesigned proforma was used to record baseline data such as age, gender, time of having asthma, and initial Asthma Control Test (ACT). The lottery method was then used to randomly assign the participants to two groups. Ketotifen was given to Group A, and montelukast was given to Group B. The patients were followed within a period of three months with a monthly follow-up. ACT scores were measured and recorded at every visit. There was also strict confidentiality as each participant

got a unique identification number and no personal identifiers were taken.

DATA ANALYSIS

The analysis and the entry of data were carried out with SPSS version 20. Mean \pm standard deviation were used to represent quantitative variables (e.g. age, duration of asthma, Asthma Control Test (ACT) scores) and frequencies and percentages were used to represent categorical variables (e.g. gender). The data were stratified based on age, gender, and length of time having asthma to control possible modifiers of effects. A stratified independent sample t-test was then used to compare the mean post-treatment ACT score of ketotifen versus montelukast group. A p-value of ≤ 0.05 was considered statistically significant. Results were tabulated and charted where necessary to help in interpretation and comparison of results between the two groups in the study.

RESULTS

A total of 60 children with mild to moderate persistent asthma were enrolled in the study and equally allocated into two groups: ketotifen (n=30) and montelukast (n=30). The average age of the subjects was 9.3 ± 2.9 years. The baseline characteristics were similar between the two groups and there was no statistically significant difference ($p > 0.05$).

Baseline Demographic Characteristics

Variable	Ketotifen (n=30)	montelukast (n=30)	sum (n=60)
Mean Age (years)	9.2 ± 3.0	9.4 ± 2.8	9.3 ± 2.9
Male	16 (53.3%)	16 (53.3%)	32 (53.3%)
Female	14 (46.7%)	14 (46.7%)	28 (46.7%)

Clinical Baseline Characteristics

Variable	Ketotifen (n=30)	Montelukast (n=30)	p-value
Asthma Duration (months)	18.6 ± 6.4	19.1 ± 6.1	0.74
Baseline ACT Score	13.1 ± 2.4	13.4 ± 2.6	0.65

There were no statistically significant differences between baseline clinical parameters of the two groups.

Comparison of ACT Scores before and after.

Time Point	Ketotifen (Mean ± SD)	Montelukast (Mean ± SD)	p-value
Baseline	13.1 ± 2.4	13.4 ± 2.6	0.65
1 Month	15.2 ± 2.6	17.8 ± 2.4	0.002
2 Months	17.0 ± 2.7	19.9 ± 2.2	0.001
3 Months	18.6 ± 2.9	21.4 ± 2.3	0.001

All follow-up intervals revealed a steady increase in ACT scores with montelukast over ketotifen.

Asthma Control 3 Months.

Asthma Control Group	Ketotifen (n=30)	Montelukast (n=30)
Well Controlled (≥20)	13 (43.3%)	22 (73.3%)
Not Well Controlled (13-19)	14 (46.7%)	7 (23.3%)
Very Poorly Controlled (≤12)	3 (10.0%)	1 (3.3%)

FINAL INTERPRETATION

The current randomized clinical trial indicates that both ketotifen and montelukast are effective in asthma management of children with mild to moderate persistent asthma. Nevertheless, montelukast demonstrated much greater effectiveness in comparison to ketotifen in all the results measured.

Sequential measurement of ACT scores indicated that the improvement was statistically significant at 1, 2, and 3 months follow-up and the difference in the montelukast group was statistically significant ($p \leq 0.002$). After three months, the mean ACT score was much higher in montelukast group (21.4 ± 2.3) than in ketotifen (18.6 ± 2.9). Moreover, a greater percentage of children had well-controlled asthma in the montelukast group (73.3) than in the ketotifen group (43.3). The ketotifen group continued to have poor asthma control.

Generally, montelukast proved to be clinically more effective in the management of asthma symptoms, asthma control and the overall disease outcomes among children with mild to moderate persistent asthma.

DISCUSSION

The current study has proven that montelukast is better than ketotifen in the management of asthma in children with mild to moderate persistent asthma. The much higher ACT scores and higher percentage of well-controlled asthma in

the montelukast group indicates that it has better clinical activity. The results are in agreement with the study conducted by Al-Hamdani (9) which has indicated a much lower asthma severity score in those patients who are treated with montelukast than with ketotifen. In the same way, Nawaz et al. (10) also showed superior clinical outcomes of montelukast, which supports its position as an effective controller therapy.

Montelukast works by inhibiting cysteinyl leukotrienes receptors (CysLT1) which reduce airway inflammation, bronchoconstriction, and mucus (18). Conversely, ketotifen mainly stabilizes mast cells and has antihistaminic properties which may not be effective in chronic eosinophilic airway inflammation long-term control (11).

The clinical effectiveness of montelukast in the management of childhood asthma has been supported by recent evidence. Recent research has revealed that montelukast can be used to control symptoms, decrease the frequency of exacerbations, and increase the quality of life in children with persistent asthma, especially those with allergic phenotypes or low adherence to inhaled corticosteroids (15,16,17). Its usefulness as an alternative or add-on controller therapy was also confirmed by a 2023 systematic review, but inhaled corticosteroids are still first-line treatment of persistent asthma as per global guidelines (12,13).

Nevertheless, ketotifen has shown some small and irregular effectiveness in contemporary clinical research and its contribution to the contemporary treatment of asthma in children is negligible relative to leukotrienes receptor-blockers and inhaled corticosteroids (8,11). This also substantiates the better clinical utility of montelukast as seen in the current study.

One of the strengths of this study is the use of ACT score as a validated and objective instrument of asthma management (14). Nevertheless, they are limited to single-center design, rather small sample size, and limited follow-up period, which can impact a generalized conclusion. It is suggested that multicenter randomized controlled trials that include more extended follow-ups are necessary in the future to corroborate these results and assess long-term outcomes.

CONCLUSION

This paper comes up with a conclusion that montelukast is far more effective than ketotifen in the achievement of asthma control among children of age, 5-15 years old, with mild to moderate persistent asthma. Patients who were treated with montelukast had better ACT scores and a higher percentage of patients who had well-controlled asthma than those treated with ketotifen. Considering its high efficacy, convenient route of administration, and positive safety profile, montelukast needs to be a treatment of choice in asthma in children, especially in those settings where inhaled corticosteroids cannot be used, or where compliance is a concern. Nevertheless, ketotifen perhaps, still has a role to play as an alternative in selected patients. More multicenter researches involving larger samples are suggested to confirm these results and measure the long-term effects. Evidence-based interventions such as montelukast when incorporated in the routine clinical use would go a long way in reducing the morbidity and enhancing the quality of life of children with asthma.

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