

Comparison of Montelukast with Fluticasone for Control of Asthma in Children

Rabia Saeed, Khadeeja Mustafa and Najam u Saqib

ABSTRACT

Objective: To compare the efficacy of Montelukast and Fluticasone for control of asthma among children of age 4-10 years.

Study Design: A Randomized control trial study.

Place and Duration of Study: This study was conducted at the Department of Pediatrics Medicine Mayo Hospital Lahore from 12 January 2017 to 15 December 2017.

Materials and Methods: The ethical grant and informed consent was taken from Department of Pediatrics Medicine Mayo Hospital Lahore and parents before start of the study. The sample size of this study was 780 patients and they were randomized in two groups. Chi-square and student t test were used for categorical variables and pair t test was used to compare means. All the data was entered and analyzed by using the computer software SPSS version 21. In all the statistical interference, the p value of ≤ 0.05 was considered as significant.

Results: Overall, 780 patients were enrolled in this study and they were of both genders. The differences between both the groups were statistically insignificant except ASA ($p=0.010$) and operative time ($p=0.000$). The mean asthma RFDs and FEV₁ before treatment in group "M" was 63.1 \pm 2.15 days and 2.5 \pm 1.23 liter respectively. While, the mean asthma RFDs and FEV₁ before treatment in group "F" was 61.7 \pm 2.56 days and 2.0 \pm 1.35 liter respectively. The mean asthma RFDs and FEV₁ after treatment in group "M" was 133.50 \pm 4.59 days and 2.9 \pm 1.45 liter respectively. While, the mean asthma RFDs and FEV₁ after treatment in group "F" was 138.5 \pm 4.67 days and 3.1 \pm 1.12 liter respectively.

Conclusion: It has been concluded that Montelukast is not less effective than Fluticasone for asthma control among pediatric patients. Both the therapies of Fluticasone and Montelukast are well tolerated and can be used as first line drugs for asthma control.

Key Words: Montelukast, Fluticasone, Asthma, Pediatric patients.

Citation of articles: Saeed R, Mustafa K, Saqib N. Comparison of Montelukast with Fluticasone for Control of Asthma in Children. Med Forum 2018;29(3):25-28.

INTRODUCTION

Asthma is the long term chronic inflammation of the airway of lungs. Its characteristics and symptoms are different, chest tightness, shortness of breath, coughing, wheezing, obstruction of airway and bronchospasm^[1]. It becomes worsen in the morning and evening. It is caused due to genetic and environmental factors^[2]. Due to increasing industries, urban population, smog and air pollution, the cases of asthma are rapidly increasing up to 50 percent in the world. In 2015, nearly 358 million people had asthma throughout the world. According to Aga Khan University Hospital (AKUH), about 10 percent of the population of Pakistan has asthma^[3].

Asthma is one of the most prevailing chronic diseases of children and adults as well. A study conducted in Aga Khan University Hospital shows; 7.5 millions

Pakistani adults and 15 million children suffer from asthma^[4]. In pathophysiological mechanism of asthma, chronic inflammation leads to the narrowing of airway especially bronchioles and bronchi. It results in thickening of lamina reticularis, increased eosinophils. There is also involvement of immune system; cytokines, chemokines, histamine and leukotrienes. But cysteinyl leukotrienes play an important role in development of asthma^[5]. Therefore all the antileukotriene agents like Montelukast have been proved helpful in blocking cysteinyl leukotrienes. So, they are very useful in controlling the effects of asthma and its symptoms. These agents also reduce chronic airway inflammation in children and adults^[6].

Regarding the treatment and therapy of asthma, some very useful practical and clinical guidelines have been published by National Heart, Lung, and Blood Institute of America. According to these guidelines, anti-inflammatory drugs can be used for treatment of moderate asthma but inhaled corticosteroid (ICS) and antileukotriene should be first line drugs for asthma therapy^[7].

Many clinical trials show that Montelukast have similar effects like beclomethasone and triamcinolone. It controls symptoms of asthma and decreases the bronchial hyperresponsiveness^[8]. Many studies show

Department of Pediatrics Medicine Mayo Hospital, Lahore.

Correspondence: Dr. Khadeeja Mustafa, House Officer,
Department of Pediatrics Medicine Mayo Hospital, Lahore
Contact No: 0316-8448557
Email: msummaiya@gmail.com

Received: December, 2017; Accepted: February, 2018

variable results when comparison of Montelukast and inhaled corticosteroids (ICS) takes place. Both have different effects on lungs function and forced expiratory volume in 1 second (FEV₁)^[9]. Many large scale clinical studies have been done among aged patients, to compare the efficacy of orally intake Montelukast and inhaled corticosteroids (ICS) but no trial have yet been done on local level. So, we designed this study on local level and in pediatric patients to compare the effects of Montelukast and Fluticasone.

MATERIALS AND METHODS

This randomized control trial was held in Department of Pediatrics Medicine Mayo Hospital, Lahore, from 12 January 2017 to 15 December 2017. The ethical approval and informed consent was taken from institution and parents before start of the study. The sample size of this study was 780 patients and they were randomized in two groups. All children of both genders and age up to 10 years suffering from mild to moderate asthma were included but patients who had pulmonary TB, chronic respiratory illness, anatomic nasal disorder and severe airway obstruction were excluded in this trial.

All the patients were divided into two different groups named as 'M' group and 'F' group. Montelukast of 5-10 mg once at bedtime was given orally to patients included in 'M' group similarly, twice daily 2 puff of 50 microgram in the morning and evening of Fluticasone were inhaled to all patients of 'F' group. This study is basically conducted in house blinding procedure. All the patients were advised to have 3 clinic visits in 12 month trial. During each visit, physical examination, laboratory tests, baseline spirometry measurements, asthma symptoms and beta receptor agonists' use were performed in proper manner. All the patients were allowed to use the systemic corticosteroids if asthma is no being controlled adequately. The clinic visits were scheduled nearly 4 months during 12 month active treatment period. A standard spirometer was used to measure the FEV₁. Pre-bronchial and post-bronchial measurements were also measured on each clinic visit.

Chi-square test and student t test were used for categorical variables and pair t test was used to compare the means. All the data was entered and analyzed by using the computer software SPSS version 21. In all the statistical interference, the p value of < 0.05 was considered to be significant.

RESULTS

Overall, 780 patients were enrolled in this study and they were of both genders. 50% (n=390) patients were randomized to Montelukast (Group M) and 50% (n=390) were randomized to Fluticasone (Group F). The mean age, weight and height of the patients of group "M" was 8.25±2.47 years, 31.96±2.05 kg and

129.91±2.22 cm respectively. In this clinical trial, 67.4% (n=263) patients were boys and 32.6% (n=127) were girls. On the other, the mean age, weight and height of the patients of group "F" was 7.95±2.32 years, 29.93±2.27 kg and 127.98±1.61 cm respectively. In this group "F" 60.5% (n=236) patients were boys and 39.5% (n=154) patients were girls. The differences between both the groups were statistically insignificant except ASA (p=0.010) and operative time (p=0.000). The mean asthma RFDs and FEV₁ before treatment in group "M" was 63.1±2.15 days and 2.5±1.23 liter respectively. While, the mean asthma RFDs and FEV₁ before treatment in group "F" was 61.7±2.56 days and 2.0±1.35 liter respectively. The difference between asthma RFDs and FEV₁ of both "M" and "F" group were statistically significant. All this has been explained in (Table.1).

Table No. 1: Demographic and Baseline characteristics among the study groups

Variables	Montelukast (n=390)	Fluticasone (n=390)	Test of Sig.
Age (years)	8.25±2.47	7.95±2.32	t=0.186,p=0.853
Gender	B=67.4%, G=32.6%	B=60.5%, G=39.5%	χ ² =0.00,p=1.0
Weight (kg)	31.96±2.05	29.93±2.27 kg	t=- 0.311,p=0.757
Height (cm)	129.91±2.22	127.98±1.61	t=- 0.7.97,p=0.000
Asthma RFDs (days)	63.1±2.15	61.7±2.56	t=8.27,p=0.000
FEV ₁ , (Litter)	2.5±1.23	2.0±1.35	t=5.41,p=0.000

Table No. 2: Results after Treatment

Variables	Montelukast (n=390)	Fluticasone (n=390)	Test of Sig.
Asthma RFDs(days)	133.50±4.59	138.5±4.67	t=- 1.20,p=0.232
FEV ₁ , L	2.9±1.45	3.1±1.12	t=- 1.80,p=0.240

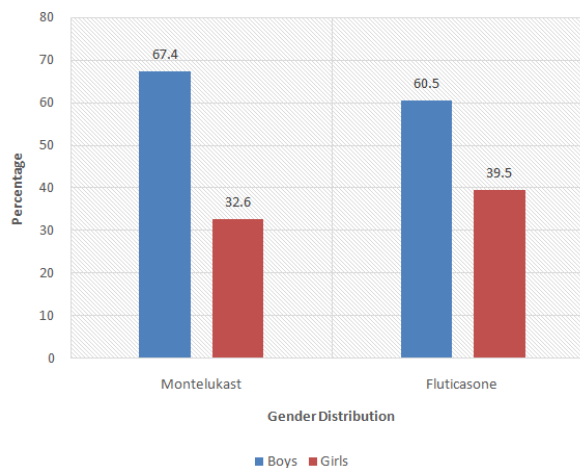


Figure No.1: Gender distribution with percentage.

The mean asthma RFDs and FEV₁ after treatment in group “M” was 133.50±4.59 days and 2.9±1.45 liter respectively. While, the mean asthma RFDs and FEV₁ after treatment in group “F” was 138.5±4.67 days and 3.1±1.12 liter respectively. The differences were statistically insignificant. (Table.2) The means asthma RFDs and FEV₁, before and after treatment was also statistically significant (p=0.232) and (p=0.240) respectively.

DISCUSSION

This randomized control study was designed to find out the comparison between effects of leukotrienes receptor antagonist Montelukast and inhaled corticosteroid (ICS) Fluticasone on mild asthma among pediatric patients of age 6-14 years. This trial explains that orally intake Montelukast is not less effective than ICS Fluticasone for asthma treatment. This 12 months treatment shows that both groups have 84% days during treatment in which they did not need any asthma medication. The difference of (RFD) rescue free days between Montelukast and Fluticasone was not greater than < 1 day / month. On the other hand, both the drugs have very significant effects on the Prebronchial FEV₁ and also decrease the peripheral blood eosinophils level.

Several clinical trials have been done among adults and children that show the efficacy of Montelukast and Fluticasone to reduce the asthma symptoms. The study by Barbara Knorr et al, in which 689 preschool children were randomly treated with 4mg Montelukast for 12 weeks^[10]. The daytime symptoms of asthma like wheezing, coughing, trouble breathing, activity limitation; and overnight cough; percentage of RFD were improved. It also explains that Montelukast has same effects regardless of sex, age and race.

There is another pediatric study by Jonathan, Bernstein, Barbara Knorr et al, 336 children with FEV₁ between 50% to 85 % of predicted value. 39% patients were receiving Montelukast and 33% receiving placebo. The result shows that FEV₁ increased from 1.85 to 2.01 liter in Montelukast group and from 1.85 to 1.93 liters in placebo group. This concludes that Montelukast improves the morning FEV₁^[11].

A multicentre, randomized, double blind trial by Theodore F, Reiss et al, demonstrates that Montelukast improves the airway inflammation and obstruction. It also increases the FEV₁ and reduces the peripheral eosinophilic level in blood. Due to its use rebound worsening effect and tolerance did not occur^[12].

An American base study by M. Luz, Garcia, Ulrich Wahn et al; that shows the comparison between Montelukast and Fluticasone for moderate asthma treatment. In this clinical trial, pediatric patients of age among 6- 14 years^[13]. This was very long study of 12 months and it was very comprehensive. This proves that Montelukast is not inferior to Fluticasone in asthma treatment. The difference between treatments was < 1

day/ month. The patients who were getting Montelukast has asthma attack 32.2% and those who were getting Fluticasone had asthma attack 25.6%.

To know the response to inhaled corticosteroids (ICS) and leukotrienes receptor antagonist (LTRA), a study was done by Stanley J. Szefer, in which children from 6-17 year were treated with Fluticasone and Montelukast for 8 weeks^[14]. The result shows that 23% patients responded to Fluticasone and just 5% responded to Montelukast. It was concluded that children with low pulmonary function and high level allergic inflammation should receive Fluticasone and other asthma patient could get either Fluticasone or Montelukast. Similarly, for comparison of Fluticasone and Montelukast, the clinical study by Robert S. Zeiger, shows that ICS Fluticasone has very significant effects and has rapid improvements in asthma patient comparative to Montelukast^[14].

There are many clinical studies to show comparison between Fluticasone and Montelukast, one of them is “low dose Fluticasone compared with Montelukast” conducted by William Busse^[15]. It concludes that low dose Fluticasone should be first line drug for asthma therapy. It has effective role than Montelukast in asthma control.

Both the ICS Fluticasone and Montelukast are generally well tolerated. They do not have any significant difference in their treatment. They are good to control the asthma and to increase RFDs and FEV₁. Both the drugs play an important role in reducing the peripheral eosinophilic blood level.

CONCLUSION

Our study concluded that Montelukast is not less effective than Fluticasone for asthma control among pediatric patients. Both the therapies of Fluticasone and Montelukast are well tolerated and can be used as first line drugs for asthma control.

Author’s Contribution:

Concept & Design of Study:	Rabia Saeed
Drafting:	Khadeeja Mustafa
Data Analysis:	Najam u Saqib
Revisiting Critically:	Rabia Saeed, Khadeeja Mustafa
Final Approval of version:	Rabia Saeed

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Khan, Ahmad A, Ambreen S, Sana. T, Tanzil J, Zafar F, Afshan AA, et al; Burden of asthma among children in a developing megacity: childhood asthma study, Pakistan. JOA 2014;51(9): 891-899.

2. Stelmach Iwona, Agata OH, Magdalena ZW. Stelmach JJP. Majak et al. Do children with stable asthma benefit from addition of montelukast to inhaled corticosteroids: randomized, placebo controlled trial. *Pul pharma & therapeutics* 2015;3(1):42-48.
3. Ahmad NA, Zafar F, Kadir MM, Nalini S. Pattern and predictors for respiratory illnesses and symptoms and lung function among textile workers in Karachi, Pakistan. *Occup Environ Med* 2013; 70(2):99-107.
4. Soriano Joan B, AAA Semaw F, Kalkidan Mukhtar B, Mani N, et al; Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet Resp Med* 2017;5(9):691-706.
5. Peddy R, Gena W, Cook S, Harrison J, Skoonmaker A. Fluticasone Propionate Combined With Montelukast Will Provide More Protection From Asthma Exacerbations During High Pollution Days Compared To Fluticasone Propionate Alone, in B53. *NAOPA* 2015;5(3):543-556.
6. Gerald Joe K, Lynne V, Monica M, Wayne J, David T, et al; Markers of differential response to inhaled corticosteroid treatment among children with mild persistent asthma. *JOACI* 2015;3(4):540-546.
7. Massingham, Messingham K, Fox S, A. Smaldone; Asthma therapy in pediatric patients: a systematic review of treatment with montelukast versus inhaled corticosteroids. *JOPHC* 2014; 28(1):51-62.
8. Chinedu N, Hitesh P, Stephen T, Sandra E, Christopher J, Knorr B, et al. Intermittent montelukast in children aged 10 months to 5 years with wheeze (WAIT trial): a multicentre, randomised, placebo-controlled trial. *Lan Resp Med* 2014;2(10):796-803.
9. Szeffler Stanley J, Lars G, Tom G, James U. Budesonide inhalation suspension versus montelukast in children aged 2 to 4 years with mild persistent asthma. *JOACI* 2013;1(1):58-64.
10. Barbara K, Matz J, Jonathan A, Bernstein. Montelukast for chronic asthma in 6-to 14-year-old children: a randomized, double-blind trial. *JAMA* 2015; 279(15): 1181-1186.
11. Barbara K, Luis M, Bisgaard H, Jan HV, Peter L, et al. Montelukast, a leukotriene receptor antagonist, for the treatment of persistent asthma in children aged 2 to 5 years. *Ped Med* 2013; 108(3):48-54.
12. Reiss Theodore F, Chervinsky P, Dockhore RJ. Montelukast, a once-daily leukotriene receptor antagonist, in the treatment of chronic asthma: a multicenter, randomized, double-blind trial. *Archives Int Med* 2015;158(11):1213-1220.
13. Luz GM. Garcia Ulrich W, Leen Gilles, Arlene S, Carol A, Peter P. Montelukast, compared with fluticasone, for control of asthma among 6-to 14-year-old patients with mild asthma: the MOSAIC study. *Ped Med* 2014;116(2):360-369.
14. Zeiger Robert S, Stanley JS, Brenda RP, Michael S, Fernando DM, et al; Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma. *JOACI*. 2016;117(1): 45-52.
15. William B, Gordon D, Raphael, Stanley G, Kalberg C, et al. Low-dose fluticasone propionate compared with montelukast for first-line treatment of persistent asthma: a randomized clinical trial. *JOACI* 2015;107(3):461-468.