Original Research Article

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20184201

Efficacy and compliance of montelukast as prophylaxis in mild persistent asthma

Sreejyothi G., Maya Menon*, Raveendranath K.

Department of Pediatrics, SUT Academy of Medical Sciences, Trivandrum, Kerala, India

Received: 14 September 2018 Accepted: 22 September 2018

*Correspondence: Dr. Maya Menon,

E-mail: dr.mayamenon94@gmail.com

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ABSTRACT

Background: Bronchial Asthma is characterized by hyperresponsiveness of airways to various triggers. The management goals of asthma therapy are to control asthma so that the affected child can lead a normal life without asthma exacerbations. In spite of several advances in the management aspects, asthma morbidity remains the same. Under diagnosis, inappropriate therapy and poor compliance are the major contributors to asthma morbidity. In the recent years the knowledge about different clinical and biological phenotypes of asthma has helped in deciding the treatment options in bronchial asthma. Montelukast has proven to be particularly effective in exercise induced asthma and asthma associated with allergic rhinitis. The aim of this study is to assess the efficacy and compliance of montelukast for prophylaxis in mild persistent asthma in children aged 1-12 years.

Methods: This is a prospective study which included children between age group 1-12 years with mild persistent asthma who was started on montelukast during the 12-month period from September 2016 to October 2017. No. of children who were controlled with moutelukast and who needed step up treatment were noted. Comorbidities of children who were controlled on montelukast were also studied.

Results: At the end of 6 months, 86.4% of children were well controlled and 13.6% were not well controlled.91.5% who were well controlled belonged to 1-5 years age group. Children with comorbidities like allergic rhinitis had good control with moutelukast. Response to montelukast was good when viral infection was a trigger.

Conclusions: It is a safe drug with modest benefits in bronchial asthma. It is useful in mild persistent asthma where ICS administration is impractical and also in patients with comorbidities like allergic rhinitis. It is also found to decrease the episode of viral induced wheeze in young children.

Keywords: Allergic rhinitis, Childhood asthma, Leukotriene antagonist, Montelukast, Phenotype

INTRODUCTION

Bronchial asthma is a disease characterized by an increased responsiveness of the airways to various stimuli. It manifests by widespread narrowing of the airways causing paroxysomal dyspnoea, wheezing or cough. The obstruction to the airflow is reversible in a large majority of cases either spontaneously or in response to treatment.

Air way obstruction in asthma is caused by oedema and inflammation of mucus membrane lining the airways, excessive secretion of mucus inflammatory cells and cellular debris and spasm of smooth muscles of bronchi. Inhalation of an allergen leads to biphasic response ultimately causing bronchoconstriction.

Leuktrienes mediate many aspects of inflammatory response. In the lung, leukotriene cascade due to activation of intracellular 5-lipoxygenase with subsequent release of leukotrienes (LTC4, LTD4, LTE4) is activated by different stimuli acting on many inflammatory cells, either resident (mast cells) or recruited in the airways (eosinophils, macrophages etc.) cysteinyl leukotrienes also have chemo attractive vascular properties for eosinophils. effect on permeability, mucus secretion and sensory nerve activation and are responsible for part of pathophysiology of asthma.1-3 They also play a role in remodelling of airways leading to progressive decline in function. Some experimental studies have demonstrated the role of Cys-LTs in inducing the proliferation and activation of mucosal fibroblasts and secretion and deposition of some component of extracellular matrix.^{4,5} In addition to inhaled allergens, viral infections, exercise, endocrine factors, emotional factors and weather change can be triggers of bronchial asthma.

The management goals of asthma therapy is to control asthma so that the affected child can lead a normal life without asthma symptoms, maintain normal activity with good sleep, can grow and develop normally, attend school regularly and participate in all school activities including sports without any asthma exacerbations. Inspite of several advances in the management aspects, asthma morbidity remains the same. Underdiagnosis, inappropriate therapy and poor compliance are the major contributors to asthma morbidity.

Asthma severity denotes the underline disease activity. Based on severity, asthma is classified as intermittent and persistent and this forms the most useful guide to asthma therapy. Once therapy is initiated, the emphasis is on asthma control. Asthma control denotes the degree to which asthma symptoms are minimized and goals of therapy are met after initiating long term management and it is a useful clinical guide to adjust therapy.

Studies on leukotriene receptor antagonist (montelukast) as monotherapy or in combination with ICS (Inhaled Corticosteroids) versus different drugs have contributed to the positioning of LTRAS in different levels of asthma treatment according to Global initiative for asthma guidelines. 1,6,7

Montelukast may be used as a monotherapy or as an alternative to low dose ICS (particularly in step down therapy) or in addition to ICS for improving clinical manifestations by an increase in anti-inflammatory effects and spraing of certicosteroids. The heterogenecity of asthma has received a large amount of attention in last few years in order to better tailor treatment according to different clinical and biological phenotypes of asthma. Montelukast has proven to be particularly effective in

exercise induced asthma and asthma associated with allergic rhinitis. 1.6

Other phenotypes were montelukast is effective include asthma in obese patients, asthma in smokers, aspirin induced asthma and viral induced wheezes. It reduces viral induced asthma exacerbations in 2-5 years.8 In comparison to adults randomized control studies comparing montelukast with inhaled corticosteroids in childhood asthma are scarce. 6,9-13 An RCT which compared montlukast with inhaled fluticasone in 6-14year-old children with mild persistent asthma had concluded that monteleukast was comparable to fluticasone in increasing the percentage of asthma rescue free days. Secondary endpoints including FEV1, β2 agonist use and quality of life improved significantly more in fluticasone treatment group. 6,11 Randomised "real world" observational studies also found relative efficacies in the two treatment groups similar.

However, patient and parent satisfaction, convenience and adherence to treatment was better with monteleukast than ICS.^{6,13} Children with low pulmonary function or high levels of inflammatory markers had a better response to ICS.⁶ Moutelukast is an attractive drug for several reasons. Oral preparations are easier to administer in young children than inhaled medications. Once daily dosing is practical and encourages compliance.^{6,14} The LTRAS have a wide therapeutic window with low toxicity at therapeutic concentration. The safety profile of montelukast is very good and the suspicion of increased risk of Churg Strauss syndrome or suicide have not been confirmed.

In short, Montelukast is not superior to ICS.⁶ It is useful in mild persistent asthma where ICS cannot be administered. Montelukast is also an alternative to LABA, as an add on Rx to ICS for moderate to severe persistent asthma. The other indications are exercise induced bronchoconstriction, allergic rhinitis and aspirin induced asthma.^{6,15-18}

Present study was done to assess the efficacy and compliance of montelukast for prophylaxis of mild persistent asthma in children aged 1-12 years.

METHODS

This is a prospective study which included children between age group 1-12 years with mild persistent asthma who was started on montelukast. The study was carried out in the ward and outpatient department of pediatrics, SUT Academy of Medical Sciences, TVM during the 12-month period from October 2016 to September 2017.

Inclusion criteria

The study group included children 1-12 years diagnosed as mild persistent asthma.

Exclusion criteria

- Children below 1 years and above 12 years
- Children diagnosed as asthma other than mild persistent asthma.

Children who satisfied the inclusion criteria were enrolled in the study. Detailed history including age, sex, triggers, night time symptoms, exacerbation and family history were taken. Detailed examination was done. The date of starting prophylaxis was noted. At the end of 6 months, children were categorized into well controlled, partially controlled and poorly controlled.

A well-controlled child is the one who leads a normal life without asthma symptoms, maintain normal activity with good sleep, can grow and develop normally, attend school regularly and participate in all school activities including sports without asthma exacerbations. Number of children who were controlled with montelukast and who needed step up treatment were noted.

Statistical analysis

Categorical variables are expressed as percent. Chi – square test was used to find association of outcome with selected variables.

For all statistical interpretations, a P<0.05 was considered the threshold for statistical significance. Statistical analysis was performed with statistical software package SPSS, version 17.0.

RESULTS

The study group consisted of 103 children out of which 72 children (69.9%) were between 1 to 5 years (Table 1). 56 children were males and 47 were females (Table 2).

Table 1: Distribution of the sample according to age.

Age	Count	%	
1yr to 5yrs	72	69.9	
>5vrs	31	30.1	

Table 2: Distribution of the sample according to sex.

Sex	Count	%	
Male	56	54.4	
Female	47	45.6	

Montelukast was started as prophylaxis for these children for a duration of 6 months and at the end of the period, these children were categorized as well controlled and not well controlled (not well controlled included children with partial control and poor control). At the end of 6 months, 89 children (86.4%) were found to be well controlled (Table 3). The remaining 14 children (Table 4) had to be changed to ICS.

Table 3: Distribution of the sample according to outcome.

Outcome	Count	%	
Well controlled	89	86.4	
Not well controlled	14	13.6	

Table 4: Distribution of the sample based on need for step up.

Changed to ICS	Count	%
Not done	89	86.4
Done	14	13.6

91.5% of children who were well controlled with montelukast belonged to 1-5 years age group Table 5.

Table 5: Age based distribution of the sample.

	Outcor					
Age (yrs)	Well		Not wel	1	χ^2	n
(yrs)	control	led	controlled		l k	P
	Count	%	Count	%		
1-5	65	91.5	6	8.5	5.14*	0.023
>5	24	75.0	8	25.0	3.14	0.023

*: Significant at 0.05 level

The response with montelukast was good in children with viral infection as a trigger Figure 2.

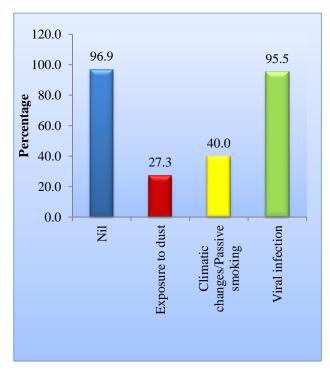


Figure 2: Distribution of triggers in well controlled children.

Children with comorbid conditions like allergic rhinitis had good control with montelukast Table 6.

Table 6: Distribution of Comorbid conditions in the study group.

Other allergies	Outcome Well Poor controlled controlled		χ2	p		
	Count	%	Count	%		
Nil	84	87.5	12	12.5		
Atopy	1	33.3	2	66.7	7.92*	0.019
Allergic rhinitis	4	100.0	0	0.0	1.92*	0.019

^{*}significant at 0.05 level

Table 7: Comparison of family history on the study group.

	Outcom					
Family	Well		Not Well		γ2	n
history	controll	ed	controlled		λ2	P
	Count	%	Count	%		
Absent	86	96.6	3	3.4	58.25**	0.000
Present	3	21.4	11	78.6	36.23	0.000

^{**}significant at 0.01 level

A position family history was also noted in children who needed step up to inhaled corticosteroids (Table 7).

DISCUSSION

According to current guidelines ICS is the preferred primary long-term treatment for asthmatic children. But leukotriene receptor antagonist can be considered to be an alternative treatment for mild persistent asthma. ¹⁹ Montelukast effectively reduced viral induced exacerbations in 2-5 years old. ⁶

Monteukast has proven to be particulary effective in exercise induced asthma and asthma associated with allergic rhinitis. Other phenotypes where monteleukast is effective include asthma in obese patients, asthma in smokers and aspirin induced asthma.

In present study, 91.5% children who were well controlled with montelukast belonged to 1-5 years age group. This is in concordance with the study by Walia M et al and also Knor et al.^{6,20} In present study, children who had viral infection as a trigger responded well with monteleukast. This is in concordance with the study by Doherty GM.¹⁴ Children with allergic rhinitis also showed a good response to montelukast which agrees with the study by Paggiaro P et al.¹

Children who needed step up to ICS had a positive family history of branchial asthma which is in concordance with the study by Walia M et al.⁶ The study by Gary et al showed that montelukast is easier to administer with only very few side effects and hence the compliance is good present study also showed a good compliance to montelukast.¹⁴

CONCLUSION

Montelukast is a safe drug with modest benefits in the treatment of asthma in young children. It is useful in mild persistent asthma where ICS administration is impractical and also in patients with comorbidities like allergic rhinitis. The drug is also found to reduce the viral induced wheezing in young children.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Oommen P. Mathew as Research investigator.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

REFERENCES

- 1. Paggiaro P, Bacci E. Montelukast in asthma: a review of its efficacy and place in therapy. Therapeutic Advances Chronic Dise. 2011;2(1):47-58.
- Holgate ST, Peters-Golden M, Panettieri RA, Henderson Jr WR. Roles of cysteinyl leukotrienes in airway inflammation, smooth muscle function, and remodeling. J Allergy Clin Immunol. 2003;111(1):S18-36.
- 3. Hamid Q, Tulic MK, Liu MC, Moqbel R. Inflammatory cells in asthma: mechanisms and implications for therapy. J Allergy Clin Immunol. 2003;111(1):S5-17.
- Asakura T, Ishii Y, Chibana K, Fukuda T. Leukotriene D4 stimulates collagen production from myofibroblasts transformed by TGF-β. J Allergy Clin Immunol. 2004;114(2):310-5.
- 5. Altraja S, Kadai M, Rekker E, Altraja A. Synthesis of tenascin and laminin beta2 chain in human bronchial epithelial cells is enhanced by cysteinyl leukotrienes via CysLT 1 receptor. Respiratory Research. 2008;9(1):44.
- 6. Walia M, Lodha R, Kabra SK. Montelukast in pediatric asthma management. Indian J Pediatr. 2006;73(4):275-82.
- 7. Global Initiative for Asthma. Global strategy for asthma management and prevention. 2007. Aavailable at www.ginasthma.org
- 8. Bisgaard H, Zielen S, Garcia-Garcia ML. Montelukast reduces asthma exacerbations in 2 to 5-year-old children with intermittent asthma. Am J Respir Crit Care Med. 2005;171:315-22.
- Stelmach I, Bobrowska-Korzeniowska M, Majak P, Stelmach W, Kuna P. The effect of montelukast and different doses of budesonide on IgE serum levels and clinical parameters in children with newly diagnosed asthma. Pulmonary Pharmacol Therapeutics. 2005;18(5):374-80.

- Szefler SJ, Phillips BR, Martinez FD, Chinchilli VM, Lemanske Jr RF, Strunk RC, et al. Characterization of within-subject responses to fluticasone and montelukast in childhood asthma. J Allergy Clin Immunol. 2005;115(2):233-42.
- 11. Garcia ML, Wahn U, Gilles L, Swern A, Tozzi CA, Polos P. Montelukast compared with fluticasone, control of asthma among 6 to 14-year-old patients with mild asthma: The MOSAIC study. Pediatr. 2005;116:360-9.
- Karamana Ö, Sünneli L, Uzuner N, Işlekel H, Turgut CS, Köse S, et al. Evaluation of montelukast in 8 to 14-year-old children with mild persistent asthma and compared with inhaled corticosteroids. Allergologia et immunopathologia. 2004;32(1):21-7.
- 13. Bukstein DA, Luskin AT, Bernstein A. Real world effectiveness of daily controller medicine in children with mild persistent asthma. Ann Allergy Asthma Immunol. 2003;90:543-9.
- Doherty GM. Is montelukast effective and well tolerated in the management of asthma in young children? Part A: Evidence-based answer and summary. Paediatr Child Health. 2007;12(4):307-8.
- Melo RE, Sole D, Naspitz CK. Exercise-induced bronchoconstriction in children: montelukast attenuates the immediate phase and late phase responses. J Allergy Clin Immunol. 2003;111:301-17.

- Pajaron-Fernandez M, Garcia-Rubia S, Sanchez-Solis M, Garcia-Marcos L. Montelukast administered in the morning or evening to prevent exercise-induced bronchoconstriction in children. Pediatric Pulmonol. 2006;41(3):222-7.
- 17. Kupczyk M, Kupryś I, Gorski P, Kuna P. The effect of montelukast (10 mg daily) and loratadine (10 mg daily) on wheal, flare and itching reactions in skin prick tests. Pulmonary Pharmacol Therapeutics. 2007;20(1):85-9.
- 18. Mucha SM, Naclerio RM, Baroody FM. Comparison of montelukast and pseudoephedrine in the treatment of allergic rhinitis. Arch Otolaryngol—Head Neck Surg. 2006;132(2):164-72.
- 19. Jartti T. Inhaled corticosteroids or montelukast as the preferred primary long-term treatment for pediatric asthma? Eu J Pediatr. 2008;167(7):731-6.
- Knorr B, Franchi LM, Bisgaard H, Vermeulen JH, LeSouef P, Santanello N, et al. Montelukast, a leukotriene receptor antagonist, for the treatment of persistent asthma in children aged 2 to 5 years. Pediatr. 2001;108(3):e48.

Cite this article as: Sreejyothi G, Menon M, Raveendranath K. Efficacy and compliance of montelukast as prophylaxis in mild persistent asthma. Int J Contemp Pediatr 2018;5:2133-7.