Efficacy and compliance of montelukast as prophylaxis in mild persistent asthma

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Received: 14 September 2018
Accepted: 22 September 2018

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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 paroxysmal dyspnoea, wheezing or cough. The obstruction to the airflow is reversible in a large majority of cases either spontaneously or in response to treatment.

Airway 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.

Leukotrienes 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 properties for eosinophils, effect on vascular 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.\(^5,8\) 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 sparing of corticosteroids. The heterogeneity 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 montelukast with inhaled fluticasone in 6-14 year-old children with mild persistent asthma had concluded that montelukast was comparable to fluticasone in increasing the percentage of asthma rescue free days. Secondary endpoints including FEV1, \(\beta_2\) 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 montelukast than ICS.\(^5,13\) Children with low pulmonary function or high levels of inflammatory markers had a better response to ICS.\(^6\) Montelukast 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.\(^5,13-18\)

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|
| >5yrs   | 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.

| Age (yrs) | Outcome          | Count | %   | Count | %   | \( \chi^2 \) | p  |
|-----------|------------------|-------|-----|-------|-----|-------------|----|
| 1-5       | Well controlled  | 65    | 91.5| 6     | 8.5 | 5.14*       | 0.023|
| >5        | Not well controlled | 24   | 75.0| 8     | 25.0|             |    |

*: 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.
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

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

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

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

*significant at 0.05 level

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

| Family history | Outcome                        | χ²   | p   |
|----------------|--------------------------------|------|-----|
|                | Well controlled                | Not Well controlled |      |     |
|                | Count | %     | Count | %     |
| Absent         | 86    | 96.6  | 3    | 3.4   |
| Present        | 3     | 21.4  | 11   | 78.6  |

**significant at 0.01 level

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. Montelukast effectively reduced viral induced exacerbations in 2-5 years old.

Montelukast 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. 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. Children with allergic rhinitis also showed a good response to montelukast which agrees with the study by Paggiaro P et al.

Children who needed step up to ICS had a positive family history of bronchial asthma which is in concordance with the study by Walia M et al. 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.
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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.