To Determine the Efficacy of Inhaled Corticosteroids Compared to Montelukast in Reducing Exacerbation in Uncontrolled Asthma in Children 6 Months to 5 Years

NAZISH JEHAN, MOBIN UR REHMAN, MUHAMMAD HUSSEIN ZARKOON

ABSTRACT

Aim: To determine the efficacy of inhaled corticosteroids compared to montelukast in reducing exacerbations in uncontrolled bronchial asthma in children 6 months to 5 years of age.

Methods: This was a randomized controlled trial study Pediatric Unit-1 Bolan Medical Complex Hospital Quetta from March 2011 to August 2011. Children 6 months to 5 years of age were admitted through OPD and emergency. The patients present with history of atopy, wheeze and nocturnal cough, children with history of use of rescue treatment in the last 4 weeks, wheezing apart from colds, sensitization to weather changes and history of exposure to pets were included. Children with acquired or congenital heart defects, those with history of pulmonary tuberculosis, pneumonia, gastroesophageal reflux, tracheoesophageal fistula, foreign body aspiration, cystic fibrosis, immune deficiency syndromes presents with recurrent infections, any comorbid condition such as hemoglobinopathy (thalassemia, sickle cell anemia) were excluded. The patients were classified into uncontrolled asthma according to the GINA guidelines. Patients were given ICS and tab Montelukast by lottery method to remove the bias. The doses for ICS were 200 microgram per day for uncontrolled asthma. Leukotriene modifiers were given in a dose of 4 mg once a day below 1 year and 5 mg once a day above 1 year. They were followed-up monthly for up to 6 months.

Results: The majority of the patients enrolled for the study were boys making up about 1383 (57.6%) out of 2400 remaining 1017 (42%) were females. The mean SD age of the patients was 2.42±1.25 with P value is significant (P<0.5). The mean±SD age for the diagnosis was 4.37±5.06 with P value for diagnosis was to be significant (P<0.5). Among the 1200 patients who were prescribed an ICS, 51.58% of patients (n=1238) were stepped down after treatment with an ICS while 153(6.375%) were stepped up. 1 patient was admitted in status when the one was treated while stepping of the treatment was considered in 771(32.125%). 2 patients were admitted in status while 7 patients were showed static response to treatment with montelukast.

Conclusion: Inhaled corticosteroids proved to be the most effective controller therapy in children 6 months to 5 years of age than montelukast.

Keywords: Asthma, Treatment, Inhaled corticosteroids, Montelukast, Children, Controller

INTRODUCTION

Asthma is the most common chronic illness in childhood with challenges that revolve around interventions that can potentially alter the course of the disease and concerns regarding the safety of regular use of controller medications. While traditional views of asthma have centered around a childhood onset disease with an allergic component, several large scale network studies are now confirming that severe asthma can present in multiple different ways, only 30-50% of which meet traditional childhood onset allergic criteria. Since asthma is a common disease, there is a great endeavor to achieve the most appropriate treatment option. In the treatment of children with mild persistent asthma, low-dose ICS are recommended as the preferred immunotherapy (referred to as step 2 of therapy). In children with inadequate asthma control on low doses of ICS (step 2), asthma management guidelines recommend adding an anti-leukotriene agent to existing ICS as one of three therapeutic options to intensify therapy (step 3). Anti-leukotriene’s (5-lipoxygenase inhibitors and leukotriene receptors antagonists) serve as alternative monotherapy to ICS in the management of recurrent and/or chronic asthma in adults and children. Asthma guidelines allow antileukotriene medications to be used as an alternative to ICSs in second-step intensity therapy. The use of montelukast as monotherapy in children presenting with persistent asthma resulted in a highly satisfactory outcome for themselves, their parents and their physicians. Leukotriene receptor antagonists, such as montelukast, provide a safe and effective treatment option with ease of administration,
particularly in preschool children and as add-on therapy in patients with difficult-to-control asthma.

A considerable number of children are not diagnosed or treated properly. And the management of asthma requires further improvement. Although clinical studies show that childhood asthma can be controlled well with inhaled corticosteroids, many children with asthma remain symptomatic despite maintenance treatment with ICSs. Adherence to treatment is often poor. Paediatric care providers should consider evaluating asthma control on a regular basis regardless of the reason for the visit. While step-up therapy is not superior to daily controller medication, symptom-based are superior to peak-flow based action plans for preventing exacerbations. Newly identified pharmacogenomics markers may be the first step in tailoring each asthmatic patient's therapy on the basis of genotype, and management tailored specifically toward each patient's level of airway inflammation is already coming into wider clinical use. Based on the current body of evidence, there is rationale for further investigation of these management strategies, including direct comparisons between inhaled corticosteroids and leukotriene receptor antagonists, as well as the role of long-acting beta-agonists, potentially targeting the subpopulations of early childhood with wheezing who are at highest risk for persistence of asthma symptoms.

PATIENTS AND METHODS

This was a randomized controlled trial study paediatric unit-1 bolan medical complex hospital Quetta from March 2011 to August 2011. Children 6 months to 5 years of age were admitted to the ward via OPD and emergency. The following patients were included in this study: children 6 months to 5 years of age presenting with history of atopy, wheeze and nocturnal cough, children with history of use of rescue treatment in the last 4 weeks, wheezing apart from colds, sensitization to weather changes and children with history of exposure to pets. After inclusion following patients were excluded: children with acquired or congenital heart defects, with history of pulmonary tuberculosis, pneumonia, gastroesophageal reflux, tracheoesophageal fistula, foreign body aspiration, cystic fibrosis, as presentation of these conditions mimics asthma, Immune deficiency syndromes presents with recurrent infections, any co morbid condition such as hemoglobinopathy (thalassemia, sickle cell anaemia). The patient's parents were informed about the study duration and informed consent was taken. Baseline tests including CBC, chest X-ray and blood sugar were done. The patients were classified into uncontrolled asthma/partially controlled asthma according to the GINA guidelines. Patient comfort and temperature maintenance were kept in consideration. Patients were given ICS and tab Montelukast by lottery method to remove the bias. Those receiving ICS were named as group 'A' and those receiving Montelukast were labelled as 'B'. The doses for ICS was 200 microgram per day for uncontrolled asthma. Leukotriene modifiers were given in a dose of 4mg once a day below 1 year and 5mg once a day above 1 year. They were followed up monthly for up to 6 months. Patients who were admitted to emergency department in exacerbation or status were considered as treatment failure. The results of the study were analyzed after six months.

RESULTS

In 6 months duration of study, out of 2400 participants, 1200 were prescribed an inhaled glucocorticosteroids and 1200 were put on montelukast. The results of the treatment response were seen after 6 months of the trial. The majority of the patients enrolled for the study were boys making up about 1383 (57.62%) out of 2400 remaining 1017 (42%) were females (Table 1). The age range of the patients selected for this study was from 6 months to 5 years. The mean age of the patients was 2.420 with standard deviation of 1.25. The majority of the patients were 3 years of age with a percentage of 11.8% (n=282), minimum age range was 39 months making up 1.0% (n=1). The P value for age is significant (<0.5). The mean age for the diagnosis was 4.3742 and standard deviation 5.06794. The P value for diagnosis was found to be significant i.e., <0.5. Among the 1200 patients who were prescribed an ICS (termed as group A), 51.58% of patients (n=1238) were stepped down after treatment with an ICS while 6.375% (n=153) were stepped up. One patient was admitted in status when the one was treated with ICS. The other group which was put on montelukast, being labelled as group B, 16.75% (n=402) of patients were stepped down when they were treated with montelukast whereas stepping up of the treatment was considered in 32.125% (n=771) who were put on montelukast. 2 patients were admitted in status while 7 patients were showed static response to treatment with montelukast.

Table 1: Frequency and percentage of genders (n=2400)

<table>
<thead>
<tr>
<th>Gender</th>
<th>n</th>
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<tbody>
<tr>
<td>Male</td>
<td>1383</td>
<td>57.6</td>
</tr>
<tr>
<td>Female</td>
<td>1017</td>
<td>42.4</td>
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DISCUSSION

Clinical asthma studies across different age groups can potentially offer insight into the similarities, differences, and relationships between childhood and adult asthma. Asthma control is suboptimal in many
children in the Asia-Pacific region\(^1\). The sample size in our study was 2400 while it was 3,021 children\(^1\), 7168 participants\(^1\) and 4531 adolescents\(^3\) in studies conducted around Asia. Thus this compares with the other studies in terms of the sample selected. Our study showed the preponderance of male 56.7\% while other workers have found that the male to female prevalence ratios increased with age from <1 at 4-5 years, peaked at 10-11 years (2.24), then reversed to 0.57 at 16-18 years\(^4\). In Brazil the predominance of females was found\(^2\). Canadian workers have found that asthma exacerbations while similar in form between the sexes, they differ in amplitude, with boys having higher risks of exacerbation in childhood and women in adult life. Rosychuk, Voaklander and others found that emergency visits or Asthma were more common by boys (61.3\%) and after age 14, more female presented\(^5\). British researchers found that the age-specific asthma prevalence was curvilinear with a peak around age 3 and somewhat higher for boys than for girls\(^6\).

The mean±standard deviation of age was 2.42±1.25. In a study conducted in Italy the mean age was 11.6±2.7 years\(^6\), while the mean age was 11.6±2.8 years reported by Bossley et al.\(^3\). During the 6 month study period comparing the efficacy of inhaled steroid with Montelukast in the context of uncontrolled bronchial asthma, it was evident that the patients who were started treatment with inhaled glucocorticosteroids had a significantly lower risk of experiencing an asthma-related hospitalization or hospitalization/emergency department visit compared with montelukast. Several randomized controlled trials demonstrate that montelukast provided effective and beneficial asthma control to children aged 2 to 14 years with mild asthma\(^2\). The results of an Israeli extensive study show that the use of montelukast as monotherapy in children presenting with persistent asthma resulted in a highly satisfactory outcome for themselves, their parents and their physicians.\(^7\) Leukotriene receptor antagonists, such as montelukast, provide a safe and effective treatment option with ease of administration, particularly in preschool children and as add-on therapy in patients with difficult-to-control asthma.\(^8\) However low-dose fluticasone had lower cost and higher effectiveness compared with montelukast in a large multicenter trial.\(^2\) In an English study it was shown that the addition of anti-leukotrienes to ICS is not associated with a statistically significant reduction in the need for rescue oral corticosteroids or hospital admission compared to the same or an increased dose of ICS in children and adolescents with mild to moderate asthma.\(^9\) Our study demonstrates that one third of patients on Montelukast were more likely to require stepping up. The patients who were put on inhaled steroids suffered less frequent asthmatic exacerbations, less school day off and less nocturnal cough in our study. This is substantiated by work done in the other parts of the world.\(^29,30\) The level of asthma control was directly proportional to adherence rate of ICS\(^3\).

Half of the patients met the criteria for atopy with typical features of parental allergies and that in the siblings. This was the group in which comprised of mostly the upper age limit of the study that is above 2½ to 3 years. They had the history of one or the other risk factor for asthma like exposure to smoke or humid environment favoring the growth of fungus and this is substantiated by other studies in the literature\(^32\). Few patients had history of contact with pets at their home. Early exposure to cat seems to increase the risk of sensitization to cat but not of asthma at 4 years of age and this is consistent with international data.\(^33\) Dog ownership, on the other hand, appears to be associated with lowered risk of sensitization to airborne allergens and asthma.\(^34\) None of the patients had history of prenatal exposure to smoke. Those who were breast-fed had otherwise more protected from diarrheal illnesses and other infections but in the context of this study, we didn’t find a consistent protective effect of breast-feeding in the context of allergies. However, older studies demonstrated that early breast feeding is associated with reduced asthmatic events\(^35\), in contrast to recent studies.\(^36\) Many of the patients had infantile eczema as a manifestation of atopic illness. Eczema was twice as common in the (PNC) persistent nocturnal cough (19\%) as in the asymptomatic children (10\%)\(^37\). Gastroesophageal reflux disease treatment may benefit patients who have asthma and complain of frequent heartburn, particularly those who have frequent nocturnal asthma symptoms.\(^38\) Wheeze is the most common presenting complaint of every age group of my study, being more common in less than 1 year because of compliant Airways. Various asthmatic phenotypes are a challenge for the physician, for differentiating it from other common infectious illnesses like tuberculosis. Most the patients coming to OPD with complaints of cough variant asthma are misdiagnosed as gastro-esophageal reflux, postnasal drip, chronic sinusitis, and vocal cord dysfunction. Cough variant asthma is an occult form of asthma of which the only sign or symptom is chronic cough\(^39\). It is characterized as a persistent, nonproductive cough with minimal or no wheezing and dyspnea and so the diagnosis is frequently overlooked.\(^40\) Nocturnal cough is the most common and important symptom and an important marker of uncontrolled bronchial asthma.\(^41\) Many of the patients had complaints of nocturnal cough.
before they get worse to exacerbation requiring systemic steroids. It is concluded from a study that the clinical features of children with persistent nocturnal cough resembled those of the asymptomatic population more closely than those of the polysymptomatic asthmatic population. In this age group persistent nocturnal cough, in the absence of wheeze, shortness of breath or tightness in the chest, is likely to be a manifestation of atypical or hidden asthma in only a minority of cases. Activity induced cough was also used as a marker of uncontrolled asthma.

Leukotriene receptor antagonists (LTRAs) have been proposed as alternative first-line therapy to ICSs for episodic or mild persistent asthma, particularly in children who have difficulty in utilizing inhalation treatment, with poor compliance, or where exercise-induced bronchospasm (EIB) is a dominant component of asthma. ICS should be introduced as initial maintenance treatment (200µg BDP equivalent) when the patient has inadequate asthma control. Atepy and poor lung function predict a favorable response to ICS. It was concluded from a study that ICS can be used to control active disease and to reduce the burden of illness, but should not be used to prevent asthma in high-risk children. In one of a study, it has been shown that early intervention with inhaled budesonide within the first 2 years of asthma diagnosis in patients with persistent asthma improves both prebronchodilator and post bronchodilator FEV1.

CONCLUSION

Inhaled corticosteroids proved to be the most effective controller therapy in children 6 months to 5 years of age then Montelukast. Early intervention with inhaled glucocorticoids achieves symptom control but does not alter the natural history of asthma. However Oral montelukast (4-mg chewable tablet) administered once daily is effective therapy for asthma in children aged 2 to 5 years and is generally well tolerated without clinically important adverse effects. This is true more so in preschool children and as add-on therapy in patients with difficult-to-control asthma.

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