Does Montelukast Reduce the Treatment Cost in Children with Moderately Severe Atopic Dermatitis

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Abstract

Montelukast use in atopic dermatitis has been evaluated in many clinical trials. It affects the clinical severity scores and some inflammatory markers.

Aim of this study was to evaluate the drug-saving effect and analyze the cost of montelukast therapy on oral antihistamines and topical steroids in children with moderately severe atopic dermatitis.

Randomized, double-blind, placebo-controlled, crossover trial with washout period, conducted from May 2002 to February 2006. The study involved 25 patients, 2-16 years old with dermatitis. Patients received oral montelukast (9 patients, Group B) or placebo (16 patients, Group A) in phase 1, and were crossed over to placebo or montelukast, respectively, for phase 2. Patients included if >10% of skin was involved and failed response to 2 week conventional treatment. At each of 2-week clinic visits, the amount of medication used was measured and cost calculated for oral antihistamines, topical steroids, and oral antibiotics.

During montelukast use, the amounts of oral histamines, or topical steroids, or oral antibiotic courses were not significantly different from their counterparts during placebo use. It did not reduce the medications cost. However, montelukast increased the direct medication cost by 138%.

In children with moderately severe atopic dermatitis, montelukast does not have any drug-sparing effect on oral antihistamines or topical steroid amounts. It increased the direct treatment cost of this disease.

Introduction

Atopic dermatitis (AD) is a common atopic disease that mainly affects infants and children [1]. It has lot of psychological, social, and functional inabilities in children affected and their families [2,3]. It has a tremendous financial impact on child's family and national health resources [4]. There has been lot of research to find alternative therapies to antihistamines and topical steroids for severe AD. This therapy included pimecrolimus [5], interferon-gamma, and leukotriene modifiers including montelukast [6,7].

To the best of our knowledge, this is the first study to investigate whether 1) daily oral montelukast treatment allows any reduction in amount of oral antihistamines, topical steroids, 2) reduces the treatment cost while maintaining control of moderately severe AD in children.

Methods

Subjects

In this study, 25 patients (9 males and 16 females), 2 to 16 years of age, with moderate-to-severe AD, with or without allergic rhinitis and or asthma who failed to respond to conventional therapy were consecutively recruited from the allergy-immunology clinics at Hamad Medical Corporation. The study was approved by the Research Committee of the Hamad Medical Corporation. All patients fulfilled the criteria of Hanifin and Rajka for the diagnosis of AD [8].

Study Design

The study was a 12-week randomized double blind, placebo-controlled trial with a crossover, and 2-week washout period between the 4-week study periods from May 2002 to February 2006. Each patient was randomi-zed to either arm of the study: receive placebo for 4 weeks, then montelukast for 4 weeks, or to receive montelukast for 4 weeks then crossed to 4 weeks placebo.

The study comprised 6 clinic visits spaced 2 weeks apart: the baseline visit was for screening and run-in, the first for allocation randomization to either arm of the study, and others were for clinical assessment, severity scoring using SCORAD (SCORing Atopic Dermatitis), and measuring the amount consumed of each medication of oral antihistamines, topical steroids, and any oral antibiotics given.

The studied subjects were patients with >10% of the skin involved by AD, and moderately severe on SCORAD. AD Severity was defined by a cutaneous index of 10% to 50% for moderate, and >50% for severe AD, and extent of disease for each patient was done by quantifying 5 manifestations of AD.

All patients or their legal guardians gave an informed written consent after the purpose, risks, and potential benefits of the study were explained to them.

The patients who had current pyoderma, or who were on any one of the following medications such as oral corticosteroids, ketotifen, montelukast, zafirlukast or zileuton within 2 weeks of enrollment or had a history of allergic reactions to one of leukotriene modifiers were excluded from the study. Nasal medications for allergic rhinitis and inhaled asthma medications were permitted provided that the dosage was unchanged during the trial.

Randomization was done by pulling one of 2 sealed envelopes with either group A or group B. Montelukast 5 mg tablets and placebo of identical appearance were supplied by Merck Inc. & Laboratory. Each patient received montelukast 5mg (one 5 mg tablet for children <12 years, and two tablets for older children) and matching placebo for 28 days.

During the screening period, each patient provided a complete history and a comprehensive examination was performed. Blood was collected for eosinophil count, total serum IgE, and specific IgE levels for a panel of common allergens. Each patient was educated on AD and its skin care, and remained on conventional treatment for 2 weeks. The amount consumed of each oral antihistamine, topical steroids, and any oral antibiotics was determined and recorded.

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) software. Comparisons of AD clinical and severity scores, and laboratory data were performed with the non-parametric Wilcoxon's rank sum sign test for the paired samples. The level $p<0.05$ was taken as the cutoff value for significance.

Results

Table 1 shows the characteristics of the studied subjects. About half (44%) of them had also asthma, and 68% of them had positive family history of allergic diseases.

Table 1: socio-demographic characteristics of children with atopic dermatitis treated with montelukast.

Variables	n (%)
Total number	25 (%) patients
Age(mean± SD, months)[a]	73.9±8.37
Sex	
Males	13 (52.0%)
Females	12 (48.0%)
M/F ratio	1.08
Other Allergies	14 (56.0%)
Asthma	11 (44.0%)
Allergic rhinitis	8 (32.0%)
Food Allergy	1 (4.0%)
Others	2 (8.0%)
Positive Family Allergy	17 (68.0%)
AEC[b]	710.0±138.0
Total serum IgE(IU/L)	2,211.9±1118.1

a: SD standard deviation
b: AEC: absolute eosinophil count

Table 2 presents the average monthly amount per patient of oral antihistamines and topical steroids, and systemic antibiotic courses during montelukast and placebo phases of the study. Evidently, montelukast use did not reduce the amount of any of these medications.

Table 3 reveals the average of treatment cost of oral antihistamines, topical steroids, and systemic antibiotic course during montelukast and placebo phases of the study. Not only there was no difference between the two phases, but when the cost of montelukast is added, the average monthly direct medication cost would increase by U$ 68.25. This represents an additional direct treatment cost of 138%.

Table 2: The monthly amount of medications used during montelukast compared to placebo in 25 children with atopic dermatitis.

Medication Amount/ month*	Placebo Group (Mean± SD)	Montelukast Group (Mean± SD)	p-value
Patient number	25	25	
Oral antihistamines	118.80±88.71	113.88±106.18	0.313
Topical steroids	31.40±30.40	27.48±24.51	0.300
Oral Antibiotics	0.28±0.45	0.40±0.58	0.183

*Amount of oral antihistamines in mg of cetirizine, topical steroids in grams of mometasone fuoarate 0.1% cream, and antibiotics in full 10-day course.

Table 3: The monthly cost of 25 children with atopic dermatitis treated with oral montelukast compared placebo treatment.

Monthly Cost (U $) Per Patient	Placebo Group (Mean± SD)	Montelukast Group* (Mean± SD)	p-value
Patient number	25	25	
Oral antihistamines	10.40±1.47	8.15±1.42	0.137
Topical steroids	10.00±2.13	10.91±2.5	0.053
Oral Antibiotics	30.68±16.8	30.40±7.40	0.160
Total	50.08±6.80	49.46±3.80	

*This excludes montelukast cost of 68.25 U$ / month.

Discussion

Montelukast has been tried in various studies on AD in both children [9], and adults [8,10]. These studies have focused on montelukast effect on AD severity scores, inflammatory marker and other laboratory tests such as total serum IgE levels, and on peripheral blood eosinophilia.

This current trial is the first study addresses the cost analysis of montelukast use and its sparing effect on oral antihistamines and topical steroids in children with moderately severe AD.

From this study, montelukast does not significantly reduce the amount of antihistamines and topical steroids used in AD in children. The drug-sparing effect of montelukast has been studied in other allergic diseases such as asthma and allergic rhinitis. Data indicate that montelukast treatment in asthma patients reduces asthma severity scores [11], improves lung function tests [12], and reduces short-acting beta-agonist (SABA) use [11]. Price et al. in retrospective, cohort, analysis on asthmatic patients who were kept on chronic montelukast therapy revealed significant ($p<0.05$) reduction in the use of SABA and antibiotics [13]. In mild-to-moderate asthma and concomitant seasonal allergic rhinitis, addition of montelukast reduced the use of asthma medications, emergency department visits, and hospitalization. However, it increased the total direct healthcare cost [14]. In a randomized, double-blind, double-dummy, cost analysis on 423 adults with persistent asthma, fluticasone/ salmeterol combination was more cost-effective than oral montelukast [15]. Inhaled steroids/ salmeterol combination has been found to be superior to montelukast/inhaled steroid combination in reducing the risk of hospitalization, SABA use, and lowering the total asthma care cost [16]. O'Connor et al, in a prospective, randomized double-blind, 12 week trial revealed that fluticasone/ salmeterol was not only a more cost-effective, but lead to cost savings compared with the addition of montelukast to the low-dose fluticasone in patients with persistent asthma [17].

In allergic rhinitis, montelukast has shown an improve-ment of nasal symptoms allergic rhinitis in children [18], seasonal allergic rhinitis [19], perennial allergic rhinitis [20], and reduces inflammatory markers [21,22]. In systematic review and met-analysis, Grainger and Drake-Lee [23] concluded that although montelukast is superior to placebo in reducing symptom score, it is not as effective as nasal steroids or antihistamines. They also concluded that it should be used with antihistamines and be regarded as second line therapy.

Although the sample size is a limitation in this study, it is the first trial to evaluate the cost of montelukast in children with AD, and larger studies should be done in the future.

Conclusion

In conclusion, in children with moderately severe AD, although montelukast could be used as an additional medication with some effect on AD severity scores, it does not have any drug-sparing effect on antihistamines or topical steroids, or reduce treatment cost.

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