THE EFFICACY OF CETIRIZINE IN THE TREATMENT OF ALLERGIC RHINITIS AND ALLERGIC BRONCHIAL ASTHMA

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ABSTRACT

Objective: The aim of this study was to describe the efficacy and safety of cetirizine in the treament of patients with allergic rhinits and allergic bronchial asthma.

Methods: We enrolled all patients diagnosed to have chronic allergic rhinitis and bronchial asthma referred to the allergy clinic between February and July 2000. The epicutaneous skin test was done for these patients. Locally developed total allergy score, frequency of exacerbations, use of broncodilators, anti-inflammatory drugs, electrocardiogram (EKG) and liver function test (LFT) assay were carried out before and after conclusion of treatment with cetirizine HCL.

Results: Forty three patients were included in the study. Other 7 patients were excluded. The age ranged between 3-15 years, 30 (69.8%) were males and 13 (30.2%) were females. The average allergic score was 27 before treatment compared to 2 after treatment with cetirizine. There was a significant decrease in total serum immunoglobin E, eosinophils, asthma exacerbations, bronchodilators and anti-inflammatory medications following treatment. The side effects were mostly transient and did not require discontinuing cetirizine HCL.

Conclusion: Cetirizine in a dose of 5-10 mg/day is safe and effective in the treatment of seasonal and perennial allergic rhinitis. It decreased asthma symptoms in patients with allergic rhinitis and mild moderate asthma and may be considered as an additional agent for treating patients with asthma.

Key words: Cetirizine, Asthma, Allergic rhinitis, Children.

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Introduction

Both allergic rhinitis and allergic bronchial asthma are relatively common disorders with rising incidence despite effective treatment and use of known preventive measures [(1)]. Patients with seasonal or perennial allergic rhinitis and/or allergic bronchial asthma experience an immediate allergic response caused by allergen-specific immunoglobulin E-mediated histamine release (IgE) [(2)]. Traditional antihistamines generally have little effect on airway responses at pharmacological doses, and the use of higher doses is limited by associated side effects [(3)]. In contrast, second generation antihistamines have a potent, nonsedating, histamine (H_1) receptor antagonist with activity in seasonal and perennial allergic rhinitis. They have effective control of allergic rhinitis and asthma symptoms and decrease the total IgE levels [(4)]. The second generation H_1 -anthistamines have become widely used in the treatment of urticaria, atopic dermatitis and allergic rhinitis [(5)]. Their use for treatment in asthma is still limited despite the fact that the same histamine is present in the upper and lower airway and can be released spontaneously. Although very effective in alleviating and preventing symptoms caused by histamine release in allergic rhinitis, antihistamines still have not gained the same popularity in the treatment of allergic bronchial asthma [(6)]. Second generation antihistamines have a potent, nonsedating, histamine (H_1) receptor antagonist with activity in seasonal and perennial allergic rhinitis. They have effective control of allergic rhinitis and asthma symptoms and they decreased the total IgE levels. They also decrease the frequency of disease exacerbations, the total amount bronchodilators

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and prophylactic cortisone treatment. This study described our experience in the efficacy and safety of cetirizine in the treament of patients with both allergic rhinitis and allergic bronchial asthma.

Methods

Between February to July 2000, fifty patients with allergic rhinitis and/or allergic bronchial asthma were referred to the allergy clinic at King Hussein Medical Center (KHMC). Patients enrolled in the study should have had their symtomps for at least two consecutive years, in addition, they should have positive skin prick test (SPT) for at least one allergen, high initial blood level for eosinophils and total serum IgE. Seven patients were excluded (14%); two with immotile cilia syndrome, three with cystic fibrosis, one with hypogammaglobulinemia, and one with bronchiectasis. Forty three (86%) were included in the study. The age ranged between 3-15 years, 30 (69.8%) were males and 13 (30.2%) were females. After detailed history and examination, all patients underwent the epicutaneous skin testing (Stallargenes^{TM}) (Table I). The daily requirement for selective β_2 agonist (Salbutamol 100 microgrmas per puff) and steroid (Beclomethasone 250 micrograms per puff), Metered Dose Inhalers (MDI) and the numbers of asthma exacerbations were documented on each follow-up visit. To evaluate the extent and severity of the condition, a locally developed allergy scoring system (Table I) was applied to these patients on the first visit and on subseqent visits. Patients were seen at 1,-3-6 weeks, 3 - and - 6 months. All patients were started on cetirizine at their initial visit. The dose of cetirizine used was 5mg for children aged two to six years and 10mg for those above 6 years according to the manufacturis recommendations. Blood was extracted for absolute eosinophil count and total IgE on the initial and the six month-visit. Total IgE was measured by Enzyme-linked Immunosorbent Assay (ELISA). Electrocardiogram (EKG) and liver function were tested before and after the end of treatment.

Results

The average allergic score was 27 before cetirizine treatment and showed progressive decrease through out the study period to reach an average score of 2 by the end of 6 months (Fig. 1). The average IgE levels dropped from 900 IU (930 IU ± 146) before adding cetirizine to 150 IU (150 IU ± 12) six months after treatment P (<0.0001), (Fig. 2). Also the average eosinophils count dropped from 2000/mm^3 (2016. /mm^3 ± 125) to 250/mm^3 (251/mm^3 ± 12) P<0.0001 (Fig. 3). Table (III) the requirements for both maintenance and rescue inhalers were significantly decreased by the end of treatment as shown in Table IV. The monthly numbers of asthma exacerbations were 3 in the initial visits while they were one at the end of the study (P<0.0001). The side effects were mostly nonspecific and did not require discontinuing cetirizine (Table IV).

Discussion

This study showed that by adding cetirizine to the treatment of patients with allergic rhinitis and/or bronchial asthma, there was improvement in the allergy score system over six months. Permanent changes like allergic salute, transverse nasal crease and orofacial abnormalities were included in the scoring system to refer to the severity and chronicity of allergic rhinitis. We do not expect improvement within six months of treatment as the case in the study. The decrease was sustained even after the onset of pollens season. At six month visit, the total IgE and absolute eosinophil counts were 6 and 20 times less than those at the initial visit, respectively. Also there was a decrease in the requirement for (salbutanol) and steroid inhalers as well as in the number of asthma exacerbations. The effect and value of non-sedating 2nd generation H_1-antihistamines were well documented in the treatment of urticaria, atopic dermatitis and allergic rhinitis [(7)]. In a double blind study Mansman *et al* showed that cetirizine was effective in reducing symptoms when compared to placebo [(8)], particularly in relieving postnasal discharge and sneezing in perennial allergic rhinitis [(8)]. Another double blind study, which looked at 263 patients with seasonal allergic rhinitis, found that both astemizole and cetirizine were well tolerated and equally effective in alleviating symptoms, with the difference that the former did not inhibit skin reactivity to histamine within 3 days of the end of the treatment [(9)]. Until recently, the use of traditional antihistamines for the treatment of patients with allergic bronchial asthma (ABA) achieved mixed results, in part because of the multiple cellular interactions stemming from release of mediators other than histamine from mast cells [(10)]. The traditional first generation H_1antihistamines generally have little effect on airway responses at pharmacological doses, and the use of higher doses to obtain beneficial effects are limited by the associated side effects [(11)]. With the recent introduction of a new generation of antihistamines that are pharmacologically different from the earlier H_1 antagonists there has been renewed interest in the role of these agents against histamine-induced bronchospasm [(12,13)]. In studies of histamine-induced bronchial hyper responsiveness in asthmatic patients, prophylactic treatment with loratidine 10 mg once daily effectively inhibited histamine induced bronchoconstriction [(14,15)] Loratidine also appeared to prevent the development of allergic asthma associated with airway infammation from pollen-induced rhino-conjunctivitis [(16)]. There is also evidence of drug sparing effect when loratidine was administered as adjunctive therapy with established standard antiasthma treatment, including theophylline, sympathomimetics, and inhaled steroids. Two randomized crossover studies of terfenadine and placebo reported improvement in

symptoms and lung function in treated patients with atopic asthma [17]. In these two studies the dose of the terfenadine was high, and as now considered contraindicated because of the risk of cardiac arrhythmias with higher doses. Studies using astemizole showed no changes in symptoms or bronchodilator use in asthmatic patients. Higher doses of the latter might be associated also with cardiac arrhytmias. Cetirizine (Zyrtec) another antihistamine was found to be safe and well tolerated and to a comparative efficacy in asthma [17,18]. Cetirizine treatment was associated with improvement in symptoms of both allergic rhinitis and asthma. Compared with placebo, cetirizine in a dose of 10 mg twice daily was associated with significant improvement in symptoms and no significant change in pulmonary functions in pollen asthma: forced expiratory volume in one second or forced vital capacity. Lower doses of cetirizine have been considered ineffective in the treatment of asthma. Recently, Andrew *et al* in a double-blind, placebo controlled study involving 93 patients with allergic rhinitis and asthma, found that a lower dose of cetirizine (10mg daily) was safe and effective in relieving both upper and lower respiratory symptoms. We used the same dose of cetirizine used in Andrew *et al* study and we have a comparable result regarding allergic score and ventolin usage. Moreover, we were able to reduce the dose of steroids inhaler in most of our patients within two weeks of starting cetirizine.

Our patients showed a significant decrease of eosinphils counts and total IgE at the end of the treatment. We do not have any explanation for this decrease. It is well known that cetirizine inhibits eosinophils accumulation at antigen-challenged skin sites and also in the airways [15] but no one looked to the effect of cetirizine on the eosinophil counts in the peripheral blood. These phenomena should be further studied. Our study was not a placebo controlled but it was unique in using cetirizine for 6 months, which is the longest duration that has been ever used in the studies. Even with this duration cetirizine proved to be a safe drug with very minimal side effects. The side effects reported by the company are illustrated in Table VI.

Conclusion

The results of this study showed that Cetirizine (5-10 mg/day) according to age, was safe and effective treatment of seasonal and perennial allergic rhinitis. In addition, cetirizine controlled asthma symptoms in patients with allergic rhinitis and mild to moderate asthma, and alleviated symptoms of asthma at the usual dose for treatment of allergic rhinitis. Slightly higher doses are needed in severe asthma. Cetirizine has excellent safety record and may be considered an additional agent for treating patients with asthma.

Table I. Locally developed allergy-scoring system*.

Index	
Frequent sneezing	Headache
Nasal itching	Fullness in the ear
Clear rhinorrhea	Hearing loss
Nasal obstruction	Ear pain or discomfort
Symptoms interfere with sleeping	Tinnitus
Eye itching	Vertigo
Throat itching	Cough
Ear itching	Shortness of breath
Allergic salute	Wheeze
Transverse nasal crease	Exercise-induced asthma
Mouth breathing	Decreased air entry
Snoring	Prolonged expiratory phase
Orofacial-dental abnormalities	Skin itch
Red eye	Skin rash
Facial discomfort	Typical atopic dermatits

- Patients were given a score of 1 for each positive item and zero for each negative item.

Table II. Changes of the allergy scores.

Initial presentation	**First week**	**Third week**	**Sixth week**	**3 Months**	**6 Months**
27	16	5	4	2	2

Table III. Changes of the total serum IgE, eosinohpils count and asthma severity.

	At initial presentation. (mean±SD)	**After six months. (mean±SD)**	***P. value***
Average concentration of serum total IgE.	900 IU (930±146)	150IU (150±12)	<0.0001
Average concentration of Eosinohpils.	2000/mm^3 (2016±125)	250/mm^3 (251±12)	<0.0001
The average number of Ventolin puffs per day.	5 (5±1)	2 (2.628± 0.952)	<0.0001
The average number of cortisone puffs per day.	4 (3±1.463)	2 (1.9±0.9)	*<0.0001*
Asthma exacerbations per month.	3 (3.023±1.0165)	1 (1.0372±0.900)	*<0.0001*

Table IV. Adverse events of Cetirizine.

Adverse events	**Number of patients experiencing at least one side effect**	**% of patients with side effects**
Abdominal pain	4	9
Agitation	1	2
Allergic reaction	0	0
Anorexia	2	4
Appetite increase	2	4
Palpitations and/or EKG* changes	0	0
Fatigue	1	2
Hyperkinesia	1	2
Insomnia	3	6
Somnolence	5	11
Decreased school performance	0	0

* EKG = electrocardiogram.

Table V. Adverse effects reported by the study conducted by the manufacturing company.

		Cetirizine	
Adverse Experiences	**Placebo (N=309)**	**5 mg (N=161)**	**10 mg (N=215)**
Headache	12.3%	11.0%	14.0%
Pharyngitis	2.9%	6.2%	2.8%
Abdominal Pain	1.9%	4.4%	5.6%
Coughing	3.9%	4.4%	2.8%
Somnolence	1.3%	1.9%	4.2%
Diarrhea	1.3%	3.1%	1.9%
Epistaxis	2.9%	3.7%	1.9%
Bronchospasm	1.9%	3.1%	1.9%
Nausea	1.9%	1.9%	2.8%
Vomiting	1.0%	2.5%	2.3%

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