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Correlation between Radiological and Total Nasal Symptom Severity Score Effect of Montelukast in Patient with Allergic Rhinitis Associated with Inferior Turbinate Hypertrophy

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ABSTRACT

Background: Allergic rhinitis (AR) is immunoglobulin E (IgE)-mediated inflammation of the nasal mucosa on exposure to allergens. Hypertrophic rhinitis (HR) is a common complication for AR, and often need turbinate surgery. Montelukast was evidenced to have an effective role in treatment in AR. **Objective:** The aim of the current work was to correlate between radiological and total nasal symptom severity score (TNSSS) effect of montelukast in patient with allergic rhinitis associated with inferior turbinate hypertrophy. **Patients and methods:** This prospective comparative case control study included a total of 100 allergic patients suffering from nasal obstruction due to inferior turbinate hypertrophy (study group) and 100 non-allergic patients (control group), attending at Outpatient Clinics, ENT Department, Al-Azhar University Hospitals, Egypt. The effect Montelukast was assessed by (TNSSS), radiologically by (CT) scan. Serum levels of IgE, TGF-β and IL13 were measured. **Result:** Montelukast showed improvement of all nasal symptoms score with highly significant improvement TNSSS (P=0.003) and significant reduction on inferior turbinate size (p=0.001) compared to control. In addition to, significant reduction in serum levels of IgE, TGF-β and IL13. **Conclusion:** Montelukast could be effective alternative treatment for inferior turbinate hypertrophy.

Keywords: Total nasal symptom severity score, Montelukast, Allergic rhinitis, Inferior turbinate hypertrophy.

INTRODUCTION

Allergic rhinitis (AR) is an immunoglobulin E (IgE)-mediated inflammation of the nasal mucosa that causes sneezing, nasal congestion, nasal itching, and rhinorrhea [1, 2]. Many studies have found a link between (AR) and Hypertrophic rhinitis (HR), which is the second most common cause of nasal obstruction [3-5]. Long Hypertrophic rhinitis may be irreversible and need turbinate surgery [6].

The total nasal symptom severity score (TNSSS) is a four-point scale used to assess the severity of individual symptoms over the previous 24 hours [7]. The scale uses four points (0,1,2,3) for (none, mild, moderate, severe) and four points (sneezing, nasal congestion, rhinorrhea, and postnasal drip) respectively. Cytokines are important mediators, originators, and maintainers of allergic inflammation [8].

Montelukast is the antagonist cysteinyl-leukotriene receptor [7], FDA approved [9] to be effective, safe down to six months of age [10] bioavailable and oral [11], well tolerated [12] and not induced tolerance in long-term studies [13].

The aim of the current work was to correlate between montelukast effects on nasal symptoms in patient with allergic rhinitis and hypertrophied inferior turbinate proved by CT scan.

PATIENTS AND METHODS

This prospective comparative case control study included a total of 100 allergic patients suffering from nasal obstruction due to inferior turbinate hypertrophy (study group) and 100 non-allergic patients (control group), attending at Outpatient Clinics, ENT Department, Al-Azhar University Hospitals, Egypt. This study was conducted between April 2015 to March 2020.

Study Group had received montelukast 10 mg for 3 months. They were 40 (40%) male and 60 (60%) female. Their age ranged from 23-44 years (mean 38±1.29 years). Control group received placebo for the same period, they were 52 (52%) male and 48(48%) female. Their age ranged from 22-44 years (mean 35±62.21 years). They were nonallergic patient without inferior turbinate hypertrophy and were chosen from those admitted for myringoplasty operations.

Exclusion criteria: Patients with sepal deviation, history of previous nasal intervention, patients who had received montelukast, any corticosteroids or antibiotics or having acute upper respiratory tract infection within one month preceding the initial study.

Both study group and control group were subjected to pre and post (after 3 months) treatment clinical and laboratory assessment by:

1. The total nasal symptom severity score (TNSSS) and computed tomography (CT) scan. Calculation of total nasal symptom severity score (TNSSS) was done by adding of four nasal symptoms (sneezing, nasal congestion, rhinorrhea, and postnasal drip). Patients were evaluated according to the symptom severity score [7]. These symptoms against the 4-point scoring scale after clarification of the scoring

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system to the patient. A checklist for TNSSS was filled before starting the treatment (over the last 24 hours) and after 6-month treatment. The mean score of TNSSS Pre- and post-treatment was compared in both groups using a t-test. P-value of less than 0.05 was considered significant.

2. Computed tomography (CT) scan of the nose (coronal plane) with 3mm slice thickness. The size of the inferior turbinate was calculated by multiplying the maximum width and height of the turbinate in the coronal plane, and the maximum length of the turbinate in axial plan. Measurements taken in an mm [103mm slice thickness in coronal plane according to [14].
3. Measurements for serum levels of IgE, TGF-β and IL13 in both control and study groups. They were measured by enzyme-linked immunosorbent assays (ELISAs) were performed using commercial kits according to the manufacturer's recommendations (Eastbiopharm kit, China).

Ethical consent:

An approval of the study was obtained from Al-Azhar University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The data were collected, analyzed, calculated using SPSS Inc., Chicago (Statistical Package for Social Sciences) Illinois, USA, version 20.0. Quantitative data were expressed as mean± SD. Qualitative data were expressed as frequency and percentage. The total nasal symptom severity score (TNSSS) was calculated by summing of all four nasal symptoms. Pre- and post-treatment mean of TNSSS was compared using a t-test. P-value of less than 0.05 was considered significant.

RESULTS

Of total 200 individuals (100 study groups compared to 100 control group) the data regarding age and gender are demonstrated in table 1.

Table (1): Demographic characteristics for group A and B.

	Group A	Group B
Age (years): Range Mean± SD	23-44 38±1.29	22-44 35±62.21
Sex [number & (%)]: Male Female	40(40%) 60(60%)	52(52%) 48(48%)

On comparing the mean values of pre and post-treatment scores symptoms including sneezing, nasal obstruction, postnasal drip, and rhinorrhea between study group and control group, Montelukast showed improvement of all nasal symptoms. Also, there were highly significant improvement TNSSS (P=0.003) while control group showed insignificant changes (p=1.062) as shown in tables 2 & 3.

Table (2): comparing mean values of pre-treatment and post- treatment scores symptoms and TNSSS in study group.

Nasal symptoms	Study group		t-Test	P value
	Before treatment	After treatment		
Sneezing	2.88±1.52	1.21±1.22		
Nasal obstruction	2.57±1.37	0.93±1.25		
Postnasal drip	2.69±1.26	1.01±1.36		
Rhinorrhoea	2.11±1.46	0.88±1.23		
TNSSS	10.25±1.53	4.03±1.26	5.321	0.003

Table (3): comparing mean values of pre-treatment and post- treatment scores symptoms and TNSSS in control group.

Nasal symptoms	Control group		t-Test	P value
	Before treatment	After treatment		
Sneezing	1.65±1.11	1.78±1.27		
Nasal obstruction	1.73±1.66	1.66±1.71		
Postnasal drip	1.47±1.42	1.51±1.36		
Rhinorrhoea	1.22±1.25	1.22±1.18		
TNSSS	5.87±2.98	5.17±2.5	2.312	1.062

Regarding to CT, study group showed significant reduction on inferior turbinate size (p=0.001) compared to insignificant reduction in control group (P=1.025) as shown in table 4.

Table (4): Comparison between study group and control group in size of inferior turbinate

	Study group	Control group
Before treatment	3.62±1.7	3.69±1.2
After treatment	2.13±1.1	3.63±1.3
Total reduction	1.49±0.6	0.06±0.1
t-Test	6.238	1.135
P value	0.001	1.025

Significant decreases in serum levels of IgE, TGF-β and IL13 study group compared to control group as shown in tables 5 & 6.

Table (5): Changes in serum levels IgE, TGF-*β* and IL13 in control group

	Control group		t-Test	P value
	Before treatment	After treatment		
IgE (U/ml)	168.43 ±7.79	174.43 ±9.83	1.751	1.341
TGF-β (ng/ml)	356.43±40.66	363.22±47.71	2.568	0.912
IL13 (pg/ml)	15.67 ±3.21	14.98±3.83	1.985	1.213

Table (6): Changes in serum levels of IgE, TGF-β and IL13 in control group

	Study group		t-Test	P value
	Before treatment	After treatment		
IgE (U/ml)	283.45±9.35	185.92±4.42	4.533	0.009*
TGF-*β* (ng/ml)	1432.38±62.52	513.53±71.67	6.486	0.001*
IL13(pg/ml)	33.53 ±6.72	19.51±3.94	4.159	0.01*

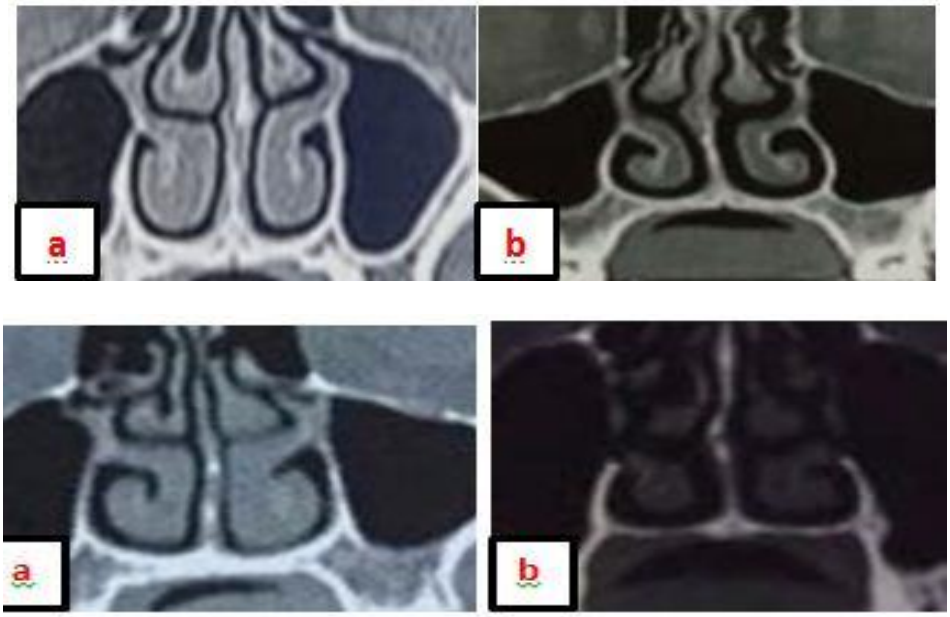

Figure (1): CT coronal section showing the effect of montelukast on size of inferior turbinate (a) before therapy, (b) after therapy.

DISCUSSION

The efficacy of montelukast in the treatment of AR has been widely examined over the years, either as monotherapy or in combination with antihistamines and intranasal corticosteroids [15, 16, 17], as well as its impact on quality of life [18].

The current work was conducted to corelate between effect of Montelukast on improving TNSSS and its effect the size of hypertrophied inferior turbinate. We included in our study a total of 200 individuals (100 allergic patients with inferior turbinate hypertrophy proved by CT scan compared to 100 non allergic individuals). To study the effect of Montelukast, 100 patients were given Montelukast while the other100 were given placebo for the same period. Follow up by TNSSS and CT of 2groups after 3 months, in addition to serum measurements for IgE, TGF-β and IL13.

On comparing severity of nasal symptoms scores and TNSSS between study and control group, we found improvement of all the mean values of nasal symptoms scores with highly significant improvement TNSSS (P=0.003) in study group while no improvement in mean values of nasal symptoms scores with insignificant improvement TNSSS (P=1.062) in control group (tables 3, 4), (Figs. 1, 2). In a recent study by **Rajput *et al.*** [7] handling the same perspective, they found that the mean TNSSS reduced from 8.25 to 2.43 after four weeks of Montelukast treatment with difference 5.82 between pre- and post-mean values which in agreement with our results. In another study**, Ciebiada *et al.*** [17] showed a gradual improvement in nasal symptom within six weeks of therapy with montelukast alone or in combination with an antihistamine in their randomized, placebo /controlled study. Similar study by **Nayak *et al.*** [18] showed that the mean symptom scores at baseline were similar for Montelukast alone or in combination. However, a prospective, randomized, controlled trial by **Mostafa *et al.*** [19] showed no significant improvements in nasal symptom scores or disease exacerbation for patients with montelukast versus INCS for 6 months.

Our findings showed significant reduction on inferior turbinate (p=0.001) in group A compared to insignificant reduction in group B (P=1.025). This may be attributed to the anti-inflammatory effect of

Montelukast by affecting cysteinyl leukotriene-1 and 2 receptors [20]. Sorrily, there is no clear data about whether Montelukast can induce reduction on size of inferior turbinate.

Our study showed significant reduction in serum levels of IgE, TGF-β and IL13 after 3 months of montelukast treatment ($P < 0.009$, 0.001 and 0.01 respectively) which confirms anti-inflammatory effect of montelukast. A number of studies demonstrated that antigen specific helper and suppressor T cells regulate the production of IgE, where it triggers production of eosinophils and activates mast cells differentiation to T helper cells into Th2 cells which secrete IL-4, IL-5, IL-10 and IL-13 [21]. **Ouyang *et al.*** [22] found that allergic rhinitis activates TGF -β expression in epithelial cells in nasal mucosa which resulted in hyperplasia in goblet cells. Montelukast can suppress the proliferation of inflammatory cells and decrease cytokines and inflammatory mediators while inhibiting airway remodeling or fibrosis [23]. Scientists found that montelukast significantly decreased of IL-4 and IL-13 and increased of IFN-γ levels in nasal lavage in children with allergic rhinitis [24].

CONCLUSION

Montelukast could be effective alternative treatment for inferior turbinate hypertrophy. So, treatment with Montelukast should be considered before surgery decision.

We recommend combination of montelukast with oral antihistamines in treatment of patients with allergic rhinitis according to their symptoms which may achieve better symptom improvement, which should be considered in future studies.

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