

The Effect on Attention Deficit and Hyperactivity Symptoms of Treatment of Paediatric Allergic Rhinitis

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ABSTRACT

Objective: Allergic rhinitis (AR) may cause neurobehavioural symptoms and impair quality of life (QoL). We evaluated the efficacy of AR treatment on QoL, attention deficit and hyperactivity symptoms in paediatric allergic rhinitis.

Methods: Twenty five children with grass pollen-sensitized seasonal AR were enrolled. They completed the Total 4-Symptom Score (T4SS), and Paediatric Rhinitis Quality of Life Questionnaire (PRQLQ). Conners' Parent Rating Scale-48 (CPRS) questionnaire was completed by the mothers to identify attention deficit and hyperactivity symptoms in children with AR. The patients were given fluticasone furoate (FF) nasal spray 27.5 microgr once daily and levocetirizine dihydrochloride (LD) 5 mg oral tablet once daily for six weeks. After six weeks, T4SS, PRQLQ and CPRS were repeated in AR group. The mothers of thirty four healthy children completed CPRS questionnaire as control group.

Results: After treatment, T4SS and PRQLQ scores improved in AR group ($p = 0.001$). Pre-treatment attention deficit and hyperactivity scores in AR group were higher than those in the control group ($p = 0.001, 0.009$, respectively). After treatment, attention deficit scores improved in AR group, and there were no differences in attention deficit scores between two groups, and hyperactivity scores in AR group were lower than those in control ($p = 0.785, 0.007$, respectively).

Conclusions: AR may show negative effect on QoL and neurobehavioural health of the patients. The combination treatment of FF nasal spray and LD tablet may improve nasal symptoms, QoL, attention deficit and hyperactivity symptoms.

Keywords: Allergic rhinitis, attention deficit, hyperactivity, symptom score, quality of life

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INTRODUCTION

Allergic rhinitis (AR) is among the world's most common chronic diseases. It is a global public health problem and is of major importance due to its large increase in world prevalence. AR in children can have several complications that have a major impairment on the child and the family (1). It can predispose to the development of comorbidities such as otitis media with effusion, recurrent and/or chronic sinusitis and asthma. Also, it causes sleep disorders, poor school performance, hyperactivity and decreased quality of life (2, 3).

In AR patients complain of fatigue, anxiety, irritability, depressed mood and apathy (4). Allergic rhinitis patients frequently have sneezing, itching, nasal congestion, nasal discharge in their nose (2). Therefore, these patients need to sniff, snort and rub in their nose. These behaviours may lead to be teased by other children and shyness in these children.

Several clinical studies have researched the coexistence of attention deficit/hyperactivity disorder (ADHD) and AR. A population-based study suggested that allergic disorders increased the risk of ADHD in paediatric patients. Their detailed analysis showed that the main contributing factor is AR (8). In another population-based study revealed that rate of ADHD among AR patients increased (9).

Recently, Kim *et al* suggested that attention performance improves after treatment in children with allergic rhinitis. But, in their study had no healthy control group. To our knowledge, our study is the first study which investigates the relationship between ADHD symptoms and treatment of allergic rhinitis in paediatric AR.

The purpose of this study was to evaluate the impact of levocetirizine dihydrochloride (LD) / fluticasone furoate (FF) combination treatment on nasal symptoms, QoL and ADHD symptoms in children with AR.

METHODS

Subjects

This prospective study was conducted at Erzurum Regional Training and Research Hospital in Turkey. We randomly recruited children who had allergic rhinitis and attended the outpatient clinics of Paediatric Allergy and Otorhinolaryngology, Head & Neck Surgery. Exclusion criteria were the following: (a) children with any acute or chronic condition that might affect the immune response; (b) children who had previously been diagnosed with ADHD or other psychiatric disorders; (c) children who had asthma, eczema, food allergy or other allergic disease.

The present study consisted of 25 children with seasonal allergic rhinitis (SAR) sensitized only grass pollen and 34 healthy children as control. Control group was selected from school. Allergic rhinitis group and control group were matched in terms of age and gender. This study was conducted in the Spring, inside the pollen season. The patients and control subjects were seen during the same time point of the pollen season. All patients with SAR were symptomatic. The study included the patients with newly diagnosed SAR. All the controls were free of symptoms of rhinitis. Neither the patients with SAR nor the control group had received antihistamines, nasal corticosteroids or immunotherapy previously.

This study was approved by the ethics committee of the Erzurum Regional Training and Research Hospital, Turkey. Written informed consent was provided by the parents of the children.

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Study design

The children with AR completed the Total 4-Symptom Score (T4SS) and Paediatric Rhinitis Quality of Life Questionnaire (PRQLQ). Conners' Parent Rating Scale-48 (CPRS) questionnaire was completed by the mothers to identify attention deficit and hyperactivity symptoms in children with AR. The patients were given combination treatment of FF nasal spray 27.5 microg once daily and oral levocetirizine dihydrochloride (LD) 5 mg tablet once daily for six weeks. After the treatment for six weeks, the T4SS, PRQLQ and the CPRS were repeated. The mothers of healthy children completed only CPRS questionnaire to compare ADHD symptoms of AR groups and healthy control groups.

Skin prick test

Diagnosis of AR was based on clinical history, physical examination, as well as a positive response to skin prick test (2, 10, 11). Symptoms of AR are rhinorrhea, nasal obstruction, nasal itching and sneezing (2). Allergic sensitization was demonstrated by the skin prick test. The skin prick test was performed the patients with AR during the pollen season. The skin prick tests were performed according to the European Academy of Allergology and Clinical Immunology guidelines. The skin prick tests were accepted to be positive if a wheal diameter was ≥ 3 mm compared with the negative control and was accompanied by erythema 15 minutes after the test was performed (12). All patients with SAR had positive skin prick test reactivity to only grass pollen extract (Allergopharma Ltd, Reinbek, Germany). These patients were not sensitized to other common environmental allergens, including dermatophagoides pharynea, dermatophagoides pteronyssinus, mold mixture, cat, grass or cereal allergen mixture (lolium preenne, festuca pratensis, phleum pratense, poa pratensis,

dactylis glomerata, hordeum vulgare, secale cereale, or triticum sativum), platanus orientalis, papulus albe, cotylus avellana, betula verrucoso and qercus robur.

Symptom score

The T4SS is a subjective scoring system for determination of symptom severity in patients with AR. It includes nasal itching, ocular itching, sneezing and nasal discharge scored from 0 (no symptoms) to three (severe symptoms). Total score is calculated by adding the scores for all four domains (13).

Paediatric rhinitis quality of life questionnaire

The Paediatric Rhinitis Quality of Life Questionnaire (PRQLQ) was developed by Juniper *et al* (14). The reliability and validity of Turkish version of PRQLQ has been made by Yuksel *et al* (15). Paediatric Rhinitis Quality of Life Questionnaire includes domains of symptoms, emotional function and activity limitations, with a total of 23 questions. Each item has Likert-type scales of seven-point responses that range from 0 to 6. All items are equally weighted and higher scores show worse outcome. Domains and total scores are the mean of the items included. “Symptoms” domain includes items 4, 6, 8, 10, 12, 14, 16, 18, 20, 23, “emotional function” domain includes 5, 7, 9, 11, 13, 15, 17, 21 and “activity limitations” domain includes items 1, 2, 3, 19 and 22.

Behavioural assessments

Conners' Parent Rating Scale-48 (CPRS) is a 48-item instrument that is widely accepted to identify ADHD behavioural problems in children (16). Turkish translation of CPRS has been validated by Dereboy and colleagues (17). It yielded six factors of oppositional, conduct, inattention, hyperactivity, anxiety and psychosomatic domains.

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Statistical analysis

The statistics were computed by SPSS 13.0. The Wilcoxon signed rank test was used for pretreatment and post-treatment comparisons, and the Mann-Whitney U test was used to compare AR and control patients. The level of statistical significance was set at $p < 0.05$.

RESULTS

The patient group comprised of 25 children (13 boys and 12 girls, mean age, 12.0 ± 2.36 year), and the control group consisted of 34 healthy children (18 boys and 16 girls, mean age, 10.0 ± 1.31 year). Age and gender were not significantly different between the groups (both $p > 0.05$).

After treatment, T4SS and PRQLQ scores improved significantly in the AR group [both $p = 0.001$] (Table 1).

Table 1. The results of conners' parent rating scale, total 4-symptom score and quality of life in the study.

	AR group ^a		<i>p</i> -value
	Pre-treatment	Post-treatment	
Hyperactivity score	7.6 ± 2.2	3.6 ± 2.5	0.001
Attention deficit score	6.0 ± 2.4	2.4 ± 2.2	0.001
T4SS score	16.7 ± 5.7	5.9 ± 3.5	0.001
Symptom score in QoL	4.6 ± 1.0	1.0 ± 0.7	0.001
Activity score in QoL	4.8 ± 1.1	1.1 ± 0.8	0.001
Emotional score in QoL	4.3 ± 0.8	1.1 ± 0.5	0.001
Total score in QoL	4.5 ± 0.9	1.1 ± 0.6	0.001

Abbreviation: AR: allergic rhinitis, T4SS: Total 4-symptom score, QoL: Quality of life

^a Data are given as mean \pm SD

Pre-treatment attention deficit and hyperactivity scores in the AR group were significantly higher than those in the control group [$p = 0.001$ and 0.009 , respectively] (Table 2).

Table 2. Hyperactivity and attention deficit scores of pre-treatment, post-treatment and control groups

	AR groups and Control Group ^a		
	AR Pre-treatment	Control	<i>p</i> -value
Hyperactivity score	7.6 ± 2.2	5.6±2.7	0.009
Attention deficit score	6.0 ± 2.4	2.7±2.7	0.001
	AR Post-treatment	Control	
Hyperactivity score	3.6 ± 2.5	5.6±2.7	0.007
Attention deficit score	2.4 ± 2.2	2.7±2.7	0.785

^a Data are given as mean ± SD

After treatment, attention deficit scores decreased in AR group (Fig. 1), and there was no difference in attention deficit scores between AR group and controls [$p = 0.785$] (Table 1).

After treatment, hyperactivity scores decreased in AR group (Fig. 2), and hyperactivity scores in AR group were lower than those in the control [$p = 0.007$] (Table 2).

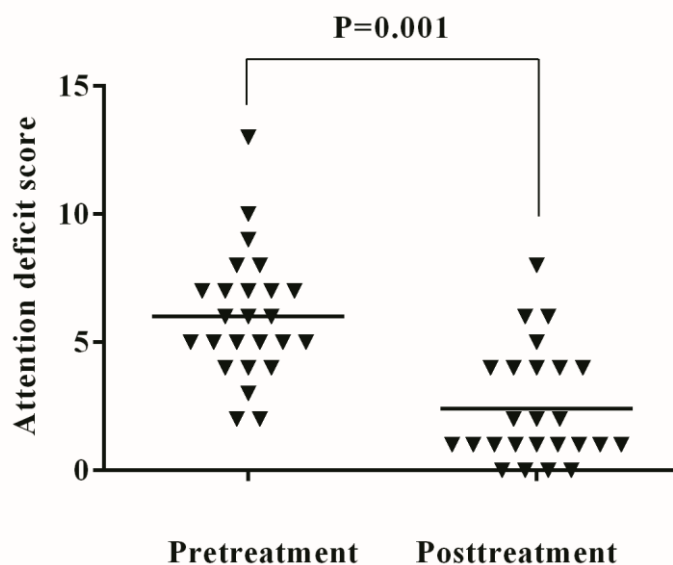


Fig. 1: Pre and post-treatment attention deficit scores in patients with allergic rhinitis.

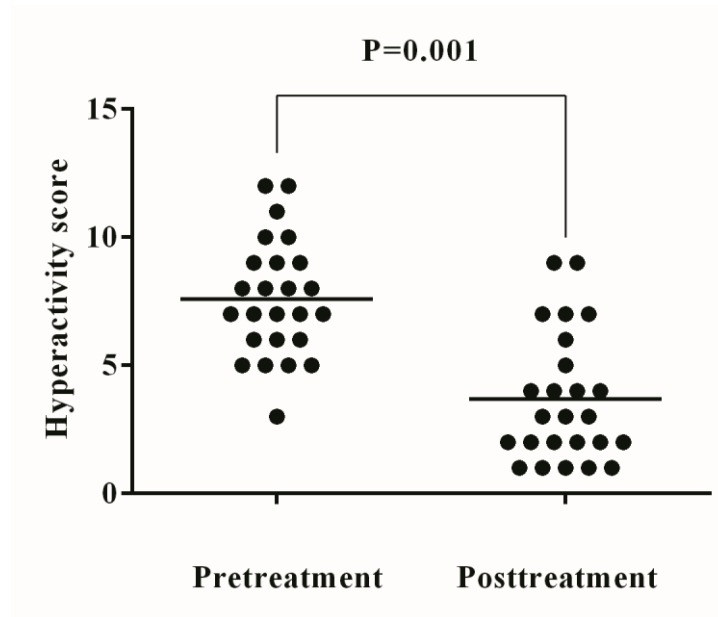


Fig. 2: Pre and post-treatment hyperactivity scores in patients with allergic rhinitis.

DISCUSSION

The results of our study indicate that attention deficit and hyperactivity scores is higher, in children with AR, when compared to the healthy control subjects. The combination treatment of FF nasal spray and LD tablet may improve scores of attention deficit/ hyperactivity, QoL scores and symptom scores in children with AR.

Allergic rhinitis in children with ADHD have been reported previously (18, 19). Conversely, ADHD symptoms among children with allergic rhinitis have also been reported (8, 9, 20). Brawley *et al* investigated children from five to 18 years of age with a diagnosis of ADHD for allergy. The researchers found that 80% of children with ADHD reported had AR symptoms, 100% had a family history of AR and 61% had at least one positive prick skin test result. Also, 43% percent showed typical physical signs of allergic rhinitis (18). Chou *et al* evaluated 469 children with ADHD in a population based study and reported an increased rate

of AR in children with ADHD patients compared with the general population (19). Tsai *et al* investigated the prevalence of atopic diseases among children with ADHD and reported prevalence of atopic diseases (especially allergic rhinitis) in ADHD patients is higher than controls (9). Shyu *et al* examined the prevalence and risk of developing ADHD among allergic patients in a paediatric group. They reported paediatric patients with allergic disorders (including AR, asthma, atopic dermatitis) had an increased rate of developing ADHD. Their detailed analysis showed that the main contributing factor is AR (8). Recently, Yang *et al* investigated hyperactivity and impulsivity in children (aged 6–15 years) with untreated allergic rhinitis. They used AR symptom score and ADHD symptom scale to study the attention and impulsivity in AR children, age matched controls and ADHD children. They reported the scores of Hyperactivity/Impulsivity subscales of ADHD symptoms were significantly higher in the AR children (20).

More recently, Kim *et al* investigated whether attention performance was improved after treatment in children with allergic rhinitis. This cohort study included 797 children with allergic rhinitis and 239 children with non-allergic rhinitis. However, there was no healthy control group in this study. The patients with AR used regularly oral medication and/or intranasal steroid sprays for one year. The patients with non-AR was performed symptomatic treatment on demand. The attention status was evaluated by using the computerized comprehensive attention test. After one year of treatment, children with allergic rhinitis showed improvement in attention. However, there was no significant difference of attention scores in children with non-allergic rhinitis. They reported that the treatment effect on attention was more effective in paediatric AR patients compared with children with non-AR (21). In our study, criteria to evaluate ADHD symptoms, study design, and study population is different from the study of Kim *et al*. We demonstrated that AR patients had higher ADHD

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scores than the healthy control children and ADHD scores improved with treatment of allergic rhinitis.

We think that two mechanisms may explain the relationship between ADHD symptoms and AR in our patients. Firstly, it has been shown that the cytokines released in atopic eczema might pass to the brain circulation and cause behavioural and emotional disorders by activating neuroimmune mechanisms (22, 23). AR is also a chronic inflammatory disease like atopic dermatitis. The inflammatory response in the nasal mucosa includes an immediate IgE-mediated mast cell response as well as a late-phase response characterized by recruitment of eosinophils, basophils, and T cells expressing Th2 cytokines (2, 24). Like atopic dermatitis, the cytokines released in the patients with AR might pass to the brain circulation and cause neurobehavioural problems by activating neuroimmune mechanisms. Secondly, AR impairs quality of life, sleep, daily activities, school and work. Also, it has chronic, stressful and troublesome symptoms (2). The sleep disturbance is one of the important complications of AR in childhood (25, 26). The cause of sleep disorders in AR is nasal congestion and obstruction and often lead to physical fatigue. Children with AR might have microarousals, snoring and obstructive apnea during sleep (27). Therefore, the patients with AR may experience high levels of psychological stress. Increased stress exposure in the children with AR might lead increased of ADHD symptoms.

Intranasal corticosteroids reduce nasal congestion, thereby improving sleep and, consequently, quality of life in patients with allergic rhinitis (27). Yuksel *et al* recently showed that nasal steroid and antihistaminic treatment for eight weeks improve nasal symptoms, quality of life and sleep disturbances in children with allergic rhinitis (25).

In conclusion, this study indicates that ADHD symptoms in children with AR are higher than those in healthy controls. Moreover, The patients have high nasal symptom scores

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and high PRQLQ scores. The combination treatment of FF nasal spray and LD tablet may improve nasal symptoms, QoL and ADHD symptoms in children with AR.

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