The effect of Enterobius vermicularis infection (oxyuriasis) on eosinophil and IgE levels in allergic rhinitis

Fevzi Solmaz[1], Oğuzhan Dikici[1], Davut Akduman[2], Mehmet Haksever[1], İsmail Necati Hakyemez[3], Muhammed Yanılmaz[4]

[1]Department of Otorhinolaryngology, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey
[2]Department of Otorhinolaryngology, Düzce University School of Medicine, Düzce, Turkey
[3]Department of Infection Diseases, Bezmialem University School of Medicine, İstanbul, Turkey
[4]Department of Otorhinolaryngology, Bezmialem University School of Medicine, İstanbul, Turkey

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ABSTRACT

Objectives: Elevated levels of serum IgE and eosinophilia are the indicators of atopy and intestinal parasitic infections. We evaluated the effect of *Enterobius vermicularis* infection (enterobiasis) on blood eosinophil count and IgE levels in allergic rhinitis.

Methods: A total of 110 patients diagnosed with allergic rhinitis (with symptoms of rhinorrhea, itchy nose and nasal congestion) consisting of 41 (37.27%) males and 69 (62.73%) females were examined. Forty-one (37.27%) patients with enterobiasis were selected as the study group. The remaining 69 (62.73%) patients accepted as the control group.

Results: In the study group the mean serum total IgE level and mean serum eosinophil count were 393.10 ± 159.83 IU/mL and 0.56 ± 0.04 10^3/mL, respectively. In the control group the mean serum total IgE level and mean serum eosinophil count were 236.91 ± 63.55 IU/mL and 0.37 ± 0.12 10^3/mL, respectively. The difference between the two groups was statistically significant for serum total IgE levels ($p < 0.05$) but not for serum eosinophil count ($p > 0.05$). The correlation coefficients between serum total IgE level and eosinophil count were statistically insignificant ($p > 0.05$).

Conclusions: More comprehensive and long-term placebo-controlled studies should be performed in order to find the answer to the question of whether helminth infections play a role in allergic disease.

Keywords: *Enterobius vermicularis* infection, allergic rhinitis, serum IgE level, serum eosinophil count

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Elevated levels of serum IgE and eosinophilia are the indicators of atopy, but intestinal parasitic infections may also play role in alterations of those parameters [1]. In atopic individuals, the secretion of IgE increases depending on type 1 immune response. Human and animal studies have revealed a relationship between allergy and parasitic infections [2]. Elevated serum total IgE levels indicate either chronic parasitic infection or atopy.

Interactions between serum IgE levels, eosinophil count and parasitic infections depend on the duration of infestation and the type of helminth [3]. This is common in the population with endemic helminthic infections [4, 5]. It has been shown that persons with the highest total IgE levels are re-infected after the treatment of helminthic infections in endemic areas.

Address for correspondence: *Fevzi Solmaz, MD., University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Otorhinolaryngology, Emniyet Caddesi No:35, 16115 Yıldırım, Bursa, Turkey*
E-mail: solmazfevzi@hotmail.com, Phone: +90 224 2955000, Fax: +902243660416

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Such elevated levels of total IgE may be due to environmental factors rather than heredity [6]. On the other hand, experimental and epidemiological studies have provided conflicting results. The phagocytic ability of eosinophils is weaker than that of neutrophils and their major functions are seen after the activation of toxic granule secretion. The main function of eosinophils in the host defense system against parasites is to attach, immobilize and kill parasites. The granular proteins secreted from the activated eosinophils kill parasites but they may cause damage to some mammalian cells. They can then lead to tissue damage and cause asthma or other inflammatory disorders. The most common inflammatory conditions, such as bronchial asthma, allergic eye inflammation, chronic fatigue syndrome, parasitic and bacterial infections, atopic dermatitis, rhinitis, allergic middle ear effusion and autoimmune diseases accompany to the eosinophil activation [7].

IgE is important both for active immunity in type I hypersensitivity reactions (such as asthma, urticaria, and high fever) and against parasites called helminths. A strong correlation is observed between allergy and increased serum IgE levels. The evaluation of serum IgE levels is therefore useful in conditions such as allergic rhinitis, extrinsic asthma, urticaria, atopic eczema, and anaphylaxis.

Eosinophils are leukocytes that eliminate antigen-antibody complexes and are capable of phagocytosis. The number of eosinophils increases in conditions such as allergy and parasitic disease. The granules of these leukocytes contain histamine at a rate of 33% in humans. The amount of IgE in mucosal secretions increases during helminthic infections and allergic diseases [7].

Enterobiasis (pinworm disease or threadworm) is caused by the small nematode *Enterobius vermicularis.* Prevalence rates up to 100% have been recorded in Northwestern Europe and the USA. It is probably the most common helminth to infect humans. *E. vermicularis* eggs have been displayed in a coprolite carbon dated to 7837 BC in western Utah [8].

Routine examination of a fecal sample gives a positive diagnosis in only 5-15% of infected subjects [8]. The best way of diagnosis depends on identification of adult worms or eggs, or both - which can be visualized in perianal region, usually at night [9, 10]. Application of a Sellotape strip to the perianal region is of value; when adherent (sticky side downwards) to a microscope slide, visualization of worms and eggs is straightforward (the debris is cleared with a drop of toluene). Three tests can detect 90% of infections while six consecutive negative results on separate days virtually exclude this diagnosis.

The aim of this study was to determine the effect of *E. vermicularis* infection (enterobiasis) on blood eosinophil count and IgE levels in allergic rhinitis, and to discuss the role of helminths in allergic rhinitis. We compared patients diagnosed with allergic rhinitis who were positive or negative for enterobiasis regarding IgE levels and eosinophil counts.

METHODS

Patients who presented to the Ear, Nose and Throat Clinic and diagnosed with Allergic Rhinitis were evaluated. Informed consent was received from all patients. The Ethical Committee Approval was received from the study center. The diagnosis of allergic rhinitis was established by patient's history, a positive prick test and elevated serum IgE levels (higher than 100 U/mL). Patients diagnosed with both allergic rhinitis and enterobiasis was included in the study group. The diagnosis of enterobiasis was confirmed by 3 consecutive anal cellotape microscopy evaluations while 6 consecutive negative results were required to rule out enterobiasis. Feces microscopy was used to rule out other parasites and patients whose feces were positive for parasite eggs other than *E. vermicularis* were excluded.

After informed consent was received from the patients, a clinical history was taken and a physical examination including nasopharyngeal examination performed. A total of 110 patients diagnosed with allergic rhinitis (with symptoms of rhinorrhea, itchy nose and nasal congestion) consisting of 41 (37.27%) males and 69 (62.73%) females were included in the study. The 41 (37.27%) patients with positive result for *E. vermicularis* eggs were selected as the study group. The remaining 69 (62.73%) patients evaluated as the control group. Factors affecting allergy or atopy were ruled out with questions. We were unable to include a healthy control group and our control group consisted of the subjects with allergic rhinitis in whom

Table 1. The demographic characteristics and laboratory findings of the patients.

	With *E. vermicularis* (n = 41)	Without *E. vermicularis* (n = 69)	*p*
Age (year)	34.25 ± 10.58	34.94 ± 10.84	> 0.05
Gender (M/F)	13/28	28/41	> 0.05
IgE (IU/mL)	393.10 ± 159.83	236.91 ± 63.55	< 0.05
Eosinophil count (10^3/mL)	0.56 ± 0.04	0.37 ± 0.12	> 0.05

Data are shown as mean±standard deviation or number

E. vermicularis eggs were not found on microscopy.

Patients who had used oral antibiotics or corticosteroids and inhaled corticosteroids within the prior 30 days were excluded from the study. A detailed history was taken and an examination was performed and the patients were referred for blood and stool samples.

The samples were evaluated for *E. vermicularis* eggs with a light microscope at a magnification of 10× and 40× by an infectious diseases specialist. Eosinophil levels above 0.5 103/ml in the complete blood count were considered as positive or elevated. The association of total serum IgE levels and eosinophil count with the presence of *E. vermicularis* infections or allergic rhinitis was investigated.

Single-dose mebendazole treatment with a repeated dose a week later used for treatment. The pre-treatment results were also compared with the post-treatment results.

The relationship between total serum IgE and eosinophil count was analyzed using Pearson's Correlation and Spearman's rank tests due to the non-normal distribution of the variables. These analyses can potentially create a basis for treatment. All data were analyzed using the SPSS for Windows v.16.0 software by IBM, USA.

Statistical Analysis

The relationship between total serum IgE and eosinophil count was analyzed using Pearson's Correlation and Spearman's rank tests due to the non-normal distribution of the variables. These analyses can potentially create a basis for treatment. All data were analyzed using the SPSS for Windows v.16.0 software by IBM, USA.

RESULTS

The 110 patients included in the study consisted of 41 (37.27%) males and 69 (62.73%) females. The average age was 32.50 ± 7.42 years. The blood serum IgE levels were 138.00 to 850.00 IU/mL (282.69 ± 129.93 IU/mL). Our patients were selected from subjects with allergic rhinitis and elevated serum IgE levels. Table 1 presents the total IgE level, eosinophil count, and gender and age values of the allergic rhinitis patients. The mean serum total IgE level and mean serum eosinophil count for the 41 patients who were positive for *E. vermicularis* eggs and 69 patients in the control group were also presented in Table 1. The difference between two groups was statistically significant for serum total IgE levels ($p < 0.05$), but not for serum eosinophil count ($p > 0.05$). Table 2 presents the pre- and post-treatment serum eosinophil counts and total serum IgE levels of patients with helminth infections and allergic rhinitis. The difference between the groups was statistically significant for serum total IgE level ($p < 0.05$) but not for serum eosinophil count ($p > 0.05$).

Eggs of *E. vermicularis* were found in 41 (37.27%) patients with the sellotape evaluation repeated 3 times. The correlation coefficients between serum total IgE level and eosinophil count are shown in Tables 3 and 4 and the results were statistically insignificant ($p > 0.05$).

Table 2. Pre- and post-treatment IgE level and eosinophil count.

	Pre-treatment (with *E. vermicularis*)	Post-treatment (with *E. vermicularis*)	*p*
IgE (IU/mL)	393.10 ± 159.83	228.90 ± 84.40	< 0.05
Eosinophil (10^3/mL)	0.56 ± 0.04	0.43 ± 0.07	> 0.05

Data are shown as mean±standard deviation

Table 3. Pearson correlation of IgE level and eosinophil count.

		IgE (n = 41)	Eosinophil (n = 41)
IgE level	Pearson Correlation	1.000	0.162
	Sig. (2-tailed)		0.311
Eosinophil count	Pearson Correlation	0.162	1.000
	Sig. (2-tailed)	0.311	

Table 4. Spearman rank test analysis of IgE level and eosinophil count.

		IgE (n = 41)	Eosinophil (n = 41)
IgE level	Correlation Coefficient	1.000	0.211
	Sig. (2-tailed)		0.186
Eosinophil count	Correlation Coefficient	0.211	1.000
	Sig. (2-tailed)	0.186	

DISCUSSION

Increased serum IgE level and eosinophilia are not specific to the allergic diseases. They are also associated with helminth infections [11, 12]. Nowadays, total serum IgE level is a poor indicator of allergic respiratory diseases. High serum IgE levels resulting from polyclonal activation are caused by chronic infection by geohelmints [13, 14]. Features of helminthic infections are complex in the endemic areas and the immune system response may show individual differences in atopic subjects. Thus, the serum IgE levels may also increase in atopic persons [15].

Geohelmints may also stimulate the release of polyclonal IgE [16]. The helminths, not only increase the production of antiparasite IgE antibody, but also stimulate polyclonal IgE synthesis, resulting in highly elevated levels of total IgE in the blood circulation [17]. Although there is some doubt regarding the relationship between helminthic infections and IgE antibody levels, IgE antibody is an important component of the immune response against parasites [18].

Although helminthic infections are less common in developed countries, atopic diseases are paradoxically more common. Exposure to infections in early childhood decreases the risk of allergy according to the "Hygiene Hypothesis" [19]. Intestinal helminths may decrease polyclonal IgE production in populations with parasitic infection according to this hypothesis [20]. In contrast to the hygiene hypothesis, serum IgE levels of patients with allergic rhinitis only were lower than that of patients with both allergic rhinitis and *E. vermicularis* infection in our study. However, this may be associated with the duration and severity of these disorders in our patients. Some studies have shown no association between helminth infections and allergic diseases [21]. However, it is reported that parasitic helminths can prevent hyperresponsiveness and eosinophilic airway inflammation in experimental animal models [22, 23]. In our study we investigated patients with E. vermicularis only and it may be appropriate to study the effects of other parasitic infections as well.

Eosinophils are located in two different regions: tissue and blood. Although the maturation and life of serum eosinophils depend on interleukin-5 (IL-5), the tissue eosinophils depend on granulocyte and macrophage colony stimulating factor (GM-CSF) [24]. Eosinophil count is therefore normal in the blood, but active eosinophils are filled by eosinophil cationic protein, major basic protein, active granules, and other mediators [24, 25]. The eosinophil levels are normal in some patients since blood eosinophils are down-regulated. The peripheral circulation may not be affected and the inflammatory process may be mild with drug intake and in chronic intestinal parasitic infections [26].

A meta-analysis of the epidemiologic literature by Feary *et al*. [27] has shown that intestinal parasite infections such as geohelminth infections are related to a reduced prevalence of allergic sensitization. The levels of serum total IgE and eosinophils of allergic rhinitis patients with *E. vermicularis* infection were higher than in patients with allergic rhinitis only in our

study, possibly depending on the duration of E. vermicularis infection.

When the intestinal larvae migrate, the eosinophil numbers may decline consequently. Eotaxin is required for chemotaxis [28]. Chronic parasitic infections regulate the immune response and the allergic response is reduced especially in early life. Genetic predisposition to atopy may also provide strong resistance to geohelminth infections. It has been demonstrated that geohelmints may increase the production of specific antibodies [13]. However, the increase in nonspecific polyclonal IgE synthesis and high total IgE levels are directly related to the presence of parasites [14].

The sensitivity of stool examination can be as low as 40% in some cases. When using the stool examination to evaluate parasite infection, one needs to take into account recurrent anti-helminthic treatment and the small amounts of parasite or the larval forms of the parasite [20]. Nyan *et al*. [20] found higher serum total IgE concentration in atopic patients than in non-atopic persons. They suggested that atopic individuals are less infected with helminths than non-atopic persons and that atopy could therefore be a protective factor against helminthic infections. High concentrations of non-specific IgE may prevent the invasion of intestinal parasites. They did not find any relationship between serum IgE concentration and helminth infections.

Since the immune response against parasite infections is variable, mild helminth infections may increase the allergic response in contrast to severe infections [29, 30]. Eosinophilia and elevated serum IgE are often observed in acute illness as a form of immune response [26]. High serum IgE levels may also trigger eosinophilia.

The helminths can induce suppressor T cells and lead to a low response against environmental allergens. Interleukin-10 (IL-10) reduces the number of serum eosinophils and also produces transforming growth factor beta (TGF-B) [26]. Production of polyclonal IgE against helminths is a common characteristic in atopic individuals [30]. The host immune response against intestinal helminths is similar to the allergic response. An IgE response is associated with the helminths in children with an atopic predisposition. Helminths and other infectious agents also increase serum IgE levels by increasing the production of non-specific B cells. Wördemann *et al*. [19] have reported that various relationships are present between helminthic infections and atopic diseases depending on the type of helminth and the allergy.

Lynch *et al*. [5] reported that a history of a strong IgE response in atopic children led to an increased protective response against helminths. The infection intensity was significantly lower compared to non-atopic subjects in that study.

The impact of helminths on allergic reactions is occurred in two ways. Nonspecific IgE synthesis may occur in patients with sporadic helminthic infections as a result of stimulation of the immune system and it may increase the allergic sensitivity in these individuals. Mast cell receptors can also be blocked due to excessive polyclonal IgE development in recurrent infections leading to the inhibition of specific IgE production against allergens [30]. Geller *et al*. [31] found no difference in serum IgE levels between the patient group and control group. Arıdoğan *et al*. [32] detected an elevated total IgE rate of 73.77% in the group infested with helminths and 35.14% in the group without helminths. Herrström *et al*. [33] found *E. vermicularis* in the 23 of 102 nonallergic control subjects and 26 of 70 allergic patients and the difference was statistically significant ($p = 0.037$).

Ganguly *et al*. [34] reported that total and specific IgE levels increased in hookworm-infected patients and then decreased significantly after treatment. In the present study, consistent with the literature, a significant decrease in the serum IgE level after treatment was observed. There was also a decrease in serum eosinophil levels but this was not statistically significant. The results reported in the literature lead to questions about the relationship between parasite infection and allergy. Long-term studies need to be conducted to clearly investigate the causal relationship between helminthic infections and atopic diseases

CONCLUSION

More comprehensive and long-term placebo-controlled studies should be performed in order to find the answer to the question of whether helminth infections play a role in allergic disease.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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