Evaluating the relation between pruritus, serum IgE levels and severity of clinical manifestations in atopic dermatitis patients

Avaliação da relação do prurido e níveis sanguíneos de IgE com a gravidade do quadro clínico em pacientes com dermatite atópica

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Abstract: BACKGROUND - Atopic dermatitis patients often have high serum immunoglobulin E (IgE) levels and pruritus is a major symptom of the disorder. OBJECTIVE - To describe the characteristics of pruritus in atopic dermatitis (AD) patients and to correlate severity of eczema with plasma IgE levels METHODS - Patients with atopic dermatitis seen at the Dermatology Service of Hospital de Clínicas de Porto Alegre and at the Dermatology and Pediatrics Service of Universidade Luterana do Brasil filled out a questionnaire on AD symptoms and had their blood collected for serum IgE levels. Severity of dermatitis was assessed according to criteria adopted by Rajka et al. Data were analyzed by SPSS program. RESULTS: Eighty-nine patients completed the study. The mean age was 9.6 ± 9 years and 51% were female. The relation between frequency of pruritus and severity of dermatitis was significant (p=0.003). Forty-five percent of patients with mild atopic dermatitis presented pruritus every day. Ninety percent of severe patients showed daily symptoms, and only 4.5% remained symptom-free for more than seven days. The median serum IgE level was 347 UI/ml. The median serum IgE levels for mild, moderate and severe cases were 279 UI/ml, 347 UI/ml and 952 UI/ml, respectively (p=0.699). Females showed significantly lower serum IgE levels when compared to males (212 UI/ml vs. 2067 UI/ml, p=0.004). CONCLUSIONS- Although IgE levels were higher in severe patients, this study did not demonstrate a trend toward greater levels in patients with severe eczema as compared with mild eczema. Males have significantly higher serum IgE levels than females. Keywords: Dermatitis, atopic; Immunoglobulin E; Pruritus

INTRODUCTION

Atopic dermatitis (AD) is a very common disease, mainly in childhood, which affects from 10 to 20% of children in developed countries.1-3 Forty to sixty percent of patients with this dermatosis present associated respiratory allergic manifestations.2,4-6 The etiopathogenesis of AD has not been com-
pletely clarified, and it is considered a multifactorial
disease, with intrinsic and extrinsic factors involved. As
to humoral immunity, the main laboratory finding is
increased total serum IgE levels in 70-80% of cases.
Some authors correlated total serum IgE levels with
severity of clinical manifestations; however it has not
been defined yet.9-13

Allergic or atopic individuals produce IgE after
contact with allergens even at low concentrations. This
response occurs in the site where the allergen pene-
trates the body (mucosal surfaces, skin and/or local
lymph nodes). The produced IgE first sensitizes local
mast cells, causing immediate allergic reactions (histo-
amine release); the exceeding IgE enters circulation and
binds to receptors both in circulating basophils and
mast cells fixed in tissues throughout the body, and
thus triggering systemic reactions.14,15

Pruritus is the main symptom in all AD patients,
in any phase of the disease, and the act of scratching
leads to most skin lesions.16,17 In a study with 100
Chinese patients with atopic dermatitis, Yosipovitch et
al. demonstrated that most of them suffered form pru-
ritus every day, primarily in the cervical region and in
joints, and pruritus was at least twice more intense
than that related to insect stings.18

Different methods have been proposed to assess
severity of AD.20,8 Past or family history, age at onset of
eczema and pruritus intensity are some factors men-
tioned as extremely important to quantify the clinical
manifestation of the disease.21

The most used method to verify intensity of the
clinical picture of atopic patients was proposed by
Rajka et al.,20 and it takes into account the extension of
body surface with lesions, the natural history of the dis-
ease and intensity of pruritus.

To understand and manage the situations that
trigger and aggravate pruritus in atopic patients may
lead to significant improvement of clinical manifesta-
tions and less severe cases. Thus, this study aims to
evaluate the relation between pruritus and IgE levels in
AD patients, as well as to correlate these levels with
severity of AD symptoms.

METHODS

A cross-sectional analytical study was carried out
and the sample comprised AD patients seen at the out-
patient's clinics of the Dermatology Service of the
Hospital de Clínicas de Porto Alegre and at the
Dermatology and Pediatrics Services of the Universidade
Luterana do Brasil. The sample size to detect difference
in IgE levels and moderate intensity of the disease (effect
size of 1, that is, one standard deviation) should have a
minimum of 17 patients in each severity level. If we es-
imate that there are fewer severe patients (20%), we
would need approximately 86 patients.

The inclusion criteria adopted were clinical man-
ifestations of AD when enrolling in the study and to
agree to take part in it. The following patients were
excluded: individuals presenting pruritic dermatoses
different from AD, patients on medications that cause
pruritus as side effect, and suffering any disease that
induces higher blood IgE levels, except for asthma or
allergic rhinitis, which were analyzed during the study.

Data were collected based on a questionnaire
applied during the routine visit. Parents of illiterate chil-
dren were asked to help them filling in the questionnaire,
which comprised questions regarding symptoms and activ-
ities of daily life of patients. The questions were adjusted
from the questionnaire validated by Yosipovitch et al.,
in 2002, describing pruritus in atopic dermatitis patients.18

The physical examination to assess severity of disease
was performed by a dermatologist, according to the criteria
established by Rajka and Langeland,20 who divided AD into
mild, moderate and severe disease.

The serum IgE results of patients who had been
recently submitted to examination (during the last atopic
dermatitis exacerbation) were retrieved from the medical
record. Patients who had no IgE results were asked to
have the test performed during the enrollment visit.

This study was approved by the Research Ethics
Committee of the Hospital de Clínicas de Porto Alegre
in March 2003, as to its scientific and methodology
(protocol number 03-17) and approved by the Ethics
Committee of Ulbra, in May 2003.

The SPSS program was applied to analyze data,
and we used frequencies, medians, 25 percentile (p25)
and 75 percentile (p75). In order to compare IgE level
with severity of AD, the Kruskal-Wallis test was used.
Mann-Whitney and chi-squared tests were used for
analysis. The significance level was \( \alpha = 0.05 \).

RESULTS

From April 2003 to January 2004, 89 atopic der-
matitis patients were examined and had the following
demographic characteristics (Table 1).

Concerning frequency of pruritus, most patients
had symptoms every day (71.90%); 15.7% complained of
itching during some days per week and 12.40% presented
this symptom with at least a seven-day interval. Evaluating
frequency of pruritus and severity of manifestations, a sig-
nificant relation (p=0.003; chi-squared test) was observed.
Forty-five percent of patients with mild AD presented itch-
ing every day, 20% every week and 35% had less than once
a week. As to patients with a moderate condition, 74.5%
had daily symptoms, 19.1% weekly symptoms, and only
6.4% presented an interval longer than seven days. On the
other hand, in seven severe individuals, 90.9% presented
symptoms every day, and only 4.5% reported an interval
longer than seven days between itching episodes.

The median IgE levels of the patients studied
were 347UI/ml; and the 25 and 75 percentiles corre-
sponded to 98 UI/ml and 3.222.50 UI/ml, respectively.
In 24% of patients IgE levels were lower than 100UI/ml
(normal); in 31.5% they ranged from 100 to 500UI/ml;
in 21.3%, from 501 to 4000UI/ml; and in 22.5% they
were greater than 4001UI/ml.
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Correlating clinical severity of AD with IgE levels, in mild patients we found a median of 279UI/ml (p25=103UI/ml and p75=2431UI/ml); in patients with moderate manifestations, a median of 347UI/ml (p25=56UI/ml and p75=2267UI/ml); and in severely affected individuals, a median of 952UI/ml (p25=135UI/ml and p75=4.085UI/ml) (p = 0.699; Mann-Whitney test) (Graph 1).

The median IgE found in females was 1440.89UI/ml (p25=62UI/ml and p75=758UI/ml), whereas in males it was 2067UI/ml (p25=155UI/ml and p75=4.190UI/ml) (Graph 2), and the IgE level difference was statistically significant (p= 0.004).

The patients reporting daily pruritus had a median IgE of 388.50UI/ml (p25=143.50UI/ml and p75=3435.25UI/ml), whereas those with this complaint every week had 365UI/ml (p25=90.50UI/ml and p75=3709.50UI/ml), and for patients suffering at intervals longer than one week it was 86UI/ml (p25=20UI/ml and p75=935UI/ml) (p = 0.129; chi-squared test).

Only 33.7% of patients presented an isolated manifestation of AD; 42.7% of sample had associated bronchial asthma and 43.8% presented allergic rhinitis.

Many patients (25.8%) presented asthma and allergic rhinitis associated with AD.

**DISCUSSION**

AD is a disease that may cause physical and psychological suffering to affected individuals. Its high incidence shows the need to better understand its etiological mechanism.

Asthma and rhinitis are conditions usually associated with AD and are observed in 20-60% of patients.10-14 In the present sample, an association with asthma or rhinitis was found in 66.3% of patients, and the percentage was slightly higher than that described in the literature.

Pruritus is a predominant symptom in AD patients, and the main cause of suffering of patients.15-18 Although most patients of this study (74.2%) presented pruritus every day, this value was lower than that reported by Yosipovitch et al.,18 who demonstrated that 87% of their sample presented daily symptoms.

In this study, the relation between severity of clinical manifestations and pruritus was as follows: 45% of patients with mild, 74.5% with moderate and 90.9%...
with severe manifestations experienced itching every day. These findings indicated that patients with more severe AD were also more symptomatic as to pruritus. This may be related to the fact that pruritus causes and maintains eczematous lesions in AD. In most cases, patients with more pruritus are those with larger lesions and consequently classified as more severe.

There is evidence that total serum IgE levels are increased in AD patients. However, it is difficult to define normal levels, since IgE levels fluctuate in serum, likewise other immunoglobulins.

Several reports in the literature state that IgE would tend to present higher levels in patients with more severe allergy. In this study, these data were not significant (p=0.699), unlike findings of previous works. Nevertheless, maybe there was no significant difference due to a high incidence of severe patients.

A significant relation was found in frequency of pruritus and severity of AD, and over 90% of severe patients presented pruritus every day. These findings are in accordance with the literature, confirming pruritus as an important symptom in atopic patients.

The mean IgE level found in males was significantly higher than that of females (p=0.001). This agrees with the findings reported by Spalding et al., who observed a mean of 78.5UI/ml in male patients and 30.2UI/ml in female patients. There is no explanation for this difference between sexes.

The presence of positive IgE dendritic cells in the skin of AD patients shows that there might be a pathogenic relation between the serum levels of this immunoglobulin and AD. Since pruritus is the main symptom reported by AD patients, we sought a relation between patients with frequent itching and their IgE levels. There was no statistical significance between the groups of patients, but it was possible to verify that the median serum IgE level was higher in patients suffering from pruritus every day when compared with those with longer symptom intervals. These data enable speculating there might be a correlation between these factors and further studies with larger samples could demonstrate this suspicion.

CONCLUSION

Analyzing together these data, we concluded that more severe AD patients presented pruritus much more often than those with milder cases. Although serum IgE levels were higher in more severe patients, they were not statistically significant to demonstrate a correlation with severity of clinical manifestations. Male AD patients presented higher serum IgE levels than females.

REFERENCES


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