We have analysed the relationship of blood eosinophil count and serum eosinophil cationic protein (ECP) levels in patients with acute and chronic idiopathic urticaria. The ECP levels and eosinophil counts were measured in the peripheral blood of 15 patients with acute urticaria, 25 with chronic idiopathic urticaria and 10 normal healthy subjects. Blood eosinophil counts and serum ECP levels increased in all patients with acute urticaria. Concerning patients affected by chronic urticaria, taking into account the recrudescence of the disease at the moment of taking the blood sample, only symptomatic patients showed increased eosinophil blood values whereas serum ECP levels were increased both in symptomatic and asymptomatic patients. Furthermore, serum ECP levels in chronic urticaria did not correlate with the peripheral eosinophil counts, as they did in acute urticaria. The results of the present study indicate that eosinophils may play a role in the inflammatory mechanisms in patients with acute and chronic urticaria showing a positive correlation between serum ECP levels and disease activity.

Key words: Acute urticaria, chronic urticaria, ECP, eosinophil

Blood eosinophils and serum eosinophil cationic protein in patients with acute and chronic urticaria


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Introduction

Circumscribed, raised, erythematous, evanescent areas (weals) of oedema that involve the superficial portions of the dermis are known as urticaria. Recurrent episodes of urticaria, characterized by transitory itchy weals, lasting longer than 8 to 12 weeks, are termed chronic. Many cases of acute urticaria are triggered by IgE antibodies to various foods, drugs, inhalants, or other allergens. There is a strong consensus that it is rarely possible to demonstrate IgE antibodies as a cause of chronic urticaria, although in this case autoantibodies against the high-affinity IgE receptor may be involved.

In chronic urticaria, previous studies have demonstrated that an increased number of mast cells, monocytes, T-lymphocytes and eosinophils are present in biopsy specimens. Yet the role played by eosinophils in the pathogenesis of skin lesions is not completely understood. The activated eosinophil itself elaborates a variety of inflammatory mediators, including, leukotrienes, the major basic protein, eosinophil cationic protein (ECP), the eosinophil protein X/eosinophil-derived neurotoxin and eosinophil peroxidase. The elaboration of these different mediators is consistent with the hypothesis that the eosinophil can be involved in both allergic and nonallergic mechanisms. Particularly, ECP may affect neurogenic responses and might therefore play a role in itching conditions. Previous studies have provided evidence that ECP may mediate cutaneous tissue damage and, in particular, be involved in chronic idiopathic urticaria. Samples from local venous blood in cold urticaria have shown raised levels of histamine and eosinophil chemotactic factor. To gain insight into the role of eosinophils in chronic urticaria, we have analysed the relationship of eosinophils to serum ECP levels in patients with acute and chronic idiopathic urticaria.

Patients and Methods

Patients: Fifteen patients with acute urticaria and 25 patients with chronic idiopathic urticaria took part in the study. Acute and chronic urticaria were respectively defined as weals lasting less than 24 h and as recurrent weals lasting at least 6 weeks or more than 2 months (median 100 weeks). Patients affected by chronic urticaria were split in two groups, taking into account the recrudescence of the disease, at the moment of taking the blood sample. Thirteen patients were symptomatic with daily eruptions, whereas 12 patients were asymptomatic for at least 3 weeks. Patients with urticaria, resulting predominantly...
from physical causes were excluded. Anti-
histamine treatment was stopped at least 48 h
before the serum samples were collected. None
of the patients was taking steroids or immuno-
suppressive drugs at the time of the study. The
control group consisted of ten healthy members
of the laboratory staff without urticaria or a
history of atopy. All the subjects examined were
women. Informed consent was obtained from all
participants.

**Eosinophil blood count:** A venous blood sample
was collected, and the eosinophils were counted
in a Fuchs Rosenthal chamber after staining with
eosinophil staining solution.\(^5\)

**Quantification of ECP:** The blood samples were
stored for 1 h at room temperature before cen-
trifugation at 1600 \(\times g\) at 4\(^\circ\)C for 10 min. Serum
was collected and recentrifuged at 1600 \(\times g\) at
4\(^\circ\)C for 10 min. The collected samples were
stored at -70\(^\circ\)C until assay. A double antibody
radioimmunoassay test has been used to quantify
serum ECP. The assay was performed with com-
mercially available kits purchased from Pharmacia
Diagnostics (Uppsala, Sweden), according to
manufacturers' instructions. The intra-assay coef-
ficient of variation was less than 70%, and the
detection limit was less than 2 \(\mu g/l\).

**Statistical analysis:** All data are expressed as
means \(\pm\) S.D. Correlations were calculated by
linear regression. The values for the different
group were compared with Student’s \(t\)-test.

**Results**

Table 1 shows mean values of the eosinophil
blood counts from the ten normal healthy sub-
jects, the 15 patients with acute urticaria and the
25 patients with chronic urticaria. The mean eos-
inophil counts were significantly higher both in
patients with acute urticaria and in patients with
chronic symptomatic urticaria compared to that
of the healthy subjects. Patients affected by acute
urticaria showed eosinophil count values signifi-
cantly higher than patients affected by chronic
urticaria. No significant difference was found
between the healthy subjects and the patients
with asymptomatic chronic urticaria.

Diversely, the mean ECP serum concentrations
were significantly higher both in patients with
acute urticaria and in patients with chronic urti-
caria compared to that of the healthy subjects; but
patients affected by acute urticaria did not show
ECP serum concentrations higher than patients
affected by chronic urticaria. Taking into account
the recrudescence of the chronic urticaria, signifi-
cant differences were found between the healthy
subjects and both symptomatic and asymptomatic
patients. Finally, in the asymptomatic chronic
patients mean ECP serum concentrations were
significantly lower than both in patients affected
by acute urticaria and in patients affected by
chronic symptomatic urticaria (Table 2).

**Table 1. Eosinophil blood counts (mean \(\pm\) S.D.) in healthy
subjects and in patients with acute or chronic urticaria**

<table>
<thead>
<tr>
<th></th>
<th>Eosinophils (\times 10^3/\mu l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy subjects</td>
<td>0.190 (\pm) 0.045(^a)</td>
</tr>
<tr>
<td>Acute urticaria</td>
<td>0.513 (\pm) 0.211(^b)</td>
</tr>
<tr>
<td>Chronic urticaria (symptomatic)</td>
<td>0.230 (\pm) 0.090(^d)</td>
</tr>
<tr>
<td>Chronic urticaria (asymptomatic)</td>
<td>0.186 (\pm) 0.068(^e)</td>
</tr>
</tbody>
</table>

\(^a\) vs. \(^b\) \(p = 0.001\)
\(^a\) vs. \(^c\) \(p = N.S.\)
\(^a\) vs. \(^d\) \(p = 0.001\)
\(^a\) vs. \(^e\) \(p = N.S.\)
\(^b\) vs. \(^e\) \(p = 0.002\)
\(^c\) vs. \(^d\) \(p = N.S.\)

**Table 2. Serum ECP values (mean \(\pm\) S.D.) in healthy
subjects and in patients with acute or chronic urticaria**

<table>
<thead>
<tr>
<th></th>
<th>ECP ((\mu g/l))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy subjects</td>
<td>4.04 (\pm) 0.64(^c)</td>
</tr>
<tr>
<td>Acute urticaria</td>
<td>36.84 (\pm) 17.25(^b)</td>
</tr>
<tr>
<td>Chronic urticaria (symptomatic)</td>
<td>25.28 (\pm) 16.68(^c)</td>
</tr>
<tr>
<td>Chronic urticaria (asymptomatic)</td>
<td>37.77 (\pm) 12.60(^d)</td>
</tr>
</tbody>
</table>

\(^a\) vs. \(^b\) \(p = 0.0001\)
\(^a\) vs. \(^c\) \(p = N.S.\)
\(^a\) vs. \(^d\) \(p = 0.0001\)
\(^a\) vs. \(^e\) \(p = N.S.\)
\(^b\) vs. \(^e\) \(p = 0.0001\)
\(^c\) vs. \(^d\) \(p = N.S.\)

**Discussion**

The aim of the present study was to investigate
the relationships between the blood eosinophil
counts and serum ECP levels in patients with
acute and chronic urticaria. Blood eosinophil
counts and serum ECP levels increased in all
patients with acute urticaria. Concerning patients
affected by chronic urticaria, taking into account
the recrudescence of the disease at the moment
of taking the blood sample, only symptomatic
patients showed increased eosinophil blood
values whereas serum ECP levels were increased
both in symptomatic and asymptomatic patients.
Furthermore serum ECP levels in chronic urti-
Eosinophils and ECP in urticaria

The second is the content of ECP of the eosinophil population and the third is the propensity of the eosinophils to secrete their ECP. In acute urticaria the ECP levels are completely paralleled by blood eosinophil counts. This could be due to a parallel change in the production of eosinophils in the bone marrow and in the activation of the eosinophil population. In chronic urticaria discrepancies between blood eosinophil counts and serum ECP levels are found. In this case the induction of eosinophil production and activation are dissociated, as we have observed in asthma patients treated with a long-acting β2-agonist. In other words, some of the factors involved in the induction and enhancement of eosinophilopoiesis process are not involved in the activation process, and vice versa. Thus, depending on the factors produced in the urticaria process, the response of the eosinophil may vary. These variations in the response of the eosinophils probably give rise to the different patterns of blood eosinophil counts and serum ECP levels. Our data show a positive correlation between serum ECP levels and disease activity and support the concept that acute urticaria and chronic urticaria may represent a spectrum of disease activity rather than separate entities.

References


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