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CLINICAL REPORT

Comparison of Severity Scoring of Atopic Dermatitis Values and Serum Levels of Eosinophil Cationic Protein and Mast Cell Tryptase for Routine Evaluation of Atopic Dermatitis

ULRICH AMON, ULRIKE MEMMEL, RICHARD STOLL and SABINE AMON

PsoriSol-Center for Dermatology and Allergy, Hersbruck, Germany

In this study the routine use of different parameters for evaluation of the overall therapeutic outcome in atopic dermatitis was investigated. The disease activity of 117 randomly selected hospitalized patients suffering from atopic dermatitis was routinely assessed using the Severity Scoring of Atopic Dermatitis (SCORAD) index on admission and at discharge. Serum levels of eosinophil cationic protein and mast cell tryptase were determined in parallel both on admission and at discharge. After a mean treatment period of 24 ± 12 days a decrease in the SCORAD index from 47.6 ± 19.5 to 7.7 ± 8.2 was achieved ($p < 0.001$). Serum levels of eosinophil cationic protein decreased from 22.8 ± 19.7 µg/l to 15.4 ± 17.5 µg/l, whereas serum tryptase levels did not change. However, there was no significant correlation between the changes in SCORAD, eosinophil cationic protein and tryptase in our cohort. Thus, routine determination of serum eosinophil cationic protein or tryptase levels, in addition to evaluation of disease activity using the SCORAD index, is not recommended in unselected patients with atopic dermatitis. ***Key words: eosinophils; outcomes measures; quality assurance.***

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Ulrich Amon, MD, PsoriSol-Center for Dermatology and Allergy, Mühlstraße 31, D-91217, Hersbruck, Germany. E-mail: amon@psorisol.de

In the past decade many techniques have been described to evaluate the disease activity of atopic dermatitis. There is increasing evidence that some mediators or markers of eosinophils, mast cells, lymphocytes and other cell types may reflect the severity of atopic dermatitis (1–7). In combination with clinical scores, such as the Severity Scoring of Atopic Dermatitis (SCORAD) index (8), these markers may therefore be used as outcomes measures.

According to the literature, eosinophil cationic protein (ECP), a potent cytotoxic protein of eosinophils, appears to be involved in the pathogenesis of atopic dermatitis as indicated by elevated serum levels (2–4, 9–12). However, the small numbers of patients included in these studies limit the significance of these observations. Additionally, it is still uncertain whether mediators released from mast cells, such as histamine, tryptase or tumour necrosis factor-α, can indicate the clinical activity of atopic dermatitis (12–16).

This study was designed to compare serum levels of two main mediators of eosinophils (ECP) and mast cells (tryptase) in a large cohort of randomly selected patients with atopic dermatitis and thereby assess these mediators for routine quality assurance during therapy in correlation to the clinical activity of the disease.

PATIENTS AND METHODS

Patients

All 117 patients (77 females, 40 males, 24.2 ± 15.6 years, range 1–80 years) admitted to our hospital with atopic dermatitis within a 3-month period in 1997 were included in the study. The diagnosis was made according to the criteria of Hanifin & Rajka (17). The status of the disease was evaluated on admission and at discharge using the SCORAD index (8). This clinical index combines objective (extent and intensity) with subjective (loss of sleep, pruritus) parameters.

All patients were screened for serum concentrations of ECP and mast cell tryptase using specific immunoassays (Uni CAP ECP, geometric mean of healthy adults: 4.4 µg/l; Uni CAP Tryptase, geometric mean of healthy adults: 5.6 µg/l; Pharmacia & Upjohn, Freiburg, Germany). Venous blood (10 ml) was taken on admission and at discharge for the above purposes. Serum preparation and assays were performed according to the manufacturer's instructions. In addition, total IgE serum levels were measured (Uni CAP IgE, Pharmacia).

Method

Therapy for atopic dermatitis consisted of a combination of classical dermatological treatments, such as emollients, phototherapy and, as required, topical glucocorticosteroids of the fourth generation (18), combined with behavioural and educational elements (19, 20). None of the 117 patients received systemic corticosteroids. According to the clinical status and individual experiences of the patients an individual interdisciplinary concept for treatment was initiated on admission. This study focused on the efficacy of the clinical outcome rather than on the efficacy of a single element of the therapeutic concept.

Statistics

The differences between the SCORAD index and the serum levels of the mediators before and after treatment were calculated using the Wilcoxon test. Differences associated with probability values of $p < 0.05$ and $p < 0.02$ were considered to be significant and highly significant, respectively. The correlation index (r) was calculated with the Spearman's rank correlation coefficient matrix (SPSS 6.01, SPSS Inc., Chicago, IL, USA). Probability was assessed using Student's t-test.

RESULTS

SCORAD index

The SCORAD index (mean ± SD) was 48.0 ± 19.2 when patients were admitted to the hospital (range 5.7–87.4). A statistically significant difference between female and male

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patients was not observed. After a mean period of hospitalization of 24 ± 12 days the clinical status of all patients as measured by the SCORAD index had significantly ($p < 0.001$) improved by $85.1 \pm 13.4\%$. Again, no differences were observed between female and male patients.

ECP and tryptase

We observed a significant correlation ($p = 0.0014$) between the clinical activity (as measured by the SCORAD index) and the ECP values on admission.

At discharge, serum ECP had decreased from 22.8 ± 19.7 μg/l to 15.4 ± 17.5 μg/l and this decrease was statistically significant ($p < 0.001$). There was no significant correlation between the clinical improvement (ΔSCORAD) and the change in the ECP level ($p = 0.28$). Calculations with five different overlapping subgroups of patients subdivided according to their SCORAD value on admission (< 30, $n = 53$; 30 – 60, $n = 27$; > 50, $n = 53$; > 60, $n = 37$; > 70, $n = 17$) also did not reveal a significant correlation between ΔSCORAD and ΔECP (data not shown). Total IgE level showed a marginal but not significant ($p = 0.07$) correlation with serum ECP values.

Mean tryptase levels on admission were 5.2 ± 3.4 μg/l (range 1 – 18.3). At the end of hospitalization tryptase levels were almost unchanged. There was no statistically significant correlation between either tryptase levels and SCORAD values or between tryptase levels and ECP levels on admission ($p = 0.16$ and $p = 0.05$, respectively). No significant regression between ΔSCORAD and Δtryptase was observed ($r = 0.006$, $p = 0.30$). ΔECP and Δtryptase also did not correlate significantly ($p = 0.37$).

DISCUSSION

This study demonstrates significant improvement in the clinical status of a cohort of randomly selected patients suffering from atopic dermatitis as measured by the SCORAD index. This scoring system reflects the consensus of the European Task Force on Atopic Dermatitis (8) and has been widely used in the past (7, 9, 21, 22). The combination of information concerning the intensity of skin involvement and measures of pruritus and sleep loss (visual analogue scale) has, however, been criticized (22). Recently, the score has been used in a modified fashion without including subjective symptoms (21). As a parameter for quality assurance (23) the SCORAD index is therefore routinely used in our hospital in all patients with atopic dermatitis. The mean percentage improvement is regularly calculated to assess whether the therapeutic concept is efficacious for this group of patients.

Because the SCORAD index is complicated for routine clinical use (22) objective measures to record disease activity may be helpful. A number of serological parameters, such as soluble (s) IL-2 receptor (1, 10, 24), sCD14 (4), sCD30 (7), sICAM-1 (5) and sE-selectin (6, 25, 26), have been investigated for association with the clinical score of atopic dermatitis. Numerous studies have focused on the role of ECP and have calculated a variable degree of correlation with the severity of the disease (2 – 4, 9 – 12). The present study showed a statistically significant correlation between the serum levels of this mediator and actual clinical status in a larger population of patients with atopic dermatitis as measured by the SCORAD index. We did not observe a pronounced increase in ECP with increased disease severity. However, individual ECP concentrations on admission were in the range 2.9 – 121 μg/l, which was comparable to the ranges found in previous studies with smaller numbers of patients (2 – 4, 9 – 12). Recently, Wolkerstorfer et al. (21) could not confirm a significant relationship between ECP serum levels and clinical activity in 40 children suffering from mild-to-moderate disease activity. With respect to the present results, determination of ECP levels as outcome parameters appears not to be sufficient in patients with even severe forms of the disease. The lack of correlation between ΔSCORAD and ΔECP may indicate distinct ongoing eosinophil activity, even if the clinical status has improved. It is still uncertain whether high ECP serum levels at discharge are of prognostic value for predicting a relapse or whether they instead indicate an activation of other atopic diseases, such as allergic asthma or allergic rhinitis. The latter aspect has not been focused on in the present study. Longitudinal studies are therefore necessary to investigate changes in ECP concentrations during the interval of atopic dermatitis following discharge. Such studies should be combined with other measures of disease activity (22).

Mast cell tryptase is a neutral protease which exerts a number of (pro)inflammatory activities (27). Serum tryptase levels have been shown to correlate well with acute systemic mast cell activation, e.g. in anaphylactic reactions (27). However, in atopic dermatitis subacute or chronic mast cell activation (e.g. late-phase reaction or piecemeal degranulation) is more relevant for the pathogenesis than acute mast cell degranulation (16, 28). Serum tryptase levels as measured by the Uni Cap method did not significantly correlate with disease activity. This confirms previously published data from a radio immunoassay system for tryptase determination (12, 15). However, evaluation of serum levels of α-protryptase may be worth studying in this disease (29).

In summary, this study demonstrates that the combined determination of serum ECP levels and evaluation of the SCORAD index in atopic dermatitis is not superior to assessment of disease severity by the SCORAD index alone. Owing to the absence of a significant correlation between ΔSCORAD and ΔECP in our population we conclude that evaluation of serum ECP levels on admission and at discharge may not be a valid tool for routine quality assurance in unselected patients with atopic dermatitis.

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