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Basal Serum Cortisol and Adrenocorticotropic Hormone Levels in Patients with Atopic Dermatitis

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Abstract

Background: Atopic dermatitis (AD) is an inflammatory skin disease with eczematous pruritic lesions. Topical corticosteroids are the most widely used and the mainstay of treatment for AD. There are some studies that percutaneous systemic absorption of topical steroids may occur and lead to suppression of hypothalamic-pituitary-adrenal axis (HPAA). However, almost in all of these studies, "basic" HPAA function (before application of topical steroids) was not evaluated.

Aim: The aim of this study was to investigate basal serum cortisol, adrenocorticotropic hormone (ACTH), and IgE levels in patients with AD and their correlation with disease severity.

Methods: Levels of basal serum cortisol, ACTH, and IgE were assessed by ELISA in 31 patients with AD and 31 control subjects. Clinical severity of AD was evaluated by the SCORAD (SCORing Atopic Dermatitis) index.

Results: Data analysis showed no statistical difference for basal serum cortisol and ACTH levels between two groups. The serum IgE level was significantly higher in AD group (P=0.02). The SCORAD index was correlated with serum IgE level, but not with the basal serum cortisol level and ACTH level.

Conclusions: Basal serum cortisol and ACTH levels are normal in AD patients. Serum IgE level is significantly higher in AD patients and correlated with disease severity.

Keywords: Adrenocorticotropic hormone (ACTH); Atopic dermatitis; Cortisol; Eczema; IgE; SCORAD; Atopy

Introduction

Atopic dermatitis (AD) is an inflammatory skin disease with an onset in infancy or early childhood. It is characterized by severe pruritus, chronic and relapsing course, and typical clinical morphology including xerosis and eczematous lesions [1,2]. The incidence of AD has been increasing during past 30 years, whereas its current prevalence is estimated 12%. Atopic dermatitis is often associated with remarkable morbidity which results in patient hospitalization, absence from work or school, and loss of several work days [3,4]. In children, one of the most hazardous effects of AD is sleep disorders which may lead to behavioral disturbances [5,6]. Furthermore, children are at risk of growth retardation as a complication of the disease [7]. Unpredictable course, chronic and relapsing nature of the disease and disturbing pruritus can impose extensive psychological and emotional burden to patients with AD and their families [8-11].

Topical corticosteroids are the most widely used and the mainstay of treatment for AD [12], but there is increasing concern about their systemic side effects, especially adrenal suppression. There is some evidence that percutaneous systemic absorption of topical steroids may occur after prolonged use of these drugs and this may lead to suppression of hypothalamic-pituitary-adrenal axis (HPAA) [13,14]. However, almost in all of these studies, "basic" HPAA function (before application of topical steroids) was not evaluated. In other words, in most of these studies, function of HPAA was compared with controls only "after" the application of topical steroids. There are few studies which have evaluated the basic function of HPAA, mostly in children, with conflicting results [15-17].

The aim of this study was to investigate basal serum cortisol, adrenocorticotropic hormone (ACTH), and IgE levels in patients with AD (without any age limitation) and their correlation with disease severity.

Patients and Methods

Patients

Thirty-one patients (22 females and 9 males) with mean age of 34.1 ± 19.2 years (range 0.5-78) who were visited by dermatologists and diagnosed as AD, according to the criteria of Hanifin and Rajka [1], and 31 age and sex-matched control subjects were included in the study. The control subjects had neither self-reported allergies or allergic symptoms, nor any inflammatory skin disease. Subjects with history of any treatment with systemic steroids during the last one year, or topical steroids during the last 1 month, history of adrenal insufficiency, Cushing's syndrome, any active inflammation, alcoholism and depression were excluded from the study.

Informed consent was obtained from the subjects or their parents (if age <16 years), before their involvement in the study.

Investigations

Morning basal serum cortisol level was measured at 8 am using enzyme link immunosorbent assay (ELISA) (Dia plus Inc/USA) (expected value: male 5-22 mg/dl; female 5.2-21.7 mg/dl; sensitivity 0.25 mg/dl) in patients and control subjects. Serum ACTH level was measured using ELISA (Biomerica, CA, USA) (expected value: 17-58.2 pg/ml; sensitivity 0.22 pg/ml) in case and control groups. Serum IgE level was measured by ELISA (Research and Production Company, Diagnostic, systemic Ltd, Nizhuy Novgorod) (positive expected value>190 Iu/ml; sensitivity 25 Iu/ml)

Disease severity

Clinical severity of the disease was evaluated by the SCORAD (Scoring Atopic Dermatitis) index and graded as mild (SCORAD<25), moderate (SCORAD: 25-50), and severe (SCORAD>50) [18].

Statistical analysis

All statistical analyses were performed using SPSS 16.0 (SPSS Inc, Chicago, IL, USA). To assess quantitative variables, student's t-test and Mann-Whitney U test were used for independent groups and categorical variable, as appropriated. Spearman correlation test was used to assess the correlation between variables. The level of statistical significance was set at P<0.05.

Results

This study included 31 patients with vitiligo and 31 healthy controls. Demographics and clinical data of patients and controls were summarized in Table 1. Basal serum cortisol level was higher than reference range in one patient in the AD group (3.2%), but none of the subjects in the control group had high basal serum cortisol level. This difference was not significant (P=0.63). The mean of basal serum cortisol level was 10.09 ± 5.24 mg/dl (range 5.1-29.4) in AD group and 9.32 ± 3.59 mg/dl (range 5-17.5) in control group. There was no statistical difference in the mean of basal serum cortisol level between two groups (P=0.67).

	Patients (N=31)	Controls (N=31)	P value
Age, years			
Mean ± SD	34.1 ± 19.2	35.6 ± 17.3	0.75
Range	0.5-78	1-80	
Median	28	30	
Gender			
Female	22	23	0.86
Male	9	8	
Disease Duration, years			
Mean	7.1	-	
Range	0.5-21	-	

Table 1: Demographics and clinical data of patients and controls.

The mean of ACTH level in AD group was 26.76 ± 17.57 pg/ml (range 6.8-66.8) while it was 26.42 ± 14.92 in control subjects. No statistical difference in the mean of ACTH level was observed between two groups (P=0.74).

The mean of serum IgE level was 328.48 ± 362.77 Iu/ml (range 8-1033) in AD group and 121.55 ± 185.47 (range 5-932) in control group. As it was expected, the serum IgE level was significantly higher in AD group (P=0.02) (Figure 1).

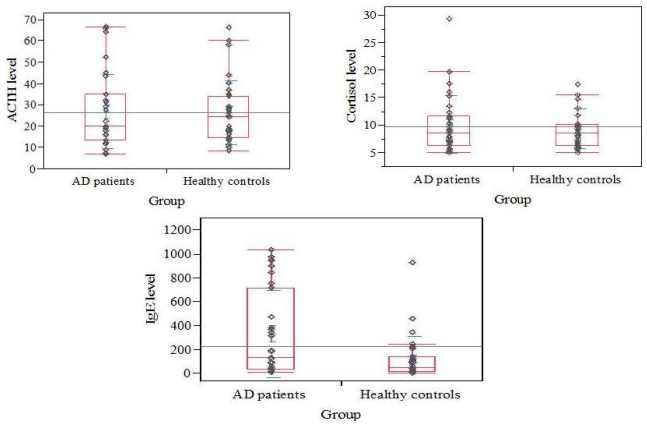

Figure 1: Comparison of serum levels of (A) ACTH (p>0.05), (B) cortisol (p>0.05), and (C) total IgE (p<0.05) in patients with atopic dermatitis and healthy controls. Data shown as median (horizontal line), 25th to 75th percentiles (box), and range (capped lines).

Most of our patients had moderate AD according to SCORAD index. Table 2 summarizes SCORAD grading in our patients. The SCORAD index was correlated with serum IgE level (P<0.05; rs=0.41), but not with the basal serum cortisol level (P=0.87; rs=0.03) and ACTH level (P=0.53; rs=0.12) (Figure 2). SCORAD index was not correlated with age, sex and clinical features of AD.

Disease severity	N (%)
Mild (SCORAD<25)	6 (19.86)
Moderate (SCORAD:25-50)	19 (61.28)
Severe (SCORAD>50)	6 (19.36)

Table 2: Disease severity evaluated by SCORAD index in patients with atopic dermatitis.

Discussion

In this case-control study, we found no significant difference in basal serum cortisol and ACTH levels in patients with AD and healthy objects. Interestingly, we found that severity of AD (SCORAD index) was correlated with serum IgE level, but not with the serum cortisol value. A literature review gives us different studies with various research designs and methodologies and conflicting results.

Evidence of impaired HPAA function in patients with AD comes from a study by Matsuda et al., who reported significantly lower basal cortisol levels and response to ACTH in AD children in comparison with control group [17]. However, the main pitfall of this study was that their control group consisted of asthmatic patients. As asthma

itself is in the spectrum of atopia and is one of the three legs of allergic triad (atopic dermatitis, allergic rhinitis and asthma), selection of controls from asthmatic patients could result in an inappropriate and biased comparison.

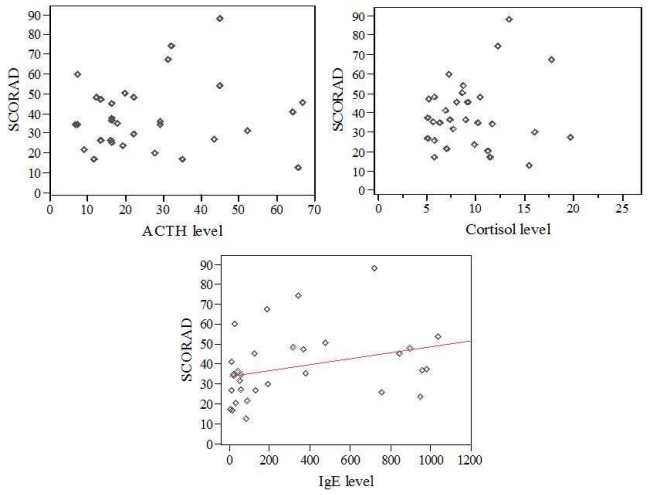

Figure 2: Correlation between SCORAD index and serum levels of ACTH, cortisol, and total IgE. There was no correlation between serum ACTH (A) or basal cortisol levels (B) and SCORAD index. Total serum IgE level was positively correlated with SCORAD index.

Patel et al. studied the adrenal function in 14 children with moderate to severe AD who were under regular treatment with topical corticosteroids and found no difference in their basal cortisol levels compared with controls [19].

A study which has been the mainstay and reference of most of recent investigations is the report of Haeck et al. which demonstrated lower basal cortisol level in patients with severe, active AD (group 1) compared with the patients with moderate, controlled AD (group 2). Furthermore, they found no significant correlation between the amount of prescribed topical corticosteroid and serum cortisol level. This study concluded that disease activity, rather than the use of topical corticosteroids, is responsible for the low basal cortisol values in patients with severe AD [16]. However, two years later, the authors of this article confessed that they had made a fatal flaw in the execution of their study which led to wrong interpretation and incorrect conclusion [20]. Surprisingly, none of the recent studies has referred to this corrigendum.

Nutan et al. in an investigation on 62 children with AD demonstrated that half of the patients had low basal cortisol levels and this was more remarkable in severe AD. Patients with severe AD had low basal and post ACTH stimulated cortisol levels even before initiation of treatment with topical steroids. After the application of topical steroids, there was a recovery of the HPAA in 98% of patients [21]. However, this study was performed only on pediatric patients with AD.

Afsar et al. reported that none of the pediatric patients with AD were found to have basal serum cortisol levels under the lower limit of the reference range, and no difference was found in the basal cortisol values when they were compared with those of the control group. They also reported that the severity of AD was not correlated with serum cortisol values in the pediatric AD group [22]. The results of this study were compatible with our findings, although it was performed only on pediatric patients.

We found a positive correlation of total serum IgE and disease severity. This is comparable with the results of Choen et al. [23].

In conclusion, this study demonstrated that there was no difference in both basal cortisol levels and ACTH values between AD group and control group. The basal cortisol levels were not correlated with disease severity. Serum IgE level was significantly higher in AD patients and correlated with disease severity. To our knowledge, this was the first case-control study evaluated HPAA in AD patients without any age limitation. The limitation of our study was its sample size, thus further studies with larger sample size to investigate the complex interaction of the neuroendocrine, metabolic and immune systems are recommended to explain the available conflicting results.

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