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Basal serum cortisol and adrenocorticotropic hormone levels in patients with atopic dermatitis

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ABSTRACT

Background: Certain studies suggest that percutaneous absorption of topical steroids may cause suppression of hypothalamic–pituitary–adrenal axis (HPAA) in atopic dermatitis (AD) patients. This study aimed to investigate the basal serum cortisol, adrenocorticotropic hormone (ACTH), and IgE levels in patients with AD and their correlation with the disease severity.

Methods: Levels of basal serum cortisol, ACTH, and IgE were assessed by ELISA in 31 patients with AD and 31 controls. Clinical severity of AD was evaluated by the scoring of atopic dermatitis (SCORAD) index.

Results: No statistical difference was observed between the two groups for basal serum cortisol and ACTH levels. The serum IgE level was significantly higher in the AD group. The SCORAD index was correlated with serum IgE level.

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

Introduction

Atopic dermatitis (AD) is an inflammatory skin disease with an onset in infancy or early childhood and 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 increased in the past 30 years, whereas its current prevalence is estimated to be 12%. Atopic dermatitis is often associated with remarkable morbidity, which results in patient hospitalization, absence from work or school, and loss of several working days [3,4]. In children, sleep disorders leading to behavioral disturbances are known to be one of the most hazardous effects of AD [5,6]. Furthermore, this disease may cause growth retardation in children [7]. Unpredictable course, chronic and relapsing nature of the disease, and disturbing pruritus can impose extensive psychological and emotional burden on patients with AD and their families [8-11].

TABLE 1. Demographics and clinical data of patients and controls

	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	-	

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 the percutaneous systemic absorption of topical steroids may occur after the prolonged use of these drugs and may lead to the suppression of hypothalamic–pituitary–adrenal axis (HPAA) [13,14]; however, in the majority of these studies, "basic" HPAA function (before application of topical steroids) remained unevaluated. In other words, in most of these studies, the HPAA function was compared with controls only "after" the application of topical steroids. Few studies have evaluated the basic HPAA function, especially in children; however, the results are conflicting [15-17].

This study aimed to evaluate the basal serum cortisol, adrenocorticotropic hormone (ACTH), and IgE levels in patients with AD (without any age limitation) and their correlation with the disease severity.

Patients and Methods

Patients

This study included 31 patients (22 females and 9 males) with mean age of 34.1±19.2 years (range 0.5–78 years) who were visited by dermatologists and were diagnosed as AD, according to the criteria of Hanifin and Rajka [1], and 31 age- and sex-matched control subjects. The control subjects had neither self-reported allergies or allergic symptoms, nor any inflammatory skin disease. Subjects with history of treatment with any systemic steroids during the previous year or topical steroids during the previous month, history of adrenal insufficiency, Cushing's syndrome, active inflammation, alcoholism, and depression were excluded from the study. The study was carried out in accordance with the ethical standards established in the Declaration of Helsinki, and informed consent was obtained from all participants or their parents (if age <16 years), before participation.

Investigations

Morning basal serum cortisol levels at 8 AM (expected value: male 5–22 mg/dL; female 5.2–21.7 mg/dL; sensitivity 0.25 mg/dL, serum ACTH levels (expected value: 17–58.2 pg/mL; sensitivity 0.22 pg/mL), and serum IgE levels (positive expected value>190 IU/ml; sensitivity 25 IU/ml) were measured using the enzyme link immunosorbent assay (ELISA; Biomerica, CA, USAin the case and control groups.

Disease Severity

Clinical severity of the disease was evaluated by the scoring of atopic dermatitis (SCORAD) index and was 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 the 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. P<0.05 was considered as statistically significant.

Results

This study included 31 patients with vitiligo and 31 healthy controls. Demographics and clinical data of patients and controls are summarized in Table 1. Basal serum cortisol level was found to be higher than the reference range in one patient from the AD group (3.2%); however, none of the

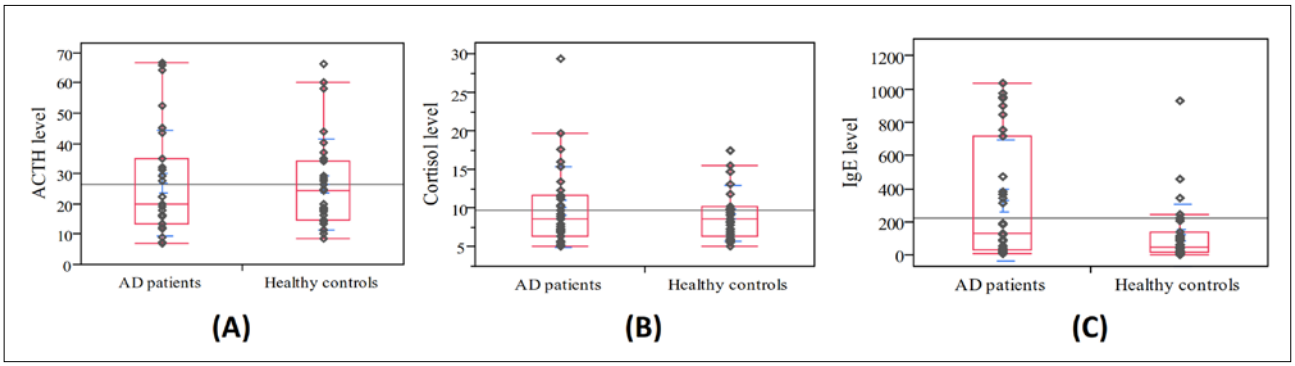

Figure 1. Comparison of serum levels of (A) ACTH (p>0.05), (B) cortisol (p>0.05), and (C) total igE (p<0.05) in patients with atopic dermatitis and healthy controls. Data shown as median (horizontal line), 25th to 75th percentiles (box), and range (capped lines). [Copyright: ©2017 Tehranchinia et al.]

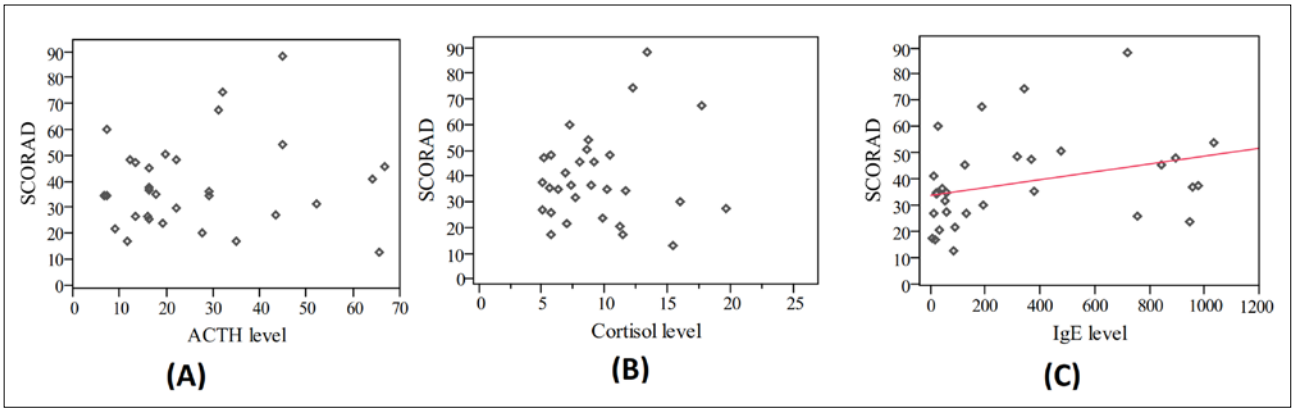

Figure 2. Correlation between SCORAD index and serum levels of ACTH, cortisol, and total IgE. There was no correlation between serum ACTH (A) or basal cortisol levels (B) and SCORAD index. Total serum igE level was positively correlated with SCORAD index. [Copyright: ©2017 Tehranchinia et al.]

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

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

subjects from the control group displayed 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 the AD group and 9.32±3.59 mg/dL (range 5–17.5) in the control group. The mean of basal serum cortisol level between the two groups showed no statistical significant difference (*P*=0.67).

The mean of ACTH level in the AD group was 26.76±17.57 pg/mL (range 6.8–66.8), whereas it was 26.42±14.92 in the control subjects. The mean of ACTH level between two groups showed no statistical significant difference (*P*=0.74)

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

Most of our patients displayed moderate AD according to the 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.

Discussion

In this case–control study, no significant difference was observed in the basal serum cortisol and ACTH levels in patients with AD and the control group. Interestingly, we found that the severity of AD (SCORAD index) correlated with serum IgE level, but not with the serum cortisol level. The literature review reveals various studies with distinct research designs and methodologies and conflicting results (Table 3).

A study by Matsuda et al., reported significantly lower basal cortisol levels and lower response to ACTH in AD

TABLE 3. Different studies evaluating serum cortisol levels in patients with atopic dermatitis

Authors	Study population	Result	Comments
Matsuda et al. [17]	Children with AD	↓Response to ACTH	Control group was selected from asthmatic children
Patel et al. [19]	Children with moderate to severe AD who were under regular treatment with corticosteroid	Normal basal cortisol levels	
Haeck et al. [16]	Patients with moderate or severe AD	AD activity is responsible for low basal cortisol levels	Two years later, the authors confessed that their results were incorrect [20]
Natan et al. [21]	Children with AD	↓Basal cortisol level in 50% of patients, which was in correlation with disease severity ↓ACTH response. Recovery of the HPAA after application of topical steroid	
Afsar et al. [22]	Children with AD	Normal basal cortisol level with no correlation with disease severity	

AD: atopic dermatitis; ACTH: adrenocorticotropic hormone; HPAA: hypothalamic-pituitary-adrenal axis.

children than the control group, providing an evidence of impaired HPAA function in patients with AD [17]; however, the main pitfall of this study was that their control group consisted of asthmatic patients. As asthma itself lies in the spectrum of atopia and forms one of the three parts of allergic triad (AD, allergic rhinitis, and asthma), selecting controls from asthmatic patients may result in an inappropriate and biased comparison.

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) than the patients with moderate, controlled AD (group 2). Furthermore, this study found no significant correlation between the amount of prescribed topical corticosteroid and serum cortisol levels, and 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]. Nevertheless, 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.

Afsar et al. reported that none of the pediatric patients with AD had basal serum cortisol levels below the lower limit of the reference range, and no difference was observed in the basal cortisol values when they were compared with those of the control group. They also reported that the severity of AD did not correlate with the 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 between the total serum IgE values and disease severity, and our study is in correlation with the results of Choen et al. [23].

In conclusion, in the present study no difference was observed in both basal cortisol levels and ACTH values between the AD and control groups. The basal cortisol levels were not correlated with the disease severity, whereas the serum IgE level was significantly higher in AD patients and correlated with the disease severity. To the best of our knowledge, this was the first case–control study that 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 are necessary to investigate the complex interaction of the neuroendocrine, metabolic, and immune systems and to explain the available conflicting results.

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