ORIGINAL ARTICLE

Serum Concentration of Dehydroepiandrosterone Sulfate and Testosterone in Women With Severe Atopic Eczema/Dermatitis Syndrome

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Abstract

Background: Although a growing body of evidence indicates that androgens modulate immune response and certain alterations in sex hormone metabolism and balance are thought to predispose an individual to immune-mediated diseases, few studies have investigated the role of androgens in atopic eczema/dermatitis syndrome (AEDS).
Objective: We evaluated serum concentration of dehydroepiandrosterone sulfate (DHEA-S) and total testosterone in women with severe AEDS to characterize the hormonal milieu of such patients.
Methods: Serum concentrations of DHEA-S and total testosterone in 13 female patients with severe AEDS were compared with concentrations in weight- and age-matched healthy controls. Measurement was by electrical chemiluminescence immunoassay.
Results: There were no significant differences in serum concentrations of DHEA-S or testosterone between the 2 groups. We found no correlation between serum concentrations of DHEA-S and total immunoglobulin E.
Conclusion: This small study suggests there may be no abnormalities in peripheral blood concentrations of DHEAS-S and total testosterone in women with severe AEDS.

Key words: Dehydroepiandrosterone. Testosterone. Atopic eczema/dermatitis syndrome.

Resumen

Antecedentes: Aunque cada vez existen más pruebas sobre la modulación de la respuesta inmunitaria por los andrógenos y sobre ciertas alteraciones en el equilibrio y metabolismo de las hormonas sexuales que pueden predisponen a padecer enfermedades mediadas por el sistema inmunitario, hay pocos estudios que hayan investigado el papel de los andrógenos en el síndrome de dermatitis y eccema atópico.
Objetivo: Valoramos las concentraciones séricas de sulfato de dehidroepiandrosterona (DHEA-S) y el nivel total de testosterona en mujeres con síndrome de dermatitis y eccema atópico grave con el fin de caracterizar el medio hormonal de dichas pacientes.
Métodos: Se compararon las concentraciones séricas de DHEA-S y el total de testosterona en 13 mujeres con síndrome de dermatitis y eccema atópico grave con controles sanas de peso y edad coincidentes. La medición se realizó mediante un inmunoanálisis de electroquimioluminiscencia.
Resultados: No se detectaron diferencias significativas en las concentraciones séricas de DHEA-S o testosterona entre los dos grupos. No existe correlación entre las concentraciones séricas de DHEA-S y la inmunoglobulina E total.
Conclusión: Este pequeño estudio sugiere la posibilidad de la ausencia de alteraciones en las concentraciones de DHEAS-S en sangre periférica y en la testosterona total en las mujeres con síndrome de dermatitis y eccema atópico grave.

Palabras clave: Dehidroepiandrosterona. Testosterona. Síndrome de dermatitis y eccema atópico.

Introduction

Atopic eczema/dermatitis syndrome (AEDS) is a chronic inflammatory skin disease, the consequence of immunoregulatory and neuro-endocrine abnormalities, and it has been characterized as an autoimmune phenomenon [1,2]. Stress also seems to play an important role in AEDS, as an association between emotional stress, especially of stressful life events, and exacerbation of AEDS symptoms has been suggested [3]. Certain alterations in sex hormone metabolism and balance may be a predisposing factor to immune-mediated diseases [4]. Dehydroepiandrosterone (DHEA) and its sulfate ester (DHEA-S) are the major androgens secreted by adrenal glands. Those very abundant hormones are converted into testosterone and estrogens in systemic circulation. DHEA-S circulates as an inactive prohormone and has both a longer half-life and a markedly higher blood concentration than DHEA [5]. The most important androgen, testosterone, is secreted by the adrenal gland and the ovarian stroma [6]. Androgens such as DHEA, DHEA-S, and testosterone may be able to modulate the immune response [7,8]. For example, DHEA may affect the balance between type 1 and 2 helper T cells (T_H1/T_H2), immunoglobulin (Ig) E synthesis and eosinophil proliferation, therefore playing a role in modulating the development of allergic reactions [9-11]. This hormone effectively prevented allergic sensitization in a study [12] and suppressed progression of allergic airway inflammation in mice in another study, probably via modification of the cytokine network involved in these processes [11]. Thus DHEA appears to be an endogenous modulator involved in the development of allergic reactions [10].

It has been suggested that the concentration of DHEA-S in peripheral blood may decrease with stress [13] and during chronic inflammatory and immune-mediated processes. However, the significance of such a phenomenon has not yet been determined [14]. The behavior of DHEA-S and testosterone in the systemic circulation of AEDS patients is under debate [10,15]. Therefore, in the present study we evaluated the serum concentration of DHEA-S and total testosterone in female patients suffering from severe AEDS and in a matched control group.

Materials and Methods

Thirteen nonsmoking AEDS women (median age, 24 years; range, 18–32 years) with severe AEDS as determined by the Hanifin and Rajka severity score [16] were enrolled. All of the subjects had a positive skin prick test to common airborne allergens. They did not suffer from concomitant rhinoconjunctivitis or asthma. None had received any systemic steroids for at least 4 weeks preceding the study. Only small amounts of topically applied emollients and steroids were used to control symptoms. The weight-matched control group consisted of 14 healthy, nonatopic women (median age, 25 years; range, 18–31 years). All the subjects gave informed oral and written consent and the study was approved by the university ethics committee.

To evaluate serum concentrations of DHEA-S and testosterone, blood samples were obtained in the morning (8:00 AM to 9:00 AM) and processed by automated electrochemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany). Allergic status was evaluated by skin prick tests using a panel of common inhalant allergens (Allergopharma, Reinbek, Germany). Saline and histamine solutions were the negative and positive controls, respectively. A wheal diameter 3 mm larger than the negative control was accepted as a positive response.

Statistical Analysis

Data were expressed as medians and ranges, and comparisons between groups were performed by a Mann–Whitney U test. Correlation was assessed with the Spearman coefficient (ρ). A *P* value less than .05 was considered significant.

Results

Serum concentrations of total testosterone and DHEA-S did not differ significantly between female AEDS patients and the control subjects (table). The median serum concentration of total IgE was 546 kU/L (range, 175-598 kU/L) in the AEDS patients. We did not find any correlation between serum concentrations of DHEA-S and total IgE ($\rho = 0.13$, $P = .75$) or total testosterone and total IgE ($\rho = 0.11$, $P = .78$) in the patients.

Discussion

Decreasing serum concentrations of DHEA and DHEA-S have been observed in chronic inflammatory diseases, suggesting a shift to cortisol at the expense of adrenal androgens [17]. Abnormalities in circulating sex hormone concentrations have been demonstrated in both male and female patients suffering from AEDS; however, available data on this subject are inconsistent. Tabata et al [10] demonstrated decreased serum DHEA in male patients with AEDS who had mild to moderate skin lesions [10]. There was no significant correlation between DHEA concentration and disease severity or serum IgE concentration. Based on this study, the authors suggested that DHEA might be one of the regulators involved in AEDS pathogenesis, controlling interleukin (IL) 4 and IL-5 production. In our study, however, the serum concentration of DHEA-S, the precursor of DHEA and total testosterone, did not differ significantly between female patients with severe AEDS and healthy controls. Moreover, we found no relationship between serum concentrations of these hormones and IgE in the AEDS group. Our findings are consistent with those of Ebata et al [15], who demonstrated no differences in serum concentrations of DHEA-S and testosterone between females with AEDS and controls. In male patients with AEDS, on the other hand, serum concentrations of total testosterone and free testosterone were significantly lower than those of the controls. There were no significant differences in serum concentrations of DHEA and DHEA-S between the patient groups in that study.

Data are scarce regarding the behavior of DHEA-S and testosterone in the peripheral blood of patients with the other 2 clinical manifestations of the so called atopic triad, namely asthma and allergic rhinitis. Circulating DHEA-S levels were

Serum Concentrations of DHEA-S and Total Testosterone in AEDS Patients and in Healthy Controls*

Parameter	Healthy Controls, n = 14	AEDS Patients, n = 13	*P*
DHEA-S, µg/dL	253 (116 – 324)	242 (188 – 413.5)	.8
Testosterone, ng/dL	45.3 (10.9 – 142)	57.4 (42.4 – 132.5)	.36

* Data are expressed as median (range). AEDS indicates atopic eczema/dermatitis syndrome; DHEA-S, dehydroepiandrosterone sulfate.

shown to be lower in some asthmatic patients [18], and in certain percentages of patients with severe (37.76%) and moderate asthma (40.00%), but very rarely in patients with mild asthma (8.51%) low testosterone levels have been reported, probably in relation to stress, hypoxia, and corticosteroid treatment [19]. In untreated children with perennial rhinitis alone or rhinitis and mild asthma symptoms, there were no statistically significant differences of DHEA and DHEA-S concentrations in the peripheral blood as compared to nonatopic individuals as compared to normal values [20]. It is tempting to speculate that degree of systemic inflammatory response and/or stress may influence these hormone concentrations in patients with asthma, possibly explaining why the hormone concentrations are not lower in mild asthma.

Interestingly, we observed that DHEA-S serum concentration is significantly lower in both female and male patients with chronic idiopathic urticaria (CIU), as compared with sex- and age-matched healthy controls [21,22]. In contrast, serum testosterone did not differ significantly between male CIU patients and controls (unpublished data), while women with CIU did tend to have lower levels. While it seems likely that a lowered circulating DHEA-S concentration accompanies CIU, but its significance in urticarial inflammation and its underlying mechanisms remain unknown. Taken together, the data in this study and the unpublished one may indicate complexity of changes in concentration of DHEA-S and testosterone in the systemic circulation of patients with different clinical manifestations of atopic diathesis and chronic skin inflammatory diseases.

In conclusion, we failed to detect significant differences between the concentrations of DHEA-S or total testosterone in the peripheral blood of female patients with severe AEDS and the blood of nonatopic matched controls. However, a limitation of this study was the small number of patients enrolled.

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