



Letter to the Editor

Serum concentration of dehydroepiandrosterone sulphate in female patients with chronic idiopathic urticaria

KEYWORDS

Chronic urticaria;
Dehydroepiandrosterone

Dear Sir,

Aetiology of chronic idiopathic urticaria (CIU) is unknown, but in some cases an autoimmune pathogenic mechanism is proposed [1,2]. Chronic urticaria is approximately twice as common in women as in men [2], suggesting that sex differences in hormone patterns may play a role in this phenomenon. Extensive evidence suggests that, abnormalities in sex hormones metabolism and/or secretion may modulate activity of some immunologic diseases [3]. It has been reported that adrenal androgens, dehydroepiandrosterone (DHEA) and its ester dehydroepiandrosterone sulphate (DHEA-S) show immunomodulatory properties and their deficiency has been associated with immune-mediated diseases, including systemic lupus erythematosus, rheumatoid arthritis and autoimmune thyroiditis, which predominantly affect women [4,5]. The question raised by the data is whether there appears any role for DHEA-S in CIU. Therefore, the aim of this study was to evaluate circulating DHEA-S concentration in female patients suffering from CIU.

The study group consisted of 34 non-atopic women (median age: 31 years; range: 19–42) with active CIU of 5 months to 10 years duration and in which all identified causes of urticaria had been excluded by appropriate investigation. The patients had not taken systemic steroids for more than 12 months preceding the study. All other therapies had been discontinued at least 10 days before the study. Patients with CIU were divided into two subgroups based on the results of autologous skin serum test (ASST), performed according to the method by Sab-

roe et al. [6]. Twenty-two patients showed negative wheal response to intradermal injection of autologous serum (negative-ASST CIU subgroup) and 12 patients proved strong reactivity to ASST (positive-ASST CIU subgroup). This test is extensively used in clinical practice and positive ASST suggests the autoimmune basis of the disease [6]. Thirty-two non-atopic healthy women (median age: 35 years; range: 18–41) were included in the control group. None of the patients or controls had anti-thyroid and anti-nuclear autoantibodies. Moreover, the individuals were not enrolled into the study if they had a personal history of disorders or were taking any medication, which could affect sex hormone concentrations.

Serum DHEA-S concentration was measured by using electrochemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany).

The statistical analysis of the results was made using Kruskal–Wallis test as well as Mann–Whitney *U*-test. Correlation coefficient was obtained by Spearman test.

Data obtained are specified in Table 1. In CIU patients serum concentration of DHEA-S was significantly lower than the control values ($P = 0.003$). No difference was observed in DHEA-S concentration between the two subgroups of patient (data not shown). No significant correlation was found between DHEA-S concentration and the duration of the disease ($r = 0.073$; $P = 0.679$).

To our knowledge there have been no earlier reports on significance of DHEA(-S) in CIU.

In our study, there appeared statistically significant differences in the serum concentration of DHEA-S between female patients with CIU and healthy controls. DHEA-S concentration was similar in the negative-ASST CIU subgroup and the positive-ASST CIU subgroup. Obviously, larger studies are needed to confirm our observations and answer the question why DHEA-S concentration decreases in this disease. Interestingly, relative reduction in serum DHEA(-S) concentration has also been reported in subjects with various immune-mediated diseases, including autoimmune disorders, suggesting that its deficiency might contribute to their pathophysiology. It is noteworthy

Table 1 Serum concentration of DHEA-S in CIU women and in healthy controls

Analysed parameters (unit)	DHEA-S ($\mu\text{g/dl}$)
Healthy controls ($n = 32$), median range	268.3 (116.2–479.8)
CIU patients ($n = 34$), median range	180.5 (45.0–443.9)
Statistical analysis P	0.003

n , Number of subjects.

that in some disorders of the immune system, clinical improvement has been observed after oral DHEA administration [4,5,7]. Moreover, DHEA was successfully used to prevent attacks in hereditary angioedema, the therapeutic effect resulted probably from inhibition of the classical complement pathway activation [8]. Taking these results into consideration, we speculate that DHEA-S might have a role in urticarial inflammation. So far, the specific molecular mechanism of action for DHEA(-S), including mechanisms of DHEA(-S) effect upon the immunological function and inflammation is unclear [4]. Nevertheless, as the adrenal androgens have been reported to exert multiple immunomodulatory and anti-inflammatory effects [4], it is interesting to speculate that DHEA-S deficiency might facilitate or induce the processes, including complement activation involved in pathogenesis of the disease. Such possibility may be strengthened by the findings of the complement contributing to activation of effector cells in chronic urticaria [9]. In addition, since androgens may regulate cell-mediated and humoral response [4], the decline in DHEA-S concentration may contribute to dysregulation of immune responses, which could have appeared significant upon the onset and/or progression of urticarial inflammation.

It is unknown whether the lowered DHEA-S concentration in CIU patients is a primary or merely a secondary phenomenon, caused by other factors, which modulate its secretion, including endogenous hormones, inflammatory mediators and stress. For example, it is necessary to evaluate the function of the hypothalamic–pituitary–adrenal axis and the adrenocortical steroidogenic cascade in CIU patients. Nevertheless, interesting observation related to DHEA-S concentrations was made, therefore the questions whether lower circulating DHEA-S concentration may contribute to CIU or if higher DHEA-S concentration may protect against the disease development call for the answers.

Finally, the results of the present study indicate that the serum DHEA-S concentration is significantly

lower in CIU women than in healthy controls. Our observation could provide a basis for further research into androgen secretion and respective role in CIU as well as for a new concept of therapy of this disease, such as dehydroepiandrosterone administration.

References

- [1] Hide M, Francis DM, Grattan CEH, Hakimi J, Kochan JP, Greaves MW. Autoantibodies against the high-affinity IgE receptor as a cause of histamine release in chronic urticaria. *N Engl J Med* 1993;328:1599–604.
- [2] Greaves MW. Chronic urticaria. *N Engl J Med* 1995;332:1767–72.
- [3] Schwartz KE. Autoimmunity, dehydroepiandrosterone (DHEA), and stress. *J Adolesc Health* 2002;30S:37–43.
- [4] Dillon JS. Dehydroepiandrosterone, dehydroepiandrosterone sulfate and related steroids: their role in inflammatory, allergic and immunological disorders. *Curr Drug Targets Inflamm Allergy* 2005;4:377–85.
- [5] Tagawa N, Tamanaka J, Fujinami A, et al. Serum dehydroepiandrosterone, dehydroepiandrosterone sulfate, and pregnenolone sulfate concentrations in patients with hyperthyroidism and hypothyroidism. *Clin Chem* 2000;46: 523–8.
- [6] Sabroe RA, Grattan CEH, Francis DM, Barr RM, Kobza Black A, Greaves MW. The autologous serum skin test: a screening test for autoantibodies in chronic idiopathic urticaria. *Br J Dermatol* 1999;140:446–53.
- [7] Barry NN, McGuire JL, van Vollenhoven RF. Dehydroepiandrosterone in systemic lupus erythematosus: relationship between dosage, serum levels, and clinical response. *J Rheumatol* 1998;25:2352–6.
- [8] Hidvegi T, Feher GK, Feher T, Koo E, Fust G. Inhibition of the complement activation by an adrenal androgen, dehydroepiandrosterone. *Complement* 1984;1:201–6.
- [9] Fiebiger E, Hammerschmid F, Stingl G, Maurer D. Anti-Fc ϵ RI α autoantibodies in autoimmune-mediated disorders. *J Clin Invest* 1998;101:243–51.

Alicja Kasperska-Zajac*

Zenon Brzoza

Barbara Rogala

*Clinical Department of Internal Diseases,
Allergology and Clinical Immunology,
Medical University of Silesia, Katowice, Poland*

*Corresponding author. Present address: Clinical Department of Internal Diseases, Allergology and Clinical Immunology, ul. 3-go Maja 13-15, 41-800 Zabrze, Poland. Tel.: +48 32 2718110; fax: +48 32 2718110
E-mail address: kasperska@plusnet.pl (A.K.-Zajac)

29 June 2005

Available online at www.sciencedirect.com

SCIENCE @ DIRECT®