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CONCISE COMMUNICATION

Sex hormones in male psoriasis patients and their correlation with the Psoriasis Area and Severity Index

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ABSTRACT

Modulation of psoriasis severity by estradiol during pregnancy, menstruation and menopause has been investigated previously. The correlation between sex hormones and Psoriasis Area Severity Index (PASI) has not been studied in male psoriasis patients. We investigated serum sex hormones in male psoriasis patients compared with healthy controls and correlated these findings with PASI. Estradiol, testosterone, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were measured in 47 male patients with psoriasis and 20 healthy controls. Patients with psoriasis showed higher body mass index and higher serum levels of FSH and LH relative to healthy controls, although this difference was not statistically significant. However, serum levels of testosterone and estradiol were significantly different between patients with psoriasis and healthy controls. Testosterone was significantly increased in control patients and estradiol was significantly increased among psoriatic patients. A significant inverse correlation was found between estradiol and PASI. Although the role of sex hormones in the pathogenesis of psoriasis has not been demonstrated, this is the first report of an inverse correlation between estradiol and PASI in male patients.

Key words: correlation, estrogen, male, psoriasis, sex hormone.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease characterized by red scaly plaques. Recent *in vivo* and *in vitro* studies suggest that sex steroid hormones including estrogen, progesterone or androgen may regulate a variety of pathophysiological conditions in the skin.[1] There have been reports of improvement in psoriasis[2] and psoriatic arthritis[3] patients taking high-dose oral estrogen contraceptives. In contrast, exacerbated psoriasis symptoms have been reported during the post-partum period, prior to menses, and at menopause[2,4] when estrogen and progesterone levels are low. These reports may demonstrate a potential protective role of estrogen in psoriasis by promoting a state of immune tolerance. The association between sex hormones and the Psoriasis Area and Severity Index (PASI) in male psoriasis patients has not been previously studied. The aim of this study is to measure follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen and testosterone in male psoriasis patients and to correlate these findings with PASI.

PATIENTS AND METHODS

A total of 47 male patients with chronic plaque psoriasis were included in this cross-sectional study. The local ethics committee reviewed and approved the study protocol. The control group was comprised of 20 healthy volunteers matched to the patient group for age and sex. Psoriasis symptom severity was measured using PASI.[5] Body mass index (BMI) was calculated according to standard methods.

Subjects were selected based on the following criteria: symptoms of active but clinically stable moderate to severe plaque psoriasis for at least 1 year and age greater than 18 years old. Exclusion criteria included prior medical history of any cardiovascular disease, hormone-dependent malignancy or breast cancer, venous thromboembolic disease, diabetes mellitus, renal dysfunction, liver disease, hypertension, use of lipid-reducing drugs, antidiabetics or glucocorticosteroids, and current hormone therapies. The aim of such exclusions was to avoid instances of hormonal imbalance.

Laboratory testing

Follicle-stimulating hormone, LH, estradiol and testosterone were analyzed using a ADVIA Centaur XP System (Siemens Healthcare Diagnostics Inc., New York, USA).

Statistical methods

Patients with psoriasis and healthy controls were compared according to age, BMI, FSH, LH, estradiol and testosterone using the two independent samples Student's *t*-test. Among

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the patient group, the correlation between PASI scores and BMI, estradiol, testosterone, FSH and LH was tested by Spearman's rank correlation coefficient. A *P*-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 16.0 for Windows (SPSS, Chicago, IL, USA).

RESULTS

The mean measurements of all parameters are presented in Table 1. No statistically significant differences were found between the control group and the psoriasis group in terms of age, BMI, and both serum FSH and LH levels compared ($P > 0.05$). Serum testosterone level was significantly increased in the control group (506.91 ± 117.7 ng/mL) ($P < 0.05$) compared with the psoriasis group (392.29 ± 181.91 ng/mL). In addition, significantly increased serum estradiol was found in the psoriasis group (37.52 ± 17.16 ng/mL; $P < 0.05$). An inverse correlation was detected between PASI and serum level of estradiol in the psoriasis group ($P < 0.05$; Fig. 1). Serum estradiol levels less than 43.7 pg/mL were associated with worsening PASI. There was no significant correlation between PASI and age, BMI, serum FSH, LH or testosterone (Table 2).

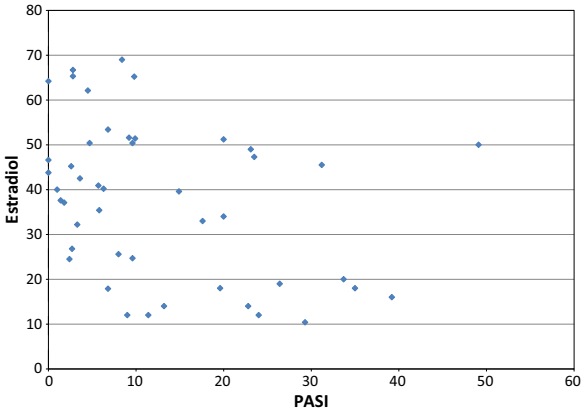

Figure 1. Dot graph showing the correlation between Psoriasis Area Severity Index (PASI) and estradiol level.

DISCUSSION

The role of sex hormones in the pathobiology of psoriasis remains unclear and understudied.[6] The present study is the first to examine sex hormone profiles in male psoriasis patients and evaluate the correlation with PASI.

Estradiol has bipotent effects on monocytes and macrophages, with low doses enhancing pro-inflammatory cytokine production (e.g. interleukin [IL]-1, IL-6 and tumor necrosis factor-α [TNF-α]) and high concentrations reducing production of these cytokines.[7] High estrogen levels promote polarization towards $CD4^+$ T (T-helper [Th]2) cell proliferation and associated cytokine production. Increased levels of IL-4 induce immunoglobulin production by B cells. Lower doses of estrogen promote the polarization towards $CD4^+$ Th1, increasing interferon-γ production and stimulating Th1 cell proliferation. Estrogens positively influence regulatory T cells (Treg), increasing their numbers during the menstrual cycle. There is also evidence for increasing programmed death 1 and perforin expression in Treg upon exposure to estrogens, which may lead to reduced Th17 cell numbers. The direct effects of estrogen on Th17 cells include induction of IL-17 production. Additionally, regulatory B-cells produce transforming growth factor-β and IL-10 in response to estrogen, which may suppress IL-17 expression.[7] Kanda *et al.* reported that 17b-estradiol acts on human keratinocytes, inhibiting production of chemokines, interferon-induced protein of 10 kDa (IP-10), monocyte chemoattractant protein-1 (MCP-1). Upon activation, estradiol regulates secretion of regulated and normal T-cell expressed and secreted in T cells, which recruit activated Th1 cells and macrophages.[8] Arnold *et al.*[9] demonstrated that estrogen inhibits the induction of epidermal ornithine decarboxylase, an enzyme required for DNA replication, indicating that estrogen may inhibit keratinocyte hyperproliferation in psoriasis, an additional anti-psoriatic effect of estrogen. Furthermore, E2 may protect keratinocytes from oxidative stress-induced apoptosis. H_2O_2 is generated in keratinocytes by ultraviolet-B irradiation and acts as an apoptotic mediator.[10] In multiple sclerosis patients, increased concentrations of estrogen enhance the production of the anti-inflammatory cytokine IL-10 while decreasing the production of pro-inflammatory cytokines such as TNF-α in $CD4^+$ T-cell clones on multiple sclerosis patients. Murase *et al.* reported that high levels of estrogen are

Table 1. Characteristics of patients and controls

Variable	Patients with psoriasis ($n = 47$)	Control ($n = 20$)	*P*
Age (years)	42.87 ± 15.56	38.05 ± 10.14	0.141
Estradiol* (range, 0–39.8 pg/mL)	37.52 ± 17.16	29.9 ± 8.77	0.02
Testosterone* (range, 229.9–799.8 ng/dL)	392.29 ± 181.91	506.91 ± 117.7	0.004
FSH (range, 1.9–18.9 IU/L)	8.84 ± 21.29	4.54 ± 2.69	0.185
LH (range, 1.7–9.6 IU/L)	6.25 ± 6.67	4.25 ± 1.3	0.056
BMI (kg/m^2)	26.86 ± 3.9	25.51 ± 5.27	0.323
PASI	12.88 ± 11.92	NA	

*Statistical significance was found between the patients with psoriasis and controls ($P < 0.05$). Data are expressed as mean ± standard deviation. BMI, body mass index; FSH, follicle-stimulating hormone; LH, luteinizing hormone; NA, not applicable; PASI, Psoriasis Area and Severity Index.

Table 2. Correlations of all parameters

Correlations						
	Estradiol	Testosterone	FSH	LH	BMI	PASI
Estradiol						
Pearson correlation	1	0.357*	−0.144	−0.096	0.045	−0.353*
P (two-tailed)		0.019	0.339	0.525	0.791	0.016
n	46	43	46	46	38	46
Testosterone						
Pearson correlation	0.357*	1	−0.295	−0.223	−0.191	−0.228
P (two-tailed)	0.019		0.055	0.151	0.264	0.142
n	43	43	43	43	36	43
FSH						
Pearson correlation	−0.144	−0.295	1	0.947**	−0.219	−0.061
P (two-tailed)	0.339	0.055		0.000	0.187	0.689
n	46	43	46	46	38	46
LH						
Pearson correlation	−0.096	−0.223	0.947**	1	−0.190	−0.105
P (two-tailed)	0.525	0.151	0.000		0.253	0.486
n	46	43	46	46	38	46
BMI						
Pearson correlation	0.045	−0.191	−0.219	−0.190	1	−0.073
P (two-tailed)	0.791	0.264	0.187	0.253		0.663
n	38	36	38	38	38	38
PASI						
Pearson correlation	−0.353*	−0.228	−0.061	−0.105	−0.073	1
P (two-tailed)	0.016	0.142	0.689	0.486	0.663	
n	46	43	46	46	38	46

*Correlation is significant at the 0.05 level (two-tailed). **Correlation is significant at the 0.01 level (two-tailed). BMI, body mass index; FSH, follicle-stimulating hormone; LH, luteinizing hormone; PASI, Psoriasis Area and Severity Index.

correlated with psoriasis improvement in psoriasis in pregnancy.[4] In addition, Ceovic *et al.*[11] reported that high levels of estrogen promote inhibition of components of the immune response, while low levels of estrogen may enhance inflammatory and immunological processes. Given the association between low serum estradiol and elevated PASI scores in the present study, we suggest that lower levels of estradiol have a stimulatory effect on psoriasis. Higher basal estradiol levels in psoriasis patients relative to controls and the inverse correlation of estradiol with PASI suggest that estradiol plays a significant role in the etiopathogenesis of psoriasis. Furthermore, the immune stimulating effect of low estradiol, reported by Ceovic *et al.*,[11]may account for the prevalence of high serum estradiol in psoriasis patients.

Previous reports have indicated that testosterone promotes an immunological shift towards the Th2 phenotype in experimental autoimmune encephalomyelitis, a model for the human demyelinating disease multiple sclerosis.[12] Testosterone levels were significantly higher among control patients relative to psoriasis patients. However, there was no significant correlation between serum testosterone and PASI in the patient group.

In conclusion, serum estradiol levels were significantly increased among psoriasis patients relative to control patients. Estradiol was inversely correlated with PASI. In addition, serum testosterone levels were significantly lower among psoriasis patients relative to control patients. This data should be considered preliminary in nature. Long-term follow-up studies are necessary to confirm the significance of these associations in a larger, more diverse population. However, the present study suggests that estrogen plays a significant role in the pathogenesis of psoriasis, potentially inhibiting inflammation and immunological activity at high doses.

CONFLICT OF INTEREST: None.

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