Serum prolactin level in psoriasis: Is it really higher than in healthy individuals?

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Background: Psoriasis is a chronic immune-mediated skin disease with a genetic predisposition. Prolactin may contribute to psoriasis pathogenesis. However, there has been a debate over the serum level of prolactin in psoriatic patients. The aim of this study was to describe the role of serum prolactin in the pathogenesis of psoriasis

Method: The serum prolactin level was measured in 45 patients with psoriasis and in 45 sex- and age-matched healthy individuals using radioimmunoassay.

Result: The mean serum prolactin concentration was not different between psoriatic patients and healthy controls (320 ± 179.38 vs. 318.18 ± 191.78 mIU/L, respectively P = 0.95). There was no sex- and age-related differences in serum prolactin between the two study groups. Hyperprolactinemia (serum prolactin >324 mIU/L in men, and >496 mIU/L for women) was observed in 11 patients with psoriasis and 12 healthy subjects, which showed no significant difference between the two groups (P = 0.81). The serum prolactin was not significantly correlated with the duration of the disease (r = -0.18, P = 0.24) or the PASI score (r = 0.10, P = 0.50).

Conclusion: The possible role of pituitary-produced circulating prolactin in the disease process needs further investigations.

Keywords: hyperprolactinemia, psoriasis, prolactin, skin

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INTRODUCTION

Psoriasis is a chronic immune-mediated and environmentally influenced skin disease with genetic predisposition, and is often associated with systemic manifestations, especially arthritis [1]. The prevalence in adults varies from 0.9% in the United States to 8.5% in Norway [2]. Cytokines, dendritic cells, and T lymphocytes are present in psoriatic lesions and all contribute substantially to its pathogenesis [3]. Prolactin has also been implicated in the pathogenesis of psoriasis, where hyperproliferation of keratinocytes is the hallmark of the disease process [4-6].

Prolactin is produced in lactotroph cells of the anterior pituitary gland. It is primarily a lactogenic and mammotrophic hormone, but also an immune modulatory cytokine. Prolactin appears to play a role in the activity of autoimmune disorders such as systemic lupus erythematosus and rheumatoid arthritis [7]. Additionally, as a result of its potent growth-regulatory effects on integumental structures in various species, prolactin has long been hypothesized to contribute to human skin biology and pathology [8].

Prolactin may contribute to psoriasis pathogenesis via stimulating keratinocyte proliferation, triggering interferon-γ production by T-cells, promoting angiogenesis, inhibiting T-suppressor cell function, and promoting the infiltration of T-helper cells into psoriatic lesions [9]. However, there has been a debate over the role of serum level of prolactin in psoriatic patients. More specifically, some researchers have recorded a significantly higher level of prolactin in the serum of patients with psoriasis compared to healthy individuals [10-13], while others found no difference [14-16]. However, the majority of these studies were consistent in finding

a remarkable reduction in serum prolactin level, following the treatment of psoriasis with a range of therapies including the topical ointments [12,13,16], phototherapy [16], and systemic regimens such as propylthiouracil [11] and methotrexate [12]. Therefore, in this study, the serum prolactin level in patients with psoriasis vulgaris and in healthy individuals were further investigated to determine the role of serum prolactin in the pathogenesis of psoriasis.

PATIENTS AND METHODS

This case-control study was carried out from September 2012 to March 2013, in the Dermatology Department of Razi Hospital, Tehran, Iran. The study protocol followed the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of Tehran University of Medical Sciences. Forty-five (45) patients with newly diagnosed psoriasis vulgaris who had not received any topical or systemic treatment for their lesions, and the same number of sex- and age-matched healthy individuals were recruited to the study. Written informed consent was obtained from all study participants. Patients who had taken drugs affecting serum prolactin levels and those with conditions causing hyperprolactinemia such as hypothyroidism, pregnancy and lactation were not included in this study.

Data regarding the type and duration of the psoriasis were recorded. The Psoriasis Area and Severity Index (PASI) was measured for all patients. The serum concentration of prolactin was determined using the radioimmunoassay technique in the hospital laboratory with the reference range being 86–324 mIU/L in men, and 102–496 mIU/L in women. The data were analyzed using SPSS version 16. Independent student's *t*-test was applied to explore significant differences between the two groups. Chi-square test was used to compare the proportion of cases with hyperprolactinemia between psoriatics and healthy controls. Pearson's correlation test was utilized to evaluate the association between the PASI score and serum prolactin. Data are presented as mean ± standard deviation (SD). A two-tailed P value less than 0.05 was considered statistically significant.

RESULTS

Overall, 45 patients with psoriasis (33 men and 12 women) and 45 sex- and age-matched healthy controls (34 men and 11 women) were included in the study. The mean age (± SD) of psoriatic patients was 39.84 ± 14.82 years and of healthy volunteers was 39.62 ± 18.13. The mean serum prolactin concentration was not different between psoriatic patients and healthy controls [320 ± 179.38 mIU/L vs. 318.18 ± 191.78 mIU/L respectively; t (88) = 0.05, P = 0.95]. The serum prolactin level was also similar in psoriatic and healthy participants in subgroups of different genders. Specifically, serum prolactin levels in psoriatic and healthy men were 313.97 ± 180.37 mIU/L and 292.65 ± 134.75 mIU/L, respectively, and there was no significant difference between both groups (P = 0.58). Similarly, serum prolactin levels in psoriatic and healthy women were 337.92 ± 183.314 mIU/L and 397.09 ± 304.70 mIU/L, respectively, and there was no significant difference between both groups (P = 0.57) (Figure 1). Furthermore, serum prolactin did not exhibit any significant difference between various age groups (<25, 25-44, 45-64, and >65 years) of psoriatic and healthy participants.

Hyperprolactinemia (serum prolactin level >324 mIU/L in men, and >496 mIU/L in women) was observed in 11 patients with psoriasis and 12 healthy participants, showing no significant difference between the two groups (P=0.81). Moreover, there was no gender-differences in the proportion of cases with hyperprolactinemia between the two groups. In the group of patients with psoriasis, the mean duration of the disease was 10.27 ± 9.24 years, and the mean PASI score was 15.78 ± 10.43. The serum prolactin was not significantly correlated with the duration of the disease (r = -0.18, P = 0.24) or the PASI score (r = 0.10, P = 0.50).

DISCUSSION

The skin is a hormone-generating and hormone-modifying organ, as well as being a hormone target. Since the mammary gland is a derivative of the epidermis and phylogenetically related to sweat glands, it has been suggested that the mammotrophic action of prolactin might have evolved from its broad action on integumental structures in other species [8]. Prolactin and prolactin receptor are expressed in human skin and human scalp hair follicles where they inhibit hair shaft elongation, promote premature catagen development, reduce

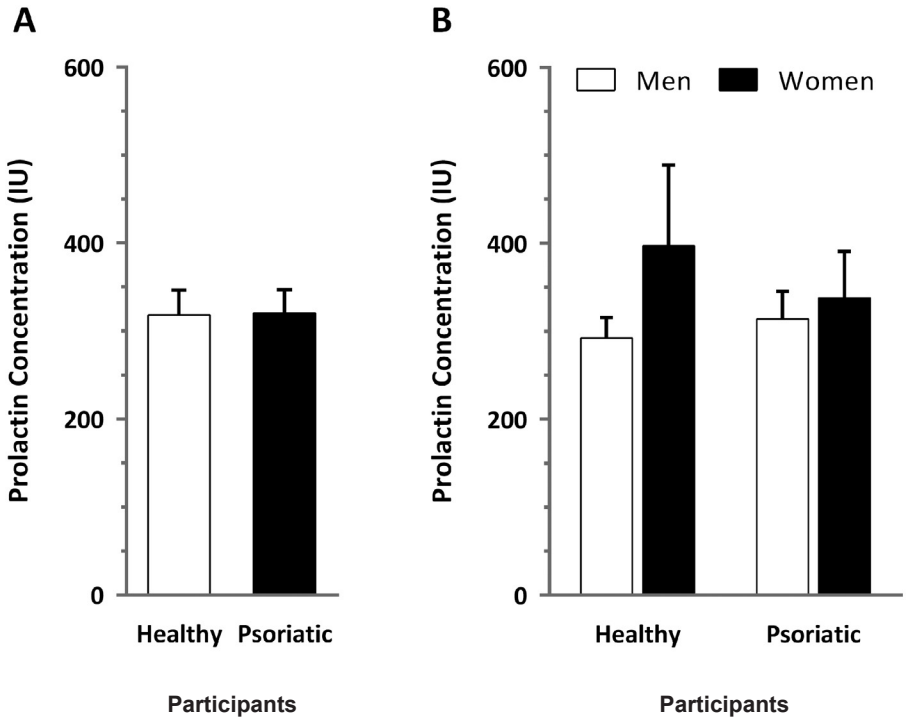

Figure 1. Serum prolactin concentration in the study participants. There was no significant difference in the serum prolactin level between the psoriatic and healthy participants (**A**). Serum prolactin also showed no significant differences between the two study groups according to the gender (**B**). Error bars display standard error of mean (SEM).

proliferation and increase apoptosis of hair bulb keratinocytes [17]. Therefore, human skin and scalp hair follicles are both a non-classical target and an extrapituitary source of prolactin. Among the key regulators of pituitary prolactin production, thyrotropin-releasing hormone, estrogen, tumor necrosis factor-α, interferon-γ, and substance P have been shown to also regulate intracutaneous prolactin production and prolactin receptor expression in different ways [18,19].

Several lines of evidence indicated that prolactin may also be implicated in the pathogenesis of psoriasis. In this regard, it has been shown that prolactin concentration was significantly elevated in blister fluid drawn from lesional, but not non-lesional skin in psoriatic patients relative to that in blister fluid from healthy controls [20]. This observation suggests a role for locally produced prolactin in the skin in the pathogenesis of psoriasis. Furthermore, a significantly higher prolactin level was found also in the serum of patients with psoriasis compared to healthy individuals [10-13], implicating the pituitary-originated circulating prolactin in the psoriasis. However, this was brought into question by studies reporting no changes in the serum prolactin level in psoriatic patients [14-16,20,21]. The findings of this study indicate that serum prolactin was neither elevated in psoriatic patients nor correlated with the severity or duration of the disease. However, these findings do not refute the role of prolactin in psoriasis.

The hallmarks of psoriasis include hyperproliferation of keratinocytes, dysregulated angiogenesis, and expression of proinflammatory T helper-1 cytokines [22]. Additionally, psoriasis is exacerbated by psychoemotional stress [23]. All of these processes proved to be influenced by prolactin. Prolactin is considered a stress hormone and potentially triggers psoriasis [8,24]. Psoriasis tends to be aggravated during the early postpartum months when a natural hyperprolactinemia occurs in relation to the lactation [25]. Prolactin stimulates human epidermal keratinocyte proliferation and vascular endothelial growth factor production *in vitro* [26,27]. Prolactin promotes the proliferation of B and T lymphocytes, increases the synthesis of the cytokines interferon-γ and interlukine-2 in T helper-1 cells, suppresses T lymphocyte apoptosis, and inhibit glucocorticoid-induced apoptosis of lymphocytes [28,29]. Prolactin also

increases the production of cytokines by T helper-1 and T helper-17, and augments inflammation in psoriasiform skin of BALB/c mice [30]. Prolactin increases basal and interlukine-17-induced CCL20 secretion, and mRNA expression in keratinocytes, and may promote T helper-17 infiltration into psoriatic lesions via CCL20 [31].

In conclusion, it seems that while intracutaneous prolactin may contribute to the pathogenesis of psoriasis, the probable role of pituitary-produced circulating prolactin in the disease process needs further investigations.

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