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Journal of Dermatology & Dermatologic Surgery 19 (2015) 104–107

Original article

Serum prolactin levels in dermatological diseases: A case–control study

Nadia Abdalhafid Elsherif [a,*], Abdalla I. El-Sherif [a], Salwa A. El-Dibany [b]

[a] Dermatology Department, Faculty of Medicine, Benghazi University, Benghazi, Libya
[b] Dermatology Department, Faculty of Medicine, Omer El-Muktar University, Elbida, Libya

Received 19 January 2015; accepted 13 March 2015
Available online 13 April 2015

Abstract

Background: Recent lines of evidence suggest that prolactin (PRL) as a neurohormone may play a role in the activity of psoriasis and some other immune-mediated diseases. Our aim was to evaluate the correlation between serum PRL levels and severity of psoriasis, vitiligo and alopecia areata.

Patients and methods: We performed a case–control study on 100 subjects: 75 patients; suffering from psoriasis, vitiligo and alopecia areata; 25 patients in each group and 25 age- and sex-matched healthy controls.

Results: Serum prolactin levels were significantly high in all three dermatological diseases in comparison with the control group ($P = 0.000$). The mean ± SD of the serum prolactin levels was 21.8 ± 11.5 ng/ml, 16.9 ± 6.8 ng/ml, and 16.6 ± 8.0 ng/ml in patients with alopecia areata, psoriasis and vitiligo respectively. Moreover, the serum prolactin levels in patients with alopecia areata and psoriasis were significantly correlated with disease severity ($P < 0.05$), however no statistically significant correlation was noted between vitiligo severity and serum prolactin levels ($P > 0.05$).

Conclusions: Prolactin may play a role in the pathogenesis of alopecia areata, psoriasis, and vitiligo; and may serve as a biological marker of disease activity in patients with psoriasis and alopecia areata.

Keywords: Prolactin; Psoriasis; Vitiligo; Alopecia areata

1. Introduction

Prolactin (PRL) is a peptide hormone secreted by the anterior pituitary gland and also by many extra-pituitary sites, including immune cells (Jara et al., 2009). PRL has a role in reproduction, calcium metabolism, osmoregulation, and behavior (Jara et al., 2009; De Bellis et al., 2005). The relationship between PRL and the immune system has been demonstrated in the last two decades (De Bellis et al., 2005). PRL has multiple immune-stimulatory effects and promotes autoimmunity. It increases the synthesis of IFN-gamma and IL-2 by Th1 lymphocytes (De Bellis et al., 2005). Moreover, PRL activates Th2 lymphocytes with autoantibody production (De Bellis et al., 2005). Many studies evaluated the clinical significance of PRL in different skin diseases with conflicting results (Foitzik et al., 2009).

2. Aim of the study

The aim of the present study was to evaluate the prevalence and clinical significance of serum PRL levels in alopecia areata, vitiligo and psoriasis vulgaris patients and to compare them with healthy controls.

* Corresponding author.
E-mail address: elsherifnadia@yahoo.com (N.A. Elsherif).
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jdds.2015.03.002

3. Patients and methods

This comparative, descriptive, case–control study was conducted at the Dermatology department at El-Jumhuriya Hospital, Benghazi city, Libya. A hundred subjects were included in the study: 75 patients; suffering from psoriasis, vitiligo and alopecia areata 25 patients in each group and 25 age and gender-matched healthy controls. A verbal consent was obtained from all patients and healthy subjects after explaining the nature of the study to them.

Exclusion criteria were presence of other autoimmune diseases and use of drugs that are known to affect levels of PRL (i.e., psychotropic drugs, thyroid hormones, glucocorticoids, and estrogens or contraceptives). Pregnant and lactating females were also not included in the study. All patients who were on either topical or systemic treatment for one month prior to blood collection were excluded from the study. Blood was collected from all subjects and serum PRL was measured by ELISA.

Psoriasis was graded according to the PASI score, presenting at the time of blood collection. The patients were divided into three groups based on the severity of the disease as mild (PASI <3), moderate (PASI 3.1-10) and severe (PASI >10). Vitiligo patients were divided into two groups as active and stable disease according to the progression of the lesions and the appearance of new lesions in the last three months. The activity of the disease among patients with alopecia areata was determined by positive pull test at the time of examination and/or progression of the lesions in the last month. Comparative analyses were carried out between age, gender, disease durations and activity and serum PRL levels.

3.1. Statistical analysis

All statistical analyses were performed using SPSS software for Windows (Version 16.0). Results are presented as mean and standard deviations for continuous variables and as a number (%) for categorical variables. Comparisons between the patients and the control group were done by *t* test. *P* values <0.05 were considered significant.

4. Results

Table 1 shows the demographic characteristics of patients and controls. No significant difference between patients and control subjects was noted.

Table 2
Serum prolactin in patients and control subjects.

Subjects	Psoriasis	Alopecia	Vitiligo	Control
Serum PRL	16.9 ± 7	21.8 ± 12	16.6 ± 8	11.2 ± 6
P value	.003	.000	.005	

The mean serum PRL of psoriasis patients was 16.9 ± 6.8 ng/ml which is statistically significantly higher than serum PRL of control subjects (Table 2). No statistically significant difference was found in serum PRL and patient's age or gender. Ten (66.7%) of the patients with severe psoriasis and 1 (10%) patient with moderate psoriasis had high serum prolactin ($P < 0.05$). About 64% of the patients had disease duration more than 5 years, and as the disease duration increased, serum PRL level also increased ($P < 0.05$).

Patients with vitiligo had a mean serum PRL of 16.6 ± 8 ng/ml which was significantly higher than the serum PRL of the control subjects (Table 2). No significant difference was found in patient's serum PRL and their age, gender, and disease durations. Regarding the activity of their disease 12 (48%) of the patients had active disease, and only 4 (36.4%) of the patients with active disease had high serum PRL ($P > 0.05$).

Among patients with alopecia areata, 9 (36%) patients had multiple patches of alopecia, 5 (20%) had alopecia totalis and 11 (44%) of the patients had alopecia universalis. Their mean serum PRL was 21.8 ± 11.5 ng/ml which was significantly higher than the serum PRL of the control subjects (Table 2). No significant difference was found in patient's serum PRL with their ages, gender and disease duration, however there was a significant correlation between the type of alopecia and serum PRL ($P < 0.05$).

Regarding the activity of their disease 48% of the patients had active disease, moreover 75% of the patients with active disease had high serum PRL ($P < 0.05$). The serum PRL was higher in patients with alopecia areata compared with that in patients with psoriasis and vitiligo but this difference was not statistically significant.

5. Discussion

Despite being known primarily as a lactogenic hormone, PRL is in fact also an immunomodulatory hormone (Jara et al., 2009). The relationship between PRL and the immune system has been demonstrated in the last two decades and has opened new windows in the field of

Table 1
Demographic data of patients under study and control subjects.

Subjects' number	Psoriasis 25	Alopecia 25	Vitiligo 25	Control subjects 25	*P* value
Age ± SD	35.8 ± 11 years	31 ± 6 years	34 ± 9 years	35 ± 9 years	.835
Gender					.387
Females	12	13	14	14	
Males	13	12	11	11	

immunoendocrinology (Jara et al., 2009). Moreover, of the currently available prolactin-lowering drugs, bromocriptine at least has been shown to decrease both peripheral and pituitary PRL production and may represent a useful adjunctive therapy in certain patients, particularly those with refractory disease (Chuang and Molitch, 2007).

At present, the best evidence of a relationship between PRL levels and disease activity exists for SLE, RA, Reiter's syndrome, and psoriasis (Chuang and Molitch, 2007). However, there are scarce reports in the literature regarding the significance of PRL in alopecia areata and vitiligo (Gönül, 2009; Gönül et al., 2009).

Although many studies found increased serum PRL in patients with psoriasis (Giasuddin et al., 1998; Dilmé-Carreras et al., 2011), there is controversy, however, as to whether raised PRL levels are associated with disease activity. Gorpelioglu et al. and Priestley et al. did not find any association between serum PRL levels and psoriasis as well as its activity (Gorpelioglu et al., 2008; Priestley et al., 1984). In contrast, a number of investigators have found a significant association between serum PRL and disease activity (Giasuddin et al., 1998; Dilmé-Carreras et al., 2011; Sanch, 2000).

Although hyperprolactinemia due to prolactinoma has been reported in severe cases of psoriasis and treatment with bromocriptine led to normalization of PRL levels and concurrent improvement of their psoriatic lesions (Sanch, 2000), none of our patients showed high serum PRL in the range of prolactinoma.

Psoriasis is a T-cell-mediated autoimmune skin disease characterized by hyperproliferation, abnormal differentiation of keratinocytes, presence of inflammatory cell infiltrate and alterations to the dermal capillaries (Gorpelioglu et al., 2008).

Several mediators and hormones have been implicated in keratinocyte hyperproliferation. Among these hormones, prolactin has been found to have a proliferative effect on epithelial cells, lymphocytes and keratinocytes in in vitro studies. Moreover, normal PRL levels are required for functions of immunocompetent T and B lymphocytes (Girolomoni et al., 1993).

A significantly elevated PRL level has been observed in the psoriatic plaques' lesions (El-Khateeb et al., 2011). Moreover functional PRL receptors are detected on epidermal keratinocytes, indicating that PRL may be involved in the hyperproliferation of keratinocytes in psoriasis (El-Khateeb et al., 2011).

A previous study of serum PRL in patients with alopecia areata reported no significant difference in serum PRL levels and in the number of hyperprolactinemic individuals between the patient and control groups and they suggested that prolactin does not play a role in the pathogenesis of alopecia areata (Gönül, 2009). In the present study, serum PRL of alopecia areata patients was significantly higher than that of the control subjects. Moreover there was a significant correlation between the type of alopecia and disease activity and the serum PRL. Alopecia areata has been considered to be an autoimmune in origin. IFN-γ is the main cytokine known to be aberrantly expressed in alopecia areata through Th1 mediated response. It has been shown that serum levels of IFN-γ are significantly higher in patients with alopecia totalis or alopecia universalis compared to those in controls, but no significant difference has been found in the levels of IFN-γ between patients with localized alopecia areata and those with more extensive forms (Arca et al., 2004). PRL has multiple immunostimulatory effects and promotes autoimmunity. It increases the synthesis of IFN-gamma and IL-2 by Th1 lymphocytes; moreover, PRL activates Th2 lymphocytes with autoantibody production (De Bellis et al., 2005).

Human skin, and and particularly scalp hair follicles, are both direct extramammary targets and extrapituitary sources of PRL (Foitzik et al., 2006). The catagen-inducing effects of PRL on human hair growth may help explain the telogen effluvium seen in patients with hyperprolactinemia (Foitzik et al., 2009). PRL has been suggested to act as an autocrine hair growth modulator with catagen promoting functions and may serve as a hair growth-inhibitory hormone (Foitzik et al., 2009).

There are scarce reports in the literature regarding the significance of PRL in patients with vitiligo. Recently, a study evaluated the significance of PRL in vitiligo and concluded that PRL does not play a role in the pathogenesis of vitiligo (Gönül et al., 2009). However, serum PRL levels among our patients with vitiligo were significantly higher than those of the control subjects, with no significant association with disease activity or durations.

PRL has multiple immunostimulatory effects and promotes autoimmunity (De Bellis et al., 2005). PRL increases the synthesis of IL-6 and IL-2 which are proinflammatory cytokines that play an important role in melanocytic cytotoxicity in vitiligo patients (Singh et al., 2012). Many workers reported high IL-6 levels in vitiligo patients. Il-6 was produced by mononuclear cells, which could induce the expression of ICAM-1 (intercellular cell adhesion molecules) on melanocytes, which might then facilitate leukocyte–melanocyte interactions, leading to polyclonal B-cell activation subsequently increasing autoantibody production, leading to immunological damage of melanocytes (Kirnbauer et al., 1992). Moreover, PRL activates Th2 lymphocytes with autoantibody production and enhances immunoglobulin production which may contribute to increased autoreactivity (De Bellis et al., 2005).

6. Conclusions

The findings of increased prolactin levels in patients with psoriasis, vitiligo and alopecia areata lead to the assumption that prolactin may play a role in the pathogenesis of these diseases; moreover PRL may serve as a biological marker for disease severity and activity.

Conflict of interest

The authors declare no conflict of interest.

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