Short Communication

Do serum prolactin levels correlate with antibodies against desmoglein in pemphigus vulgaris?

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Abstract

Background: Pemphigus vulgaris is a chronic inflammatory disease of skin, the etiology of which is not completely known. Despite the latter, anti-desmoglein antibodies play a proven role in the pathogenesis. Recent studies showed an etiologic effect for prolactin in the pemphigus vulgaris. This study aimed to quantify the correlation between serum prolactin levels and anti-desmoglein antibodies in patients with pemphigus vulgaris.

Materials and Methods: Prolactin and antibodies against desmoglein 1 and 3 measured with ELISA in 14 new subjects of pemphigus vulgaris.

Results: There was no statistically significant relation between both serum prolactin and anti-desmoglein1 levels ($r = 0.02$, $P = 0.47$) and serum prolactin and anti-desmoglein 3 levels ($r = -0.09$, $P = 0.38$).

Conclusion: This study indicates that no correlation was found between serum prolactin levels and anti-desmoglein 1 levels and serum prolactin and anti-desmoglein 3 levels. However, other studies should be initiated regarding exact molecular and cellular effects of prolactin in the pathogenesis of pemphigus vulgaris.

Key Words: Desmoglein, pemphigus vulgaris, prolactin

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INTRODUCTION

Pemphigus vulgaris (PV) as an autoimmune disease is the most common type of pemphigus with a worldwide distribution.[1] Despite the fact that it has become clear that autoantibodies against desmosomal glycoproteins including desmoglein 1(Dsg1) and desmoglein 3 (Dsg 3) play role in the pathogenesis of PV, the accurate molecular steps in initiation and perpetuation of this abnormality remain unknown. Besides the proposed pathogenic role of these antibodies, recent studies indicate a significant relation between Dsg 3 and Dsg 1 antibody titers with severity of oral and skin involvement, respectively.[2-8]

With clarification of immunomodulatory aspect of prolactin (Prl) apart from the known hormonal effects, researches on the conjectural role of this molecule in auto-immune or immune-related disorders in dermatology such as lupus erythematousus and psoriasis have been commenced.[9-12] Recently, a

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cross-sectional study showed that elevation of Prl levels in PV patients correlates with the extent of body involvement.[13]

Also, some studies showed that prolactin can accompany progress of some autoimmune diseases, such as, systemic lupus erythematosis, uveitis, rheumatoid arthritis, multiple sclerosis, autoimmune thyroiditis, psoriatic arthritis, etc.[14]

By juxtaposition of the aforementioned results on the correlation of the severity of PV with anti-desmoglein antibodies and serum Prl titers, it is interesting to perform an investigation to find out whether or not Dsg 3 and Dsg 1 antibodies correlate with serum Prl titers. This cross-sectional study is the first, to our knowledge, to measure quantitatively the correlation between anti-desmoglein antibodies with serum Prl level.

MATERIALS AND METHODS

This study was conducted at the outpatient department of Dermatology, Isfahan, Azahra Teaching Hospital. A total of 14 subjects (aged 21 to 59 years) presenting as new case of PV were enrolled in the study between December 2011 and December 2012. This study was initially approved by the ethical committee of Isfahan University of Medical Science. The Research Project Number was 291252. Written informed consent was obtained from all participants before enrollment.

The diagnosis was established on the basis of clinical findings and confirmed with histopathology and direct immunoflourescence.

The patients were divided into two different treatment groups, using a table of random numbers. Inclusion criteria included any new case of PV, aged between 20 and 60 years. Patients with bulla and erosions secondary to other causes, pregnancy and lactation, impaired kidney function, significant liver function abnormalities, hepatitis, cirrhosis, those on therapy that affecting serum Prl (phenothiazines, cimetidine, metoclopramide, and opioids), and also those with a history of abortion were excluded from the study. In other words, mild to moderate cases of PV were selected.

The serum ELISA was performed to measure antibodies against Dsg1 and Dsg3 (kits from Medical and Biological Labratories Co Ltd Nagoya, Japan). The index value of positive reactions was considered more than 20 for both Dsg3 and Dsg1. In addition, the serum Prl titers were measured by ELISA method. The samples were taken in the morning in a fasting status for at least 8 hours. In this method, the index value of positive reactions was considered more than 20 in males. In females, the values greater than 28.5 and 18.5 were considered positive in premenopausal and postmenopausal, respectively. Due to hyperprolactinemia secondary to hypothyroidism, TSH was measured in all the subjects.

The statistical analysis was done by SPSS for Windows software (SPSS Inc., Chicago, IL, USA, version 18.0) by using Chi-square and Pearson regression test. The significance level was set at *P*- value of less than 0.05.

RESULTS

Fourteen PV patients (5 men and 9 women) with an average age of 49.42 (age range of 39 to 60 years) were enrolled in the study. Characteristics of patients are shown in Table 1.

Mean serum Dsg1 antibody levels in males and females were 14.8 ± 5.8 and 0.8 ± 0.2, respectively, that were statistically significant ($P = 0.06$). However, such a comparison between male and female values of mean serum Dsg 3 antibody ($P = 0.14$) and prolactin ($P = 0.96$) revealed no significant difference [Table 2].

The Pearson regression test was used to determine the correlation between the antibodies against Dsg1 and Dsg 3 titers and Prl level. By this method, no

Table 1: Patients' characteristic

Patient number	Age	Sex	Prolactin level	Anti-Dsg1 level	Anti-Dsg3 level
1	45	F	20.5	0.1	56
2	52	M	5.4	23	209
3	57	M	5.5	0.1	40
4	54	F	6.9	0.1	40
5	47	F	6.4	0.9	175
6	52	F	22	0.1	59
7	44	M	6	25	213
8	39	F	6	1	45
9	60	M	18	1	50
10	46	F	7	2	200
11	52	F	30	1	65
12	56	M	27	25	220
13	39	F	7	1	50
14	48	F	98	1	55

Dsg: Desmoglein

Table 2: Pemphigus vulgaris parameters of male and female subjects

Levels	Male	Female	*P* value
Anti-Dsg1	148±5.8	0.8±0.2	0.006
Anti-Dsg3	146±41.46	82.78±20	0.14
Prolactin	12.38±4.37	12.64±3	0.96

Dsg: Desmoglein

correlation was detected between both serum Prl and anti-Dsg1 levels (r = 0.02, P = 0.47) and serum Prl and anti-Dsg3 levels (r = -0.09, P = 0.38).

DISCUSSION

Since the late 1980s, it is proven that autoantibodies in PV are directed against two desmosomal cadherins: mostly Dsg3 and, to a lesser extent Dsg1.[2-8] However, after 3 decades of more clarification of the cascade of events in inducing blister of PV, the initial steps in the pathogenesis remain to be determined.[1]

In the immunopathogenesis model, both humoral and cellular autoimmunity are involved in the pathogenesis of lesions of PV. Apart from the known role of auto-antibodies in inducing the blisters, T cells, especially CD4 cells with T helper 2 type cytokine profile, may also be involved in acantholysis.[1,7]

In a study of 44 patients of PV, Kumar *et al.* suggested the severity of skin and oral involvement that is related to the quantities of antibodies against Dsg1 and Dsg3, respectively.[15]

In another study of 38 known cases of PV, Mortazavi and Kiavash clarified that not only the Dsg1 and Dsg3 ELISA confirmed the disease (Sensitivity: 97.3%) but Dsg 1 index value is statistically correlated with the severity of PV in Iranian patients.[16]

Despite many theories been involved in the pathogenesis of PV, it is yet to be fully understood. With regard to the more accepted role of Prl in the pathogenesis of autoimmune disorders, investigators in the field of dermatology turn their attention to the latter.[11]

Other than considering as an endocrine hormone, Prl is a cytokine with broad distribution throughout immune cells and several immunomodulatory effects. Based on *in vitro* studies, Prl augments the interleukin-2 release and enhances tumor necrosis factor –alfa secretion. Besides antiapoptotic effects on B lymphocyte cells, it heightens the production of antibodies.[9-12,17-19]

In many autoimmune diseases, a positive correlation was suggested between serum Prl and disease activity. Reddy and Khandpur reported a significant relationship between the serum Prl levels and extension of lesions in a 21-year-old woman with hyperprolactinemia. This patient was only controlled when bromocriptine was added to the therapeutic regimen.[13]

Regarding the role of prl in inducing autoimmune diseases and the fact that PV has significant autoimmune aspects in pathogenesis, we provide the first clinical evidence that measures quantitatively the correlation between Dsg1 and Dsg3 index values (known PV activity markers) and serum Prl levels by ELISA.

In a study of 24 patients with PV, Fallahzadeh and Namazi revealed a positive correlation between serum prolactin levels, and the extent of body surface involvement (P = 0.01).[20]

In our study, no correlation was found between serum prolactin levels and anti-Dsg1 levels and serum Prl and anti-Dsg3 levels.

Azizzadeh *et al.* in a survey on psoriasis revealed no association between Prl levels and psoriasis. However, a relationship between severe forms of psoriasis and Prl levels was noticed.[21]

In comparison to aforementioned studies on the correlation of serum Prl levels and autoimmunity, it could be concluded that the role of Prl in severe forms of autoimmune diseases should be considered. In other words, by excluding mild to moderate cases of PV, a more positive correlation between serum Prl level and anti-Dsg antibody titers will be probable. In determining the limitations of study if we enrolled subjects with more extensive lesions, and those with lesions recalcitrant to therapy, the results would not be the same. Furthermore, despite the proposed role of anti-Dsg antibodies and Prl in the pathogenesis of PV, the conjectural steps between these cytokines remain unclear.

In addition, by discovery of immunomodulatory effects of Prl through studies of autoimmune diseases, caution should be performed when considering definite immune-related disorders such as PV. In fact, considering PV as a pure autoimmune disease is an oversimplification that may not be appropriate for all study patterns.

In summary, we suggest that studying the effects of Prl levels on disease activity should be done in a large sample size of PV patients with extensive disease and in cases who are resistant to therapy. Moreover, in completing the fragmented knowledge that we have gathered to date regarding PV pathogenesis, parallel experiments should be initiated regarding exact molecular and cellular effects of Prl in PV.

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