

Serum prolactin levels in psoriasis and correlation with cutaneous disease activity

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Summary

Background. Prolactin (PRL), a neuropeptide secreted by the anterior pituitary gland, possesses a variety of physiological actions. It has been implicated as an important immunomodulator and exerts a proliferative effect in cultured human keratinocytes via specific receptors. Some studies have indicated an increase in serum PRL levels in psoriasis and exacerbation of psoriasis when a prolactinoma is present.

Aim. To evaluate the correlation between serum PRL levels and Psoriasis Area and Severity Index (PASI).

Methods. Serum PRL levels were measured in 20 patients (10 men, 10 women, age range 18–88 years) with plaque-type psoriasis before and after a 6-week period of topical treatment with tacalcitol ointment. Results were compared with a group of 20 healthy volunteers.

Results. Serum PRL levels were significantly increased in the psoriatic group compared with the control group ($P < 0.001$) and were significantly reduced after treatment ($P = 0.001$). There was a correlation between pretreatment serum PRL levels and PASI ($r = 0.33$; $P = 0.02$).

Conclusions. These results indicate that serum PRL levels may serve as a biological marker of psoriatic disease activity.

Introduction

Psoriasis is a dermatological condition, with a prevalence of 1.4% in the Spanish population.¹ It is an inflammatory disease characterized by hyperproliferation of keratinocytes and accumulation of activated T cells in the epidermis and dermis of psoriatic lesions.² Evidence for the central role of T helper (Th)1 lymphocytes comes from both animal models of psoriasis and from trials of treatment with T-cell inhibitors.³ There is considerable epidemiological evidence that genes play a key role in the pathogenesis of psoriasis. It has been estimated that the human leucocyte antigen-associated

allele *PSORS1* on chromosome 6 accounts for 30–50% of the genetic contribution of psoriasis,⁴ especially in the Spanish population.⁵ In addition to the genetic influences, some environmental factors, such as injury, infection, stress⁶ drugs or hormonal disturbances, are necessary for development of the psoriatic phenotype.

There is some evidence that psoriasis worsens at ages when hormonal changes such as puberty and menopause are taking place, and may also worsen or improve during pregnancy.⁷ We previously reported three women with plaque-type psoriasis in whom an increase in severity and extent of the skin lesions correlated with development of a prolactinoma.⁸ In all three patients, administration of bromocriptine, a dopamine agonist that suppresses the secretion of prolactin (PRL), improved the therapeutic response of psoriasis. Giasuddin *et al.*⁹ evaluated serum PRL levels in 12 patients with psoriasis vulgaris (PV), and found that they were significantly higher than those of 9 patients with atopic dermatitis and 20 control subjects. In all their patients,

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hyperprolactinaemia was < 100 ng/mL; this is below the level that occurs in cases of pituitary microadenoma (100–250 ng/mL) and pituitary macroadenoma (> 250 ng/mL). In recent years, it has become apparent that PRL plays an important role in the immune reactions¹⁰ and exerts a proliferative effect on human keratinocytes by binding specific sites.¹¹

There are some clinical measures of disease severity and outcome in psoriasis. The most widely used is the Psoriasis Area and Severity Index (PASI),¹² but there is high interobserver variability. To achieve a more objective assessment of psoriasis activity, especially in clinical trials, some authors have measured a number of molecules in the sera of patients with psoriasis before and after treatment. We found in a previous study that serum neopterin level is a good objective marker of psoriatic disease activity,¹³ and that there was a good correlation between pretreatment serum neopterin levels and PASI, thus indicating that this determination may be useful for the evaluation of a therapeutic response.

In the present study, we measured serum PRL levels in patients with plaque-type psoriasis and studied the correlation between clinical disease activity and PRL.

Methods

The study was approved by the hospital ethics committee, and all participants gave informed consent.

Participants

In total, 20 patients with plaque-type psoriasis (10 women, 10 men; median age 54.7 years, range 18–88) were enrolled in the study. At the time of enrolment, none of the patients had received either local or systemic treatment for their psoriasis for at least 2 and 6 weeks, respectively. The control group comprised 20 healthy volunteers matched for age and gender (10 women, 10 men; median age 52.3 years, range 18–89). No significant demographic differences were found between groups.

Exclusion criteria were pregnancy, breast-feeding, and evidence of renal, hepatic, endocrinopathic or psychiatric disease. A complete blood analysis was performed in all potential subjects to exclude these diseases. No concomitant medication or anovulatory drugs were permitted during the study. Patients with an alcoholic intake of > 20 g per day were also excluded. The aim of such exclusions was to avoid instances of secondary hyperprolactinaemia.

Prolactin measurements

Serum PRL levels were measured before and after treatment with tacalcitol ointment 4 μ /g once a day for 6 weeks. Disease severity of psoriasis was assessed in all the patients by PASI,¹² always by the same dermatologist (MSR). Blood samples were taken in the morning between 08.00 and 10.00 hours, in both patients and controls. All the women's measurements were taken in the premenstrual phase of the cycle. The serum levels of PRL were quantitatively estimated using enzyme immunoassay (EIA).

Statistical analysis

All statistical analyses were conducted using SPSS for Windows software (SPSS Inc., Chicago, IL, USA). A stepwise multiple regression analysis was used, $P < 0.05$ was considered significant. Results are expressed as mean \pm SD.

Results

Serum PRL levels were significantly increased in the psoriasis group (21.4 ± 16.7 ng/mL) compared with the control group (8.4 ± 5.2 ng/mL) ($P < 0.001$).

In the psoriatic group, significant clinical improvement was experienced by all the patients after tacalcitol treatment, with PASI reducing from 10.7 ± 7.0 (range 2.8–32) before treatment to 3.8 ± 2.0 (range 1.8–11) after treatment ($P < 0.01$). Serum PRL levels also reduced, from 21.4 ± 16.7 before treatment to 3.6 ± 33.7 after treatment ($P = 0.001$). A good correlation was seen between PASI and PRL before and after treatment ($r = 0.33$, $P = 0.02$). We did not observe any correlation between gender and PRL serum levels.

None of our patients had hyperprolactinaemia (PRL level was always < 100 ng/mL), and none had clinical symptoms such as amenorrhoea/galactorrhoea, hirsutism, visual alterations, impotence or decreased libido. Furthermore, no serological abnormalities were found.

Discussion

PRL is a polypeptidic neuropeptide produced by lactotroph cells in the anterior pituitary gland, and is well known for its lactogenic and mammatrophic effects. In recent years it has become apparent that PRL may influence both humoral and cell-mediated immune reactions, and may play an important part in the expression of autoimmune diseases.¹⁴ PRL exerts its actions in several target organs via specific receptors

that are expressed on many cells, including on T and B lymphocytes.^{15,16} Girolomoni *et al.*¹¹ found that PRL exerts a proliferative effect on cultured human keratinocytes and, through radioligand studies, confirmed the expression of specific PRL-binding sites on keratinocyte membranes. Kanda *et al.*¹⁷ reported that PRL acts on human keratinocytes and enhances the production of chemokine (C-X-C motif) ligand (CXCL)9, CXCL10 and CXCL11, which preferentially attract Th1 cell infiltration into psoriatic lesions.

Some studies have indicated an association between PRL levels and activity of human autoimmune disorders such as systemic lupus erythematosus and rheumatoid arthritis.^{18,19} Buskila *et al.*²⁰ described a woman with psoriatic arthritis who, after treatment with bromocriptine (a dopamine agonist that suppresses the secretion of PRL), for primary infertility, had a marked improvement in her skin and joint disease. There are few reports about serum levels of PRL in psoriasis. Hedman *et al.*²¹ measured the levels of PRL and other hormones in blood and synovial fluid in patients with arthritis of the knee associated with psoriasis (seven cases), and reported that there were no significant differences between patient and control groups. More recently, Giasuddin *et al.*⁹ measured serum PRL levels in 12 patients with PV, and found that they were significantly higher than those of 9 patients with atopic dermatitis and 20 controls, but in no case was serum PRL > 100 ng/mL. We previously reported three women with plaque-type psoriasis in association with prolactinoma (PRL-secreting pituitary gland microadenoma). Interestingly, in all three patients, the severity of the skin lesions correlated with PRL serum levels, and administration of bromocriptine improved their psoriasis. Based on these studies, we are in accordance with Giasuddin *et al.*⁹, who suggested that PRL plays a role in the pathogenesis of psoriasis.

In our present study, we found that serum PRL levels were significantly higher in patients with psoriasis than in healthy controls. We also found a correlation between serum PRL levels and PASI, indicating that PRL may be a useful biological marker of psoriasis activity.

The role of PRL in psoriasis has not yet been elucidated. It could act directly, given its proliferative effect on human keratinocytes through specific PRL-binding sites.¹¹ Studies on the action of ciclosporin A have shown it inhibits PRL binding to the PRL receptors on human B and T lymphocytes.¹⁶ Furthermore, bromocriptine, a dopamine agonist that suppresses the secretion of PRL, has been used in the treatment of plaque-type psoriasis and psoriatic arthritis with very good response.^{20,22,23} Emotional disturbances are one of

the most important causes of hyperprolactinaemia,²⁴ and stress is significantly associated with exacerbations of psoriasis,⁶ thus secondary hyperprolactinaemia due to stress cannot be excluded. Nevertheless, we believe that the findings described above indicate that PRL may play a role in the pathogenesis of psoriasis. We found a significant increase in serum PRL in patients with psoriasis compared with healthy controls. In all of our patients, hyperprolactinaemia was mild, asymptomatic and transitory; after treatment cessation, serum levels returned to normal.

In conclusion, we suggest that PRL may serve as a useful biological marker of psoriatic activity. Further studies should be performed to confirm our results and to clarify the pathogenic role of PRL in psoriasis.

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