Evaluation of B-endorphin concentration in Atopic Dermatitis and Psoriatic patients

By

Khaled M.Monib, *Hamdy F. Marzouk,
Nancey Wadea, Amal A. Amin

From

*From the departments of Dermatology, Benha Faculty of Medicine,
Zagazeg University. *Department of Clinical Pathology,
Mansoura Faculty of Medicine.*

ABSTRACT

This study included 20 atopic dermatitis patients (AD) (11 males and 9 females) 10 mild and 10 severe cases as well as 20 Psoriatic patients (10 males and 10 females) 10 mild and 10 severe cases, this besides 20 healthy control subjects of matched age and sex. None of these patients had received any systemic medications for at least 3 months prior to the study. Only emollients were applied as topical treatment during a 2-week wash-out period.

B-Endorphin concentration was done on separated plasma samples from patients and controls using RIA principle. While the hormonal assay (cortisol, PRL, T4, TSH, PTH) were performed on sera of patients and controls using automated chemiluminiscent enzyme immunoassay princi-

ple.

B-Endorphin concentration was increased in AD and psoriatic patients when compared to controls. The level of B-endorphin correlates with the disease severity. B-endorphin concentration was significantly increased in psoriatic patients vs AD patients. Stress had nonsignificant effect on B-endorphin concentration in AD and psoriatic patients. While the level of cortisol and PRL were significantly increased in stressed AD and psoriatic patients vs controls as well as non-stressed patients. The level of T4, TSH and PTH showed nonsignificant change by stress. Cortisol level was found to be higher in psoriatic patients vs AD patients and controls.

It is concluded that the relationship between B-endorphin concentration and some clinical parameters of

the diseases in concordance with the elevated neuropeptide level in AD and psoriasis suggests that skin inflammation may be a factor responsible for B-endorphin production. Possibly by activation of neuropeptide generation by peripheral blood lymphocytes, tissue histiocytes as well as infiltrating lymphocytes rather than central mechanism of production.

INTRODUCTION

Atopic dermatitis is a common chronic fluctuating disease that may occur at any age (Champion and Parish, 1992). While, psoriasis is a common chronic hyperproliferative disorder of the skin that results from hyperproliferation of keratinocytes. Locally infiltrating T-lymphocytes have a crucial role (Barna et al., 1997; Harrocks et al., 1997). The exacerbation of psoriasis after stress might be related to the release of neuropeptides (Fisher et al., 1984). AD and Psoriasis have different effects on pituitary chemistry profile, cortisol, ACTH, epinephrine and B-endorphin (Rupperecht et al., 1997). B-endorphin is a 31-residue amino acid peptide, which belongs to the endogenous opiate family (Wallengren et al., 1987). It is one of the most important medications of stress (Olsen et al.,

1986) and is known to be generated by stimulating of the pituitary-adrenal axis (Morley, 1981; Fisher et al., 1984). Farber et al, (1986) suggested that this neuropeptide is of pathogenic importance in atopic dermatitis and in psoriasis. It serves as a neuromodulatory factor underlying exacerbation of psoriasis and/or persistence of psoriatic lesions.

Glinski et al, (1994) found increased serum B-endorphin concentration in Psoriasis and other inflammatory skin dermatosis. However the work of Glinski et al, (1995) found a relationship between increased B-endorphin level and disease severity, degree of skin affection and presence of other symptoms of atopy. A possible explanation of increased B-endorphin is either its generation by inflammatory cells of lesional skin or activation of pituitary-adrenal axis by psychoneural factors in the mechanism of chronic stress (Glinski et al., 1995). Thus the site of release of increased B-endorphin is still a matter of debate.

This study was planned to determine the concentration of B-endorphin in patients with AD and in patients with Psoriasis with different

disease severity. In order to clarify the site of B-endorphin release (whether local or central) a plane for estimating some stress hormones (cortisol and PRL) and nonstress hormones (T4, TSH, and PTH) were done in the main time with B-endorphin estimation; both before and after physical stress.

SUBJECTS AND METHODS

Subjects

This study included 20 atopic dermatitis patients (11 males and 9 females) with their ages ranging from 2-36 years, and the mean age was 20.4 ± 10.9 years. 10 mild and 10 severe cases were selected. The severity was determined according to the Rajka grading of AD (Rajka, 1990). The study also included 20 psoriatic patients (10 males and 10 females) with their age ranging from 10-56 years and the mean age was 38 ± 9.5 years. 10 mild and 10 severe cases were selected. The severity was determined according to PASI score (Ramsay and Lawrence, 1991).

Non of the patients had received any systemic medications for at least 3 months prior to the study. Only emollients were applied as topical treatment during a 2-week washout period. Thorough history and clinical

examination were performed to all the patients to exclude any systemic diseases. This besides 20 healthy control subjects of matched age and sex. The controls were clinically free, with no dermatological or systemic diseases. An informed consent was taken from each subject included in this study.

Blood sample was taken from each subject (12 ml each) and divided as follows: 4 ml was put in an EDTA tube, immediately centrifuged and the separated plasma was kept at -20°C until analysis of B-endorphin. 8 ml was left for 1/2 hour. The serum was separated and divided into 2 aliquots; the first one was used for routine investigations (glucose, liver function, and renal function) to exclude any systemic disease. The second aliquot was kept at -20°C until analysis of the planned hormonal profile (T4, TSH, PRL, cortisol and PTH). All patients included in this study were subjected to physical stress (exhausting exercise). Blood samples were taken after stress and treated as above to be used for estimation of B-endorphin and the planned hormonal profile.

Methods

The concentration of plasma B-

endorphin was measured by 125 -RIA using the INCSTAR kit, Stillwater, Minnesota, USA. The RIA method is based on an antibody with high sensitivity to B-endorphin (Wiedemann et al., 1979). Plasma samples and first antibody are incubated for 16-24 hours at 2-8 °C. A tracer was added and incubated at 2-8 °C for another 16-24 hours. Plasma separation was done in 2 hours at 2-8 °C with a pre-precipitated complex of second antibody, carrier and PEG (polyethylene glycol) added in a single step. This assay requires extracted plasma samples.

The hormonal assay (cortisol, T_4 , TSH, PRL and PTH) were done using a commercially available kits from Diagnostic Product Corporation (DPC), Los Angeles. They have the principle of chemiluminescent enzyme immunoassay using automated Immulite system (Babson, 1991).

Statistics

Data are mean $\pm$ SD. Statistical comparisons between means were done using student's t test and analysis of variance. Regression analysis was done using computer program SPSS PC version 7.0 for windows. Correlation between variables was calculated using the Pearson correla-

tion test. $P < 0.05$ was considered significant.

RESULTS

There is a significant increase in B-endorphin in psoriasis and AD patients vs controls. There is also a significant increase in B-endorphin in psoriasis vs AD patients (table 1).

In table 2 there is a significant increase in B-endorphin concentration in AD and in psoriasis patients vs controls. The concentration of B-endorphin in severe cases is significantly increased when compared to mild cases of AD as well as psoriasis. There is a significant increase in cortisol and PRL levels in AD and psoriatic patients vs controls. While, the severe cases show significant increase in PRL and cortisol when compared to mild cases of AD and psoriasis. T_4 concentration is increased in severe cases of psoriasis vs mild cases as well as controls. TSH and PTH levels show nonsignificant changes from the control group as well as between mild and severe cases of AD and psoriasis.

Table 3 shows that in patients with more than 10% skin affection the concentration of B-endorphin is signif-

icantly higher than the patients with less than 10% skin affection in AD as well as psoriatic patients. AD patients with severe pruritus show a significant increase in B-endorphin concentration when compared to cases of mild pruritus. While, asthma or family history of atopy has nonsignificant effect on B-endorphin concentration when compared with patients of no asthma or family history of atopy, respectively.

Stress resulted in a significant increase in cortisol and PRL concentration when compared to nonstressed AD as well as psoriatic patients. However, the concentration of B-endorphin, T4, TSH and PTH show

nonsignificant change between stressed and nonstressed atopic and psoriatic patients (table 4).

Fig. 1 and 2 show a significant positive linear regression of B-endorphin concentration on age onset of disease in patients with psoriasis and on disease severity in AD patients (14).

Fig. 3 shows a significant multiple linear regression of B-endorphin on cortisol, sex and duration of the disease in all patients. The relation is positive with sex and cortisol and is negative with the duration of the disease.

Table (1) : B-endorphin concentration in patients with psoriasis and in patients with AD vs control. In between brackets is the number of cases.

Group	B-endorphin (pg/ml)	p
Psoriasis (20)	14.2±5.9 ^{a,b}	< 0.01
AD (20)	9.3±2.2 ^c	< 0.05
Control (20)	6.9±2.3	< 0.05

^a psoriasis vs control

^b psoriasis vs AD

^c AD vs control

Table (2) : Concentration of B-endorphin, Cortisol, PRL, T₄, TSH and PTH in patients with AD and in patients with psoriasis vs control. In between brackets is the number of cases.

	AD		Psoriasis		Control
	Mild (10)	Severe (10)	Mild (10)	Severe (10)	
B-endorphin (pg/ml)	8.1±1.1 ^a	10.5±0.5 ^{a,b}	11.5±2 ^a	16.8±3 ^{a,b}	6.9±0.7
Cortisol ug/dl)	8.7±0.4	10.8±0.9 ^b	12.5±0.5	22.5±0.4 ^{a,b}	10.1±0.8
PRL (ng/ml)	9.5±0.5 ^a	11.5±0.5 ^{a,b}	7.3±0.4	10±0.4 ^{a,b}	6.8±0.3
T ₄ (ug/dl)	8.7±1	8.7±2	10±1.3	13.5±0.8 ^{a,b}	11.8±1.9
TSH (uIU/ml)	0.9±0.1	1.1±0.3	0.7±0.1	0.8±0.1	0.8±0.1
PTH (pg/ml)	10±0.3	11±0.8	9.8±0.7	9.7±0.3	9.5±0.5

^a mild and severe cases vs control

^b mild vs severe case

^{a,b} p<0.05

Table (3) : The relation between B-endorphin concentration and clinical aspects of patients with AD and patients with psoriasis .

Clinical aspects	B-endorphin concentration (pg/ml)	
	AD	Psoriasis
% skin affection < 10% > 10%	8.1±1.1 (10) 10.8±0.3 ^a (10)	11.3±2.3 (5) 14.7±1.3 ^a (15)
Pruritus mild severe	8.1±1.1 (10) 10.5±0.5 ^a (10)	14.1±2.3 (15) 14.6±1.5 (5)
Asthma No Yes	9.2±0.3 (13) 9.4±0.3 (7)	
Family history of atopy No Yes	10.2±1.3 (5) 9.1±1.2 (15)	

^a > 10% skin affection vs < 10% skin affection.^b severe pruritus vs mild pruritus.

In between brackets is the number of cases.

Table (4) : Concentration of B-endorphin Cortisol, T₄, TSH ,PRL and PTH in patients with AD and in patients with psoriasis subjected to stress vs nonstressed patients.

Group	B-end (pg/ml)	Cortisol (ug/dl)	T ₄ (ug/dl)	TSH (uIU/ml)	PRL (ng/ml)	PTH (pg/ml)
Psoriasis						
No stress (10)	12.2±1.3	12.2±1.3	17.3±1.2	0.9±0.1	9.5±0.3	10±0.4
stress	15±2.7	25±1.5 ^a	19.1±2	0.8±0.2	11.5±0.4 ^b	10.5±0.7
AD						
No stress (10)	9.9±1	10.2±0.9	9±1.7	0.9±0.2	8.1±0.6	9.7±0.5
stress	8.3±1.2	18.9±1.4 ^a	8.2±0.8	0.9±0.2	10±0.7 ^b	10±0.3

^a p < 0.01

a and b stressed vs nonstressed patients .

^b p < 0.05

In between brackets is the number of cases .

Figure (1) : Regression of B-Endorphin concentration on age of disease onset in patients with psoriasis.

Figure (2) : Regression of B-Endorphin concentration on disease severity in patients with atopic dermatitis.

N.B. For sex : 200 was assigned for a Female and 300 was assigned for a Male.

Figure (3) : Regression of B-Endorphin concentration on cortisol concentration, sex and disease duration in all patients .

DISCUSSION

B-endorphin is known to be generated by stimulation of the pituitary-adrenal axis after stress (Glinski et al., 1995). The presence of high level of B-endorphin in AD and psoriasis lesions might affect peripheral sensory nerve function and cause antinociceptive effect (Harrison, 1990; Glinski et al., 1994). In psoriasis patients POMC were consistently detected in the keratinocytes and mononuclear cells at psoriatic lesional skin. Keratinocytes could express messenger RNA for POMC in vitro (Teofoli et al., 1993). These observations indi-

cate that POMC products (B-endorphin is one of them) may accumulate locally in lesional skin (Slominski et al., 1993).

Wintzen and Gilchrest (1990) reported that the factors modulating B-endorphin release from the intermediate lobe of the pituitary were different from those regulating anterior lobe release. Endogenous opioid peptides affect pituitary hormone secretion by altering the activity of neurons carrying either biogenic amines or hypothalmo-hypophysiotropic hormones. Also, they may have a direct auto-

crine effect on the pituitary (Pico et al., 1986).

In this study B-endorphin concentration in AD patients was significantly increased ($p < 0.01$) vs controls. The highest concentration was found in patients with severe active lesions (10.5 ± 0.5 pg/ml), those with more body surface area affection (10.8 ± 0.3 pg/ml) and those with severe pruritus (10.5 ± 0.5 pg/ml). Also a positive linear regression of B-endorphin concentration and the disease severity was noticed. Georgala et al., (1994) found a concentration of 14.9 ± 2.9 pg/ml in patients with AD associated with pruritus and 9.4 ± 2.5 pg/ml in patients with AD not associated with pruritus. They suggested that the B-endorphin elevation in AD patients with pruritus confirm the hypothesis of increased activity of their opioid system, and that opioid antagonist might block itching which is their major clinical symptom. Opiate-induced hormonal release appear to be mediated through dopaminergic and/or serotonergic mechanisms (Morley, 1981). However Gliniski et al., (1995) found no relationship between B-endorphin concentration and the grade of pruritus or familial occurrence of atopy. But, a statistically significant elevation

of B-endorphin was found in patients with other symptoms of atopy as bronchial asthma (11.6 ± 3.1 pg/ml), patients with more than 20% skin affection (11.1 ± 3.6 pg/ml) and high disease severity score (18.7 ± 3.7 pg/ml) vs controls (6.1 ± 1.5 pg/ml).

In this study patients with psoriasis with more than 10% lesional affections have values (14.7 ± 1.3 pg/ml) significantly higher than those do with less than 10% lesional affection (11.3 ± 2.3 pg/ml). While nonpruritus cases have values (14.1 ± 2.3 pg/ml) nonsignificant from pruritus cases (14.6 ± 1.5 pg/ml). On the other hand the concentration of B-endorphin in severe psoriasis (16.8 ± 3 pg/ml) was significantly higher than mild cases (11.5 ± 2 pg/ml). Stress has nonsignificant effect on B-endorphin concentrations in psoriatic patients. Gliniski et al., (1994) found a statistically significant elevation of B-endorphin in patients with extensive lesions of psoriasis, a positive correlation between B-endorphin and the area of skin involved as well as PASI score. While pruritus was associated with lower levels of B-endorphin. In this study a positive linear regression of B-endorphin concentration and the age onset of the disease was present. In

psoriasis either the level of B-endorphin in the peripheral blood is below the threshold concentration for a systemic pruritic effect of opiates to occur or the peripheral antinociceptive effect of B-endorphin on the skin sensory nerve fibre receptors predominate. Both prospective and retrospective studies investigating the relation between stress and worsening of psoriasis have documented that psychological stress is important in the onset and exacerbation of psoriasis in about 40-50% of cases (Rache, 1995). In this study a nonsignificant effect of stress on B-endorphin concentration in psoriatic patients was noted.

B-endorphin was found to be increased in patients with psoriasis (14.4 pg/ml) and AD (9.2 pg/ml) vs controls (6.1 pg/ml). The highest values of B-endorphin were found in patients with actively spreading plaque of psoriasis (17.3 pg/ml), whereas lesion-free patients showed a reduction in the neuropeptide concentration (10.2 pg/ml). B-endorphin release in AD and psoriasis patients may be due to some stress generating factors, inflammatory cells in the dermal infiltrate, lymphocyte infiltrate within the skin and/or circulating lym-

phocytes. It might be produced in the peripheral tissues since it is released during the inflammatory processes from cells such as lymphocytes, macrophages, monocytes and plasma cells (Glinski et al., 1995). In this study neither the presence of stress nor the presence of itching correlated with the serum peptide concentration. A hormonal study profile was planned using some of the stress hormones (cortisol and PRL) and some of the nonstress hormones (T_4 , TSH, and PTH) in a trial to determine and evaluate the site of B-endorphin release. Serum T_4 , TSH and PTH showed nonsignificant changes between stressed and nonstressed AD as well as psoriatic patients. While, there are a significant increase in cortisol and PRL in stressed AD and psoriatic patients when compared to nonstressed cases. B-endorphins are increased in stressed patients but nonsignificantly from nonstressed ones. Rupprecht et al., (1997) found a significant increase in cortisol in AD patients with stress when compared to controls and nonstressed patients. Skin inflammation may be a factor responsible for B-endorphin production in psoriasis and AD possibly by the activation of neuropeptides generation by peripheral blood lymphocytes. This highlights

that the site of B-endorphin release is rather peripheral.

Further study to measure B-endorphin before and after treatment and to evaluate its role in the disease aetiopathogenesis is recommended.

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