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ORIGINAL ARTICLE

Somatotrophin axis hormones in patients affected with psoriasis

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Abstract

OBJECTIVES: The serum concentrations of somatotrophin axis hormones (growth hormone – GH, insulin-like growth factor-I – IGF-I and insulin-like growth factor binding protein-3 – IGFBP-3) in the patients with psoriasis in its active stage have been evaluated in relation to the control group consisting of healthy people in order to see whether these hormones may play a role in the psoriasis aetiopathogenesis.
MATERIAL AND METHODS: The subjects included 85 psoriatic patients (mean age 36,9 ± 11,2 years) in the active state of disease and 20 healthy persons (mean age 35,6 ± 6,6 years) as a control group. GH and IGFBP-3 concentrations in serum were determined by immunoradiometric assay (IRMA), IGF-I concentrations – by radioimmunological assay (RIA). Evaluation of the dermatological state also included a determination of psoriasis area and severity index (PASI).
RESULTS: In the patients with psoriasis the concentration of the growth hormone was found to be significantly higher than in the healthy people at the simultaneously much lower concentrations of the insulin-like growth factor-I and its binding protein-3. IGF-I concentrations correlated negatively to PASI value.
CONCLUSION: In the psoriatic patients the somatotrophin axis activity is disturbed and these disturbances may effect the psoriasis process modulation. However, it is impossible to determine if the disturbances are of the primary, i.e. aetiological, importance for the disease pathogenesis, or only of the secondary – psoroid character.

Abbreviations and units:

GH	– growth homone
GHR	– growth hormone receptor
IGF-I	– insulin-like growth factor-I
IGFBP-3	– insulin-like growth factor binding protein-3
PASI	– psoriasis area and severity index
μU/ml	– microunit/milliliter
nmol/l	– nanomol/liter

Introduction

Psoriasis is one of the most common skin diseases. Aetiopathogenesis of this dermatosis is complex and not yet well known. Thus, treatment may be difficult, although many methods of treatment have been developed. Lately, besides many different pathogenic factors, the hormone factors have been regarded to be important for the psoriasis aetiology. Particularly somatotrophin axis hormones should be carefully considered. Numerous observations show that skin cells may be affected by these hormones, both in physiological and pathological state. Present information on their possible participation in psoriasis origin seems to be very interesting, yet often contradictory, and first of all, very scarce. If their crucial role in psoriasis aetiology could be confirmed, some quite new therapeutic possibilities could appear soon.

The main aim of the work was to evaluate the concentrations of growth hormone (GH), insulin-like growth factor-I (IGF-I) and insulin-like growth factor binding protein-3 (IGFBP-3) in the serum of the patients with psoriasis during active stage of the disease.

Material and methods

85 patients admitted to hospital because of intensified psoriatic lesions were studied. The subjects included 35 women at the age from 18 to 50 and 50 men at the age from 18 to 55 (mean age in psoriatic patients group was 36,9 ± 11,2 years). A control group consisted of 20 healthy persons (10 women and 10 men; mean age in control group was 35,6 ± 6,6 years) in whose family history no psoriasis had been reported. The studies excluded the psoriatic patients with some other diseases (e.g. with neoplastic diseases, diseases of nervous system, cardiovascular system, kidney and liver, diabetes and other endocrinological disorders, autoimmunological and allergic diseases etc.). Evaluation of the dermatological state also included a determination of the psoriasis area and severity index – PASI [1].

Following an overnight fast, blood samples were collected at 8 a.m., in the active state of the disease, and before the beginning of the treatment. Blood samples from the control group were taken under the same conditions. After centrifugation of blood, the serum received was stored at –70°C until the determinations could be performed.

Research protocol was accepted by the Local Bioethical Committee of the Silesian Medical University. Every patient was informed about the aim of the studies and agreed in writing to participate in the studies.

Concentrations of growth hormone and insulin-like growth factor binding protein-3 (IGFBP-3) were determined by immunoradiometric assay (IRMA).

To determine the growth hormone concentration the HGH-IRMA kits (POLATOM, Otwock – Świerk, Poland) of 0.1 μIU/ml sensitivity were used. The intra-assay precision and inter-assay precision was 2.1 – 3.4% and 1.1 – 5.1%, respectively. The DSL-6600 ACTIVETM IGFBP-3 IRMA kits (Diagnostic Systems Laboratories Inc., Webster, Texas, USA) of 0.0175 nmol/l sensitivity were used to determine IGFBP-3 concentration. The intra-assay precision and inter-assay precision was 1.8–3.9% and 0.5–1.9%, respectively.

The concentration of insulin-like growth factor-I (IGF-I) was determined by radioimmunological assay (RIA) with the use of the SM-C-RIA-CT kits (BioSource Europe S.A., Nivelles, Belgium) of sensitivity equal to 0.03 nmol/l. The intra-assay precision and inter-assay precision was 4.1–6.1% and 9.3–9.9%, respectively.

The results of hormone determinations were presented with the use of basic parameters of descriptive statistics, such as: mean value, standard deviation, median, minimum and maximum values.

Compatibility of variable distribution with normal distribution was checked with a chi-square test. For group comparisons the Student's t-test and nonparametric tests by Kolmogorov-Smirnov, Wald-Wolfowitz and U-Mann – Whitney were used. Pearson's linear correlation coefficients were calculated to determine the relationship between the parameters. A significance level $p<0.05$ was accepted as statistically significant. A computer program STATISTICA was used for computations.

Results

Most of the patients under study were men (58.8%). The age of psoriatic patients and control group patients was comparable ($p=0.6$).

After hormone determination and obtaining the results the concentrations of the parameters in the active stage of the disease were compared to the concentrations in the control group. The comparison results are presented in Table I. Individual concentrations of growth hormone in psoriatic patients in the active stage of the disease compared to the control group are presented in Fig. 1.

Correlation between the parameter concentrations in the active stage of the disease and psoriasis area and severity index (PASI) was evaluated, and a statistically significant negative correlation between IGF-I concentration in the active stage of the disease and PASI values was found (Fig.2).

Discussion

In 1981 Weber et al. [2] were the first to suggest that growth hormone might play an important role in psoriasis pathogenesis. They not only pointed at the elevated concentrations of the growth hormone in serum correlated with the disease process activity, but also showed the therapeutic effectiveness (in relation to skin and joints) of GH secretion central blocking and GH overproduction source as well [3, 4, 5, 6, 7]. They ended the interpretation of the results with a hypothesis that intensified secretion of the growth hormone after puberty time is an aetiological factor in psoriasis pathogenesis [3, 4, 7]. Somatostatin – an effective growth hormone inhibitor was used in psoriasis therapy also by other authors, who achieved a significant change for

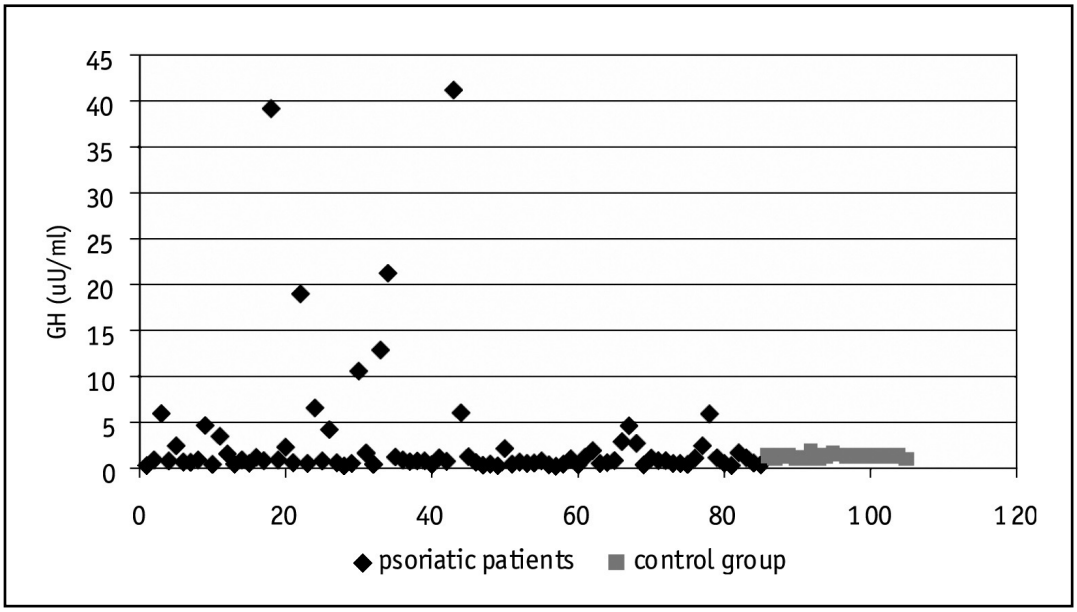

Figure 1. Individual values of growth hormone (GH) concentration in psoriatic patients at the active stage of disease in comparison to control groupmunization. Results are expressed as the mean ±SD from three separate experiments (8 rats /group per experiment); p<0.01 vs control.

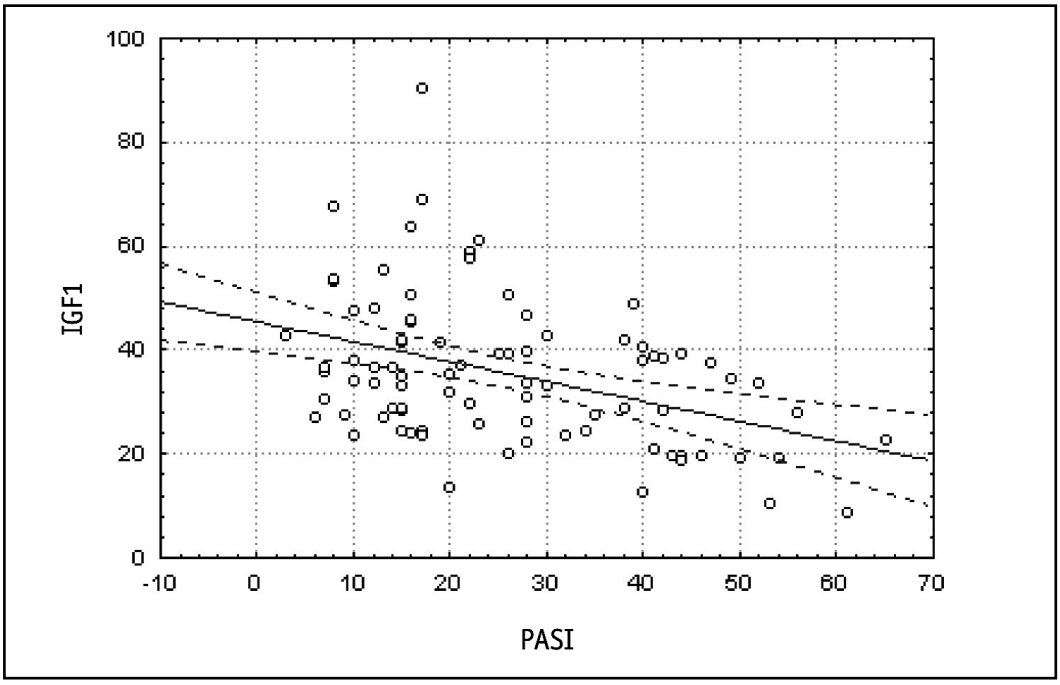

Figure 2. Relationship between insulin-like growth factor-I (IGF-I) concentration and psoriasis area and severity index (PASI) ($p < 0.05$; $r = -0.40$)

Table 1. Growth hormone (GH), insulin-like growth factor-I (IGF-I) and insulin-like growth factor binding protein-3 (IGFBP-3) concentrations in psoriatic patients at the active stage of disease in comparison to control group.

	Control group					Psoriatic patients				
	mean	**SD**	**median**	**minmum**	**maximum**	**mean**	**SD**	**median**	**minimum**	**maximum**
GH (µU/ml)	1.21	0.20	1.23	0.88	1.71	2.93+	6.81	0.83	0.24	41.17
IGF-I (nmol/l)	52.34	11.43	52.44	33.49	73.49	35.48+	14.18	34.11	8.78	90.25
IGFBP-3 (nmol/l)	159.90	39.90	165.95	95.48	239.82	123.91+	56.22	118.23	39.37	456.93

+ $p < 0.05$ in group of psoriatic patients in comparison to control group of healthy persons

better in 30–80% of the patients [5, 6, 8, 9, 10, 11]. Not all of them agree that the growth hormone concentration in psoriatic patients' serum is elevated [12, 13], and its excretion with urine is intensified [14]. In our psoriatic patients a mean concentration of GH in blood serum in the active stage of the disease was higher than in the control group (Table I), yet it did not correlate with the activity of the disease process. Particular attention should be paid to the high value of the standard deviation in the group of psoriatic patients compared to the control group, which may be related to significant variations in GH secretion in psoriatic patients (Table I, Fig.1).

Skin ability to react directly to growth hormone requires the expression of its functional receptors (GHR). They can be found both on epidermis cells, and on dermis fibroblasts [10, 14, 15]. If we only consider the differences between the mean values of GH concentrations in psoriatic patients and healthy people, the hypothesis by Weber et al. [2] seems to be true. Although the course of the somatotrophin hypophysial adenomas may differ, even according to sex [16], and is often clinically mute, yet, no tendency to psoriasis and acromegaly coexistence [12] and no correlation (observed by us) between GH concentrations and PASI values make it rather impossible that GH overproduction could be the only cause for this dermatosis. Intensified secretion of growth hormone in psoriatic patients may also suggest that higher concentration of GH is a secondary phenomenon following the psoriasis process. A similar conclusion was drawn by Priestley et al. [13], who found among their patients a group with a high concentration of GH in serum. A local production of GH in psoriasis lesions by immunocompetent cells of inflammatory infiltration may be a possible explanation for that [17] . Secondary intensified GH secretion in psoriasis may also be related to the fact that the dermatosis can be accompanied by wrong regulation of the secretion and/or GH metabolism.

The problem to be explained is whether a possible participation of growth hormone is of a direct character, or a whole axis is engaged: growth hormone – insulin-like growth factor-I (IGF-I) and its binding proteins. In psoriatic hyperplastic epidermis the number of receptors for IGF-I is increased in accordance to a larger area of proliferating epidermis [18, 19], and their density on psoriatic keratinocytes is over twice as high as on healthy ones [20]; moreover, they move from psoriatic lesions towards prickle keratinocyte layer [18, 19].

There are scarce literature data on the evaluation of IGF-I concentrations in serum in psoriatic patients. Björntorp et al. [14] and Nickoloff et al. [21] did not find a significant difference in relation to the control group. The results of our determinations are contrary (Table I). Psoriatic patients in the active stage of the disease had significantly lower concentrations of insulin-like growth factor-I than healthy persons. It is interesting that at the same time the growth hormone concentrations were higher in the patients than in the control group, when IGF-I concentration is in great part a derivative of GH concentration. After the analysis of the data it can be concluded that in psoriasis a greater 'consumption' of the growth factor takes place. Such a hypothesis is in agreement with the previous statement about the great increase in receptor number for IGF-I in hyperplastic psoriatic epidermis [18, 19, 20], and a significant negative correlation between its concentration in serum and PASI values in the patients is another evidence for that (Fig.2). IGF-I is a factor which stimulates riversibly a somatostatin production in hypothalamus. Thus, it seems likely that a primary psoroid lowering of IGF-I in circulation makes the somatostatin concentration very low [17], and hypophysis somatotrophin cells producing a growth hormone have no a negative regulation. In this sense the increased release of GH in psoriatic patients would follow the greater 'consumption' of IGF-I in psoriasis lesion.

Very few scientists have been interested so far in the evaluation of IGFBP-3 concentration in psoriatic patients' serum. The Swedish authors [14] mentioned above did not find significant differences between psoriatic patients and control group. However, in our patients we could observe that a mean concentration of binding protein was significantly lower than in healthy people (Table I), although it did not correlate with the disease activity.

A change in IGFBP-3 concentration regulation might explain why psoriatic keratinocytes react so much to IGF-I, or it might be responsible for excessive expression of the receptor for IGF-I in psoriatic epidermis [19]. Such a possible solution cannot be excluded as IGFBP-3 in the active stage of the disease was found lower in the psoriatic patients. But the concentrations of GH – the main stimulator of IGFBP production – tended to be high, while deficiency of the binding protein in the patients under study was parallel to the lowered concentrations of IGF-I. Thus, it seems likely that a greater expression of IGF-I receptors results in the shift of IGF-IGFBP as a whole from the circulation to the diseased skin. Such an assumption is in agreement with the elevated contents of IGFBP-3 found in the diseased skin extracts compared to the healthy skin or the skin without any visible changes [23]. It has been also suggested that IGFBP-3 effects negatively the increase and proliferation of keratinocyte and fibroblast cells quite independently of the system IGF-I - its receptors, possibly via its own receptors [24, 25]. And last of all, lowered concentrations of both IGF-I and IGFBP-3, in spite of high concentrations of GH in psoriatic patients' serum, might suggest that this dermatosis is accompanied by a subclinical damage of hepatic cells, which results in the disorders in the hormone inactivation and the synthesis of growth factors and binding proteins [26].

The problems presented in the work are of introductory character and still require a lot of scientific research to be carried out. As it seems likely that the disturbed regulation of GH – IGF-I – IGFBP-3 axis contributes to psoriasis aetiopathogenesis, there is more and more evidence for pharmacological interference in this axis functioning [27]. Perhaps such an interference will soon be crucial not only in psoriasis treatment, but other hyperproliferating dermatoses as well.

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