

Itching sensation in psoriatic patients and its relation to body mass index and IL-17 and IL-31 concentrations

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Postep Derm Alergol 2015; XXXII (6): 426–430

DOI: 10.5114/pdia.2015.56097

Abstract

Introduction: According to available data, pruritus is a common symptom of psoriasis, however its characteristics and pathogenesis are not clearly understood.

Aim: The main aim of this study was to assess itching sensation among patients suffering from psoriasis, including its incidence and severity. All factors triggering and worsening pruritic symptoms were also carefully analyzed. The authors assessed the relationship of itch with body mass index (BMI) and severity of disease. Moreover, serum levels of interleukin 17 (IL-17) and IL-31 were analyzed in relation to Psoriasis Activity and Severity Index, BMI and severity of pruritus.

Material and methods: The study group consisted of 60 patients with plaque-type psoriasis. Analysis of impact of pruritus on the quality of life and worsening factors was based on the questionnaire. The severity of pruritus was assessed with the use of two independent scales. Serum IL-17 and IL-31 levels were measured in 30 patients suffering from psoriasis and in 10 healthy controls using immunoassay tests.

Results: 88.3% of analyzed patients complained of itch and the most common factor which exacerbated pruritus was stress (39.6%). Pruritus in psoriasis was independent of gender, illness duration and extent of skin lesions. The average intensity of pruritus was assessed as moderate and did not correlate significantly with BMI level, IL-17 and IL-31.

Conclusions: Since the pathogenesis of pruritus in psoriasis is not fully understood, further investigation in this area needs to be conducted. Pruritus may be considered as a characteristic feature of psoriasis and, besides the skin lesions, should be a target in dermatological treatment to improve patient's quality of life.

Key words: psoriasis, pruritus, itch, body mass index, Psoriasis Activity and Severity Index, interleukin 17, interleukin 31.

Introduction

Definition of itch (from Latin “pruritus”) was proposed in the seventeenth century by the German physician Samuel Hafenreffer to name an unpleasant feeling that leads to scratching [1]. This troublesome symptom is associated with numerous diseases, both involving the skin and other organs. Pruritus is the major complaint reported by patients suffering from allergic and inflammatory skin conditions including atopic dermatitis, contact dermatitis and lichen planus. It also occurs in seborrhoeic dermatitis, bullous pemphigoid, parasitic and fungal skin infections. It may accompany different drug eruptions and have psychogenic etiology. A very interesting, but

to date underestimated, problem is an itching sensation that occurs in psoriasis [2].

Psoriasis is a very common skin disorder, which nowadays, according to recent studies, is perceived as a systemic, immune-mediated disease, characterized by inflammatory skin and joint manifestations [3]. A range of co-morbidities were recognized to be associated with psoriasis, including metabolic diseases, such as diabetes, and psychological disorders [4]. While in the past psoriasis was recognized as a non-itchy skin disorder, available literature data show that this symptom may even concern 84% of psoriatics and severely affects their quality of life [5–8]. This phenomenon needs to be emphasized,

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Received: 15.08.2013, **accepted:** 25.01.2014.

because management of itch should be considered as a significant component of psoriatic therapy.

Aim

Therefore, the aim of this study was to attempt to investigate the itch in patients suffering from psoriasis. The prevalence of itch and its severity in relation to the data obtained from the patients' examination were evaluated. A thorough analysis of the factors that trigger and worsen pruritus sensation was also made. In order to investigate the pathogenesis of pruritus serum concentrations of interleukin 17 (IL-17) and 31 were measured, which were additionally correlated with the severity of skin lesions and body mass index (BMI).

Material and methods

Sixty patients suffering from plaque-type psoriasis (15 women and 45 men) hospitalized in the Department of Dermatology at the Poznan University of Medical Sciences in the period from November 2010 to April 2011 were included in the study. The average age in the study group was 44.8 ± 15.2 years (women 39.0 ± 14.9 years, men 46.8 ± 15.0 years). In each patient the diagnosis of psoriasis was established on the basis of detailed dermatological examination. The intensity of itch was evaluated with the use of two independent systems: W-AZS I index and visual analogue scale (VAS). W-AZS I index is the part of the W-AZS scoring system, which was proposed by researchers from the Department of Dermatology in Poznan for determination of subjective and objective signs and symptoms in patients with atopic dermatitis [9]. W-AZS I allows the assessment of extent, frequency and severity of itch as well as sleep disturbances (difficulty in falling asleep, night awakenings or insomnia). These symptoms may range from 0 to 34 points [9]. W-AZS I index of 0–6 points indicates mild pruritic symptoms, 7–17 points – moderate, while > 18 points – severe itch. A VAS also allows for evaluation of severity of pruritus. Patients were asked to assess intensity of itch, on a 10-cm-long line, where 0 cm means no itching, and 10 cm – very severe sensation. In order to accurately interpret the results, they were ranked as follows: 0–3 – mild pruritus, 4–6 – moderate and 7–10 – severe.

In addition, a detailed assessment of subjective complaints was determined with the use of a self-designed questionnaire. Questions included in the survey were associated with pruritus characteristics, including description of sensation of pruritus, impact on the subject's life, effect of pruritus on the mood as well as aggravating factors.

The severity and extent of skin lesions were expressed as a PASI index score (Psoriasis Activity and Severity Index), which values are within the range from 0 to 72 points.

In all patients with psoriasis, BMI was rated by dividing body weight in kilograms by the square of height in meters. For adults, BMI value of 18.5–24.99 kg/m² is within the normal range, < 18.5 kg/m² indicates underweight, while ≥ 25.0 kg/m² – overweight.

Additionally, in 30 patients with psoriasis and in 10 healthy subjects, serum levels of IL-17 and IL-31 were measured using a commercially available enzyme immunoassay (Quantikine, R & D Systems; Platinum Elisa, eBioscience).

Statistical analysis

The results were evaluated statistically. Values of analyzed parameters were presented as percentages, minimum and maximum values as well as arithmetic means and corresponding standard deviation ($x \pm SD$). For statistical calculations, *t*-Student and *U* Mann-Whitney test for independent variables was used. An analysis of the relationship between selected variables was evaluated using Spearman's and Pearson's correlation coefficients. The differences were statistically significant at $p < 0.05$. For the calculation Statistica 9.1 PL was used.

All participants provided written informed consent and the institutional review board approved the study.

Results

The study group consisted of 60 patients diagnosed with chronic plaque-type psoriasis vulgaris. There were 15 women aged from 10 to 57 years (mean age: 39.0 ± 14.9 years) and 45 men aged from 20 to 79 years (mean age: 46.8 ± 15.0 years). In most patients, the disease lasted for many years and its average length was estimated to be 16.7 ± 13.6 years. In women it was 11.8 years, in men 18.3 years.

Thirty-three (88.3%) patients complained of pruritus, while in remaining subjects (11.7%) pruritus did not occur. The average value of the W-AZS I index was 11.7 ± 7.5 points (min. 0, max. 34 points), what indicates moderate itch intensity. Among female patients W-AZS I mean value was 12 ± 8.2 points and among men 11.6 ± 7.7 points. There was no statistically significant difference in the severity of pruritus expressed by W-AZS I index between men and women ($p = 0.64$). Detailed analysis of W-AZS I index revealed that 7.5% of individuals identified itching as mild, 67.9% of patients as moderate, while 24.5% of patients suffered from severe pruritus. The average intensity of pruritus measured using VAS was 4.9 ± 2.9 , expressing moderate severity of itch. Minimum and maximum for this parameter was equal to the limit adopted in the assessment. Similar results were obtained regardless of the patient sex (women 4.9 ± 2.9 and men 4.9 ± 2.8) ($p = 0.65$). 18.8% of patients rated their itching as a mild, 50.9% as moderate and 30.2% as severe. The comparison of the results of the severity of pruritus assessed by two independent scales is presented in Table 1.

Table 1. Intensity of itch in psoriatic patients ($n = 60$)

Variable	W-AZS I [points]	VAS
Women ($n = 15$)	12.0 \pm 8.2	5.0 \pm 2.9
Men ($n = 45$)	11.6 \pm 7.7	4.9 \pm 2.9
Total ($n = 60$)	11.7 \pm 7.5	4.9 \pm 2.9

VAS – Visual Analogue Scale.

In the presented study, 90.6% of psoriatics (48 individuals) listed factors aggravating itch. In 39.6% of cases (21 patients) the intensification of pruritus was associated with stress, in 30.2% (16 patients) with physical activity, in 28.3% (15 patients) with bathing in hot water. 20.8% of cases (11 individuals) indicated high ambient temperature and fatigue as the cause of escalating itch. 15.0% (8 patients) pointed out to dry air, 11.3% (6 patients) low ambient temperature, 9.4% (5 persons) bath in cold water, 5.6% (3 persons) observed worsening of pruritus during sleep.

In the analyzed group of patients, 43.4% (23 patients) described sensation associated with itch as delicate tickling, 24.5% (13 patients) as stinging and tingling, 22.6% (12 patients) had hot and burning feeling. Sixty-two percent (33) of patients named the accompanying pruritus as annoying, 30% (16 patients) as burdensome, 11% (6 patients) as unbearable. Most of patients – 62.3% (33 patients) confirmed that psoriasis and pruritus negatively influence their mood and cause depressed mood. 26.5% (14 patients) stated that pruritus did not affect their mood. Fifty percent (8 patients) of cases stated that itch provoked impaired concentration and in 7% (4 patients) of patients it led to anxiety.

In the study group, the mean severity and extent of skin lesions measured by PASI was 13.9 \pm 10.9 points (min. 0.3 points and max. 51.6 points). There was no statistically significant difference in PASI between men and women ($p = 0.1$). A statistically significant correlation between W-AZS I and numerical scale was demonstrated ($p < 0.01$; correlation coefficient 0.67).

There was no statistically significant correlation between the duration of disease and the severity of itching, both with regard to measuring the intensity of pruritus using a numerical scale ($p = 0.56$) and a W-AZS I index ($p = 0.32$). We also did not observe any statistically significant correlation between the severity of itching, expressed by a numerical scale and W-AZS I, and PASI ($p = 0.23$ and $p = 0.36$, respectively).

The average BMI value in psoriatics was 27.5 \pm 5.9, what is related to overweight. The weight within normal ranges was revealed in 21 (35.0%) patients. Underweight was observed in 4 (6.6%) patients, 25% of patients (15 patients) were overweight and 33.3% (20 patients) obese. In the study group, there was no statistically significant correlation between the severity of pruritus assessed both by W-AZS I index as well as the numeri-

cal scale and BMI ($p = 0.84$ and $p = 0.81$, respectively). Additionally we did not find any statistically significant correlation between BMI and PASI ($p = 0.97$).

The mean level of IL-17 in psoriatics (38.8 \pm 9.01 pg/ml) did not differ statistically significantly from the level determined in the healthy group (28.2 \pm 19.6 pg/ml) ($p = 0.052$). There was no statistically significant difference in the serum concentration of IL-31 between patients with psoriasis and healthy controls (0.69 \pm 2.3 pg/ml and 0.26 \pm 0.82 pg/ml, respectively) ($p = 0.359$). In addition, there was no significant correlation between the concentration of IL-17 and IL-31 in patients with psoriasis ($p = 0.215$) as well as between the concentrations of IL-17 and IL-31 and variables such as BMI, W-AZS I, PASI and numerical scale.

Discussion

Although many leading textbooks of dermatology do not mention pruritus as a major complaint of psoriatic patients, our study indicates that itch is a frequent symptom observed in that dermatosis. The prevalence of pruritus among patients hospitalized in our department was found to be high and reached 88.3%, what is in accordance with other studies. Yosipovitch *et al.* examined 101 patients with extensive psoriasis and noted that general pruritus was a feature in 84% of them [7], whereas Gupta *et al.* observed this symptom in 67% of analyzed cases [10]. In Szepietowski *et al.* survey, 80 of 100 psoriatic patients experienced itch mostly within affected skin regions, however 19% of patients suffered from pruritus also within uninvolved skin [11]. It was previously analyzed that taking into consideration clinical variants of psoriasis, itch appears in plaque-type psoriasis more often in comparison with a pustular, erythrodermic or guttate form of the disease [7].

In our study, intensity of itch was determined with the use of two independent scales, which showed strong agreement ($p < 0.01$, correlation coefficient 0.67). One scale known as W-AZS I is a part of overall clinical assessment in atopic dermatitis and allows for determination of extent, severity and frequency of pruritus as well as sleep disturbances [9]. The other evaluation was based on numerical scale ranging from 0 to 10 points. The pruritus intensity using W-AZS I and numerical scale was assessed as moderate and reached 11.7 and 4.9 points, respectively. Furthermore, almost every fifth person in our study presented severe itch sensation and only 7.5% of analyzed cases (W-AZS I) complained of its mild perception. This is in contrary to Amatya *et al.* report, in which 80% of patients had mild itch, which was evaluated using a visual analogue scale [8]. Another interesting result was no difference in perception of pruritus between women and men, what is also in conflict with a previously cited study, in which higher pruritus intensity has been observed in females [8].

Interestingly, we did not observe any correlation between severity of psoriasis and intensity of pruritus. Opinions on this subject are variable. In Yosipovitch *et al.* and Nakamura *et al.* [12] reports, similarly to our data, there was no relationship between PASI and itch intensity [7, 14], however Szepietowski *et al.* believe that prevalence and intensity of pruritus is dependent on the extent of psoriatic lesions [11].

Analysis of questionnaires revealed that the most common description of itch was delicate tickling, reported by 43% of patients. Another 24.5% of patients described pruritus as stinging and tingling sensation, while 22% of cases had a feeling of hot and burning skin. Similar results obtained Sampogna *et al.* [13]. Also Amatya *et al.* reported that stinging and tickling sensations were the most common accompanying feelings (even more frequently described by women), however 12% of women and 9% of men felt crawling [8]. We also detected that most of our patients (62%) found pruritus as annoying and negatively influencing their mood. This result is in concordance with previous observations on the impact of psoriasis on quality of life. Some other authors report the most common affective description of itch was bothersome, while annoying one was placed at the second place [7]. According to available data, even if there is a limited body surface involvement, psoriasis creates a feeling of shame and embarrassment as well as lack of confidence. Most of psoriatic patients report the negative impact of their dermatosis on their lives and significant association with stressful life events [14, 15].

In our research the most important aggravating factor for pruritus was stress, what is in consistence with other reports. Italian researchers identified stress as a crucial aggravating factor of itch in 67% of the patients [16]. Moreover, Szepietowski *et al.* documented a significantly higher severity of psoriasis in patients who experienced stressful life events in comparison with those without stress [11]. It has been observed that the nervous system can influence the course of psoriasis and traumatic events may even lead to the exacerbation of disease. This relationship was confirmed by Nakamura who revealed that psoriatic itchy skin is more innervated in the superficial dermis and in the epidermis compared to the non-psoriatic skin [12].

Another essential element increasing the feeling of itch in our patients was physical exercises, which are associated with intense sweating. In the Swedish report, sweating and physical exercises were aggravating factors in 35% and 10% of cases, respectively [8]. What is interesting, in our survey only 3 persons experienced worsening of pruritus at night. Generally it is stated that itch worsens at night due to the higher temperature, what is commonly observed among atopic dermatitis patients. In Yosipovitch *et al.* study, pruritus tended to appear at night in 52% of individuals, while in 69% of cases it was associated with difficulty in falling asleep [7].

However, our report revealed that high temperature as a separate aggravating factor influenced the sensation of itch in every fifth patient. The report cited above, which was performed in tropical climate, presents hot ambient temperature as an exacerbating agent in every second patient [7]. According to Cormia experiments, heat can enhance the itch sensation by its effect on dermal nerve endings [17].

In recent trials it has been shown that obesity plays an important role in many aspects of psoriasis: increases the risk of inverted psoriasis, leads to complications and affects therapy [18]. Epidemiological studies have identified a high prevalence of cardiovascular comorbidities, secondary to the metabolic alterations associated with psoriasis and obesity [19]. Similarly to previous studies, we observed mostly overweight, however we did not note any relationship between BMI and intensity of itch and between BMI and PASI. Our result is difficult to explain, because it seems that in obese patients sweating and temperature is increased and may worsen itch sensation. Contrary to our investigation, Prignano *et al.* found that overweight or obese psoriatic patients experienced more intense pruritus [16].

Despite the high frequency of pruritus in psoriasis, its exact mechanism still remains unclear. Although histamine plays an important role in pruritus in allergic skin diseases, in psoriasis a number of other mediators have been implicated. Most of the studies concern the involvement of neuropeptides, including substance P (SP), calcitonin gene-related peptide (CGRP), vasoactive intestinal peptide (VIP), somatostatin, β -endorphin or pituitary adenylate cyclase activating polypeptide (PACAP) [20]. Other molecules postulated to participate in pruritus are interleukin 2 (IL-2) and E-selectin. Interleukin 31 seems to be an interesting cytokine expressed by activated Th2 cells and suggested to be strongly involved in itching sensation of atopic dermatitis patients. However, its role in pruritus in psoriasis has not yet been evaluated [21]. Our study demonstrates no evidence for possible engagement of this cytokine in itch of psoriasis. We did not detect any difference in its mean level between healthy subjects and psoriatic patients as well as there was no significant relationship between IL-31 and PASI or intensity of itch. Despite the fact that atopic dermatitis and psoriasis are regarded as T-cell-mediated chronic skin diseases, the clinical picture of both dermatoses is completely different. Whereas in atopic dermatitis pruritus is a significant diagnostic criterion, in psoriasis (as mentioned above) it is a relatively mild concomitant symptom. Previous studies conducted in our department concerning atopic dermatitis revealed that pruritus intensity was assessed as 16.1 points W-AZS I, while in psoriatic patients this index was 11.7 points [22].

Recently, a new subset of T cells (Th 17) producing IL-17 has been identified. Interleukin 17 has pro-inflammatory action and characterizes the synergistic effect

with IL-1 and tumor necrosis factor α (TNF- α). New reports revealed that psoriasis lesions are enriched with IL-17+ T cells as well as synovial tissue in psoriatic arthritis contain lots of IL-17R. This may suggest an important role of that cytokine in the pathogenesis of psoriasis and psoriatic arthritis [23, 24]. In our study we evaluated the potential involvement of IL-17 in pruritus in psoriasis and we did not observe any significant relationship. The concentration of IL-17 in patients' serum was found to be low, what may indicate the predominant tissue-related action of that cytokine. Therefore, for better evaluation of this issue, the expression of IL-17 in tissue in relation to itch should be further evaluated.

Conclusions

Our study provides subsequent data on the intensity of itching sensation and relevance of pruritus in psoriatic patients. Due to its high prevalence, itch seems to be a characteristic feature of psoriasis and, in order to improve patients' quality of life, should be targeted therapeutically in addition to treatment of the lesional skin. Since the pathogenesis of pruritus in psoriasis is not fully understood, further investigations in this area need to be conducted. It seems that serum concentrations of IL-17 and IL-31 may not be reliable markers of these cytokines' engagement in psoriatic pruritus.

Conflict of interest

The authors declare no conflict of interest.

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