INVESTIGATIVE REPORT

Pruritus is an Important Factor Negatively Influencing the Wellbeing of Psoriatic Patients

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The aim of this study was to evaluate the relationship between itch and the well-being of patients with psoriasis. In a study of 102 patients with plaque-type psoriasis, pruritus was found in 91 (89.2%) patients during exacerbation of psoriasis. No significant correlation was found between disease severity and the presence and intensity of pruritus. However, pruritus intensity correlated significantly with patients' quality of life, feelings of stigmatization, stress experienced within a period of one month before psoriasis outbreak, and depressive symptoms. In conclusion, pruritus may have a significant negative influence on the psychosocial status of patients with psoriasis. There is a need for the development of effective antipruritic treatments in order to improve the well-being of patients with psoriasis. Key words: psoriasis; depression; quality of life; stigmatization; stress; itch.

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Psoriasis is one of the most common chronic inflammatory skin diseases; it is estimated to affect approximately 1–2% of the general population of highly developed countries. It has a complex, multifactorial aetiopathogenesis, which is not yet fully understood. Several factors are thought to play an important role in the development of psoriatic lesions, including genetic predisposition, hyperproliferation of keratinocytes, vascular alterations in the skin, upregulation of cytokines, and immunological as well as auto-immunological disturbances (1). In addition, observations of stress-induced onset or exacerbations of psoriasis, as well as a symmetrical distribution of psoriatic plaques indicate an additional, important role of the nervous system in the development of this entity (2, 3).

A number of studies have shown that pruritus is a frequent phenomenon in patients with plaque-type psoriasis, affecting more than 60% of individuals (3–10), with a reported mean severity of 5.2–6.4 points on the visual analogue scale (VAS; 0–10) (3, 5, 10–13). Despite

its high frequency, therapeutic options to alleviate or reduce itch in psoriasis are very limited (14). The lack of effective anti-pruritic treatments for psoriasis is an important issue in daily clinical practice, as it is believed that pruritus may be an unendurable symptom for patients with psoriasis (5, 15–17). In 1988, Gupta et al. (4) noted that many subjects consider pruritus to be the most troubling symptom of psoriasis, even though the mean severity of itch seems to be lower than in other pruritic skin conditions, such as atopic dermatitis (18). Furthermore, Amatya et al. (10) documented that a majority of patients with psoriasis consider pruritus to have a negative effect on their quality of life (QoL), with mood, concentration, sleep, sexual desire and appetite being the most impaired parameters. In spite of these observations, the influence of pruritus on other aspects of psoriatic patients' well-being has not been well studied so far. The current study therefore examined the relationship between pruritus in psoriasis and various psychosocial variables.

MATERIALS AND METHODS

Patient characteristics

All patients gave their informed consent prior to inclusion in the study. A total of 102 consecutive patients (both inpatients and outpatients) with plaque-type psoriasis (64 males (62.7%) and 38 females (37.3%)), age range 16–82 years (mean age 45.2 ± 17.2 years) were included in the study. Twenty-three (22.5%) subjects were also diagnosed as having had psoriatic arthritis in the past; however, at the time of examination none of these individuals had active joint symptoms. Detailed characteristics of the enrolled patients are shown in Table I.

Basic study methodology

This cross-sectional study was approved by the local ethics committee. Every patient underwent a careful dermatological examination at the first onset of psoriasis or during a new exacerbation of skin lesions. All patients were examined on the first day of admission (for inpatients) or at their visit to the outpatient clinic due to psoriasis onset/exacerbation, before any anti-psoriatic treatment was initiated. A specially designed questionnaire containing socio-demographic and clinical data was completed based on the anamnesis and physical examination. Psoriasis severity was assessed according to the Psoriasis Area and Severity Index (PASI) (19). For patients with pruritus, itch intensity was evaluated according to the 10-point VAS and the 4-item Itch Questionnaire, which had been used successfully by our group in previous studies of pruritus

Table I. Comparison of characteristics of patients with psoriasis with and without pruritus

Characteristics	Total	Patients with pruritus	Patients without pruritus	p^{a}
Number of patients: <i>n</i> (%)	102 (100)	91 (89.2)	11 (10.8)	_
Age, years				
$Mean \pm SD$	45.2 ± 17.2	45.2 ± 16.8	45.2 ± 21.2	1.0
Range	16-82	17–82	16–79	
Gender, n (%)				
Females	38 (37.3)	34 (37.4)	4 (36.4)	0.79
Males	64 (62.7)	57 (62.6)	7 (63.6)	
Marital status, n (%)				
Single	45 (44.1)	39 (42.9)	6 (54.6)	0.61
Married	52 (51.0)	47 (51.6)	5 (45.4)	
Cohabitating	5 (4.9)	5 (5.5)	0 (0)	
Education level, n (%)				
Primary school	15 (14.7)	12 (13.2)	3 (27.3)	0.33
Secondary school	25 (24.5)	22 (24.2)	3 (27.3)	
High school	45 (44.1)	40 (44.0)	5 (45.4)	
University	17 (16.7)	17 (18.7)	0 (0)	
Employment, <i>n</i> (%)	, , ,	, ,		
Employed	34 (33.3)	32 (35.2)	2 (18.2)	0.43
Unemployed	68 (66.7)	59 (64.8)	9 (81.2)	
Place of residence, n (%)	, ,	, ,	` '	
Countryside	18 (17.6)	15 (16.5)	3 (27.3)	0.08
Small town (<258100,000 citizens)	41 (40.2)	40 (44.0)	1 (9.1)	
Large city (≥100,000 citizens)	43 (42.2)	36 (39.5)	7 (63.6)	
Joint involvement, <i>n</i> (%)	- (-)	()	(1111)	
Yes	24 (23.5)	21 (23.1)	3 (27.3)	0.95
No	78 (76.5)	70 (76.9)	8 (72.7)	
Disease severity (PASI), scores	, ,	,	,	
Mean ± SD	12.5 ± 8.2	12.5 ± 8.6	12.4 ± 4.6	0.41
Range	2.5-46.4	2.5-46.4	6.6-21.7	
Disease duration, years				
Mean ± SD	16.4 ± 13.8	16.9 ± 13.4	12.6 ± 16.9	0.33
Range	0.2-55	0.2-55	0.2-51	
Duration of the last exacerbation, n (%)				
<3 months	57 (55.9)	51 (56.0)	6 (54.6)	0.82
≥3 months	45 (44.1)	40 (44.0)	5 (45.4)	
Family history of psoriasis, n (%)	, ,	,	,	
Positive	37 (36.3)	36 (39.6)	1 (9.1)	0.1
Negative	65 (63.7)	55 (60.4)	10 (90.9)	
Lesions on visible skin areas, n (%)	, ,	, ,	` '	
Face with/without hands	60 (58.8)	56 (61.5)	4 (36.4)	0.2
Only hands	42 (41.2)	35 (38.5)	7 (63.6)	
Hospitalizations due to psoriasis/year, <i>n</i>	(' /	` /	` /	
Mean ± SD	1.3 ± 1.0	1.3 ± 1.1	1.1 ± 0.8	0.54
Range	0.5–6	0.5–6	0.5–3	

^aComparison between patients with and without pruritus.

PASI: Psoriasis Area and Severity Index; SD: standard deviation.

(3, 6). The 4-item Itch Questionnaire consists of evaluations of itching severity, frequency, localization and sleep disturbances due to pruritus (6). The patients were asked to assess itch intensity during the last 24 h.

Psychosomatic assessments

Shortly after physical examination all patients were asked to complete several questionnaires that evaluated health-related QoL (HRQoL), stigmatization, stress and depression. HRQoL within the last 7 days prior to the study visit was evaluated according to the Dermatology Life Quality Index (DLQI) (20, 21). Stigmatization assessment was based on the Feelings of Stigmatisation Questionnaire (22, 23) and the 6-item Stigmatisation Scale (23, 24). Stress severity was measured within one month prior to disease exacerbation and was assessed according to the Holmes and Rahe Social Readjustment Scale (25) as well as according to the Stress Self-assessment Scale (no stress, mild, moderate, severe and extremely severe stress) (3). Severity of symptoms of depression was rated based on the Beck's Depression Inventory (BDI) (26). Both stigmatization and depression questionnaires referred to the previous 2 weeks of the patient's life.

Statistical analysis

All data were analysed statistically with Statistica® 7.0 software (Statsoft, Cracow, Poland). Student's t-test for independent variables, Mann-Whitney U test, analysis of variance and χ^2 test were used where appropriate. Correlations between parameters were measured with Spearman's rank correlation test. To assess the influence of other clinical and socio-demographic parameters on the relationship between itch and well-being the multivariative analysis of variance (MANOVA) and multiple regression analysis (results demonstrated as $\beta \pm$ standard error) were calculated. The following parameters were entered as covariates for MANOVA and multiple regression analysis: itch intensity according to the VAS, itch intensity according to the 4-item Itch Questionnaire, psoriasis severity according to the PASI, age, gender, marital status, education level, employment, place of living, joint involvement, disease duration, duration of the last exacerbation, family history of psoriasis, presence of psoriatic lesions on visible skin areas and the number of hospitalizations due to psoriasis per year. Statistical significance was set at p < 0.05.

RESULTS

Itch frequency and intensity

Pruritus was observed in 91 patients (89.2%). The severity of psoriasis did not markedly influence the existence of itch (the mean PASI in subjects with and without pruritus was 12.6 ± 8.6 and 11.8 ± 4.3 points, respectively; p=0.66). The presence of pruritus was also independent of the analysed demographic and clinical parameters, including patients' age, gender, marital status, education level, employment, place of living, type of psoriasis, disease duration, duration of current psoriasis exacerbation, family history of psoriasis, presence of psoriatic lesions on visible skin areas, and number of hospitalizations due to psoriasis (data not shown).

The intensity of pruritus according to the VAS ranged between 0.3 and 8.9 points (mean 4.2 ± 2.4 points). Regarding the 4-item Itch Questionnaire, the severity of itch ranged between 4 and 19 points (mean 10.1 ± 4.3 points). A significant correlation was found between the results obtained using both methods of itch severity assessment (ρ =0.41, p<0.001, n=91).

There was no significant correlation between itch intensity and psoriasis severity assessed by the PASI

(n=91) (Table II). However, the intensity of pruritus correlated positively with the number of hospitalizations per year due to psoriasis (VAS: $\rho=0.24$, p=0.02; 4-item Itch Questionnaire: $\rho=0.31$, p=0.003, n=91). Remarkably, psoriasis severity was another parameter determining the annual number of hospitalizations in psoriatic subjects ($\rho=0.23$, p=0.02, n=102). Other clinical and socio-demographic parameters studied did not influence the intensity of pruritus, except for disease duration, which, interestingly, correlated positively with the 4-item Itch Questionnaire scoring ($\rho=0.26$, p=0.01, n=91), but not with the VAS results ($\rho=0.11$, p=0.3, n=91).

Itch and quality of life

The HRQoL assessed by the DLQI ranged between 0 and 29 points (mean 12.2 ± 7.0 points). Based on the explanation of DLQI scoring proposed by Hongbo et al. (27), 5 patients (5.4%) had normal, 12 (13.0%) slightly impaired, 26 (28.3%) moderately impaired, 36 (39.1%) very severely impaired and 13 (14.1%) extremely severely impaired HRQoL.

Patients with pruritus had significantly decreased HRQoL (on average a very large effect on the patient's life) compared with patients without pruritus (on average moderate effect on patient's life): DLQI scoring 12.2 ± 7.0 compared with 6.8 ± 7.1 , respectively (p=0.02, n=102). We have also found significant correlations between the DLQI scoring and both assessments of itch intensity in pruritic subjects (n=91) (Table II). Accordingly, significant differences were found regarding itch intensity between patients with normal, slightly impaired, moderately impaired, very severely impaired and extremely severely impaired HRQoL (Table III).

Table II. Relationship between pruritus intensity, psoriasis severity and psychosocial assessments (n = 91)

	Pruritus intensity					
	Visual analogue scale		4-item Itch Questionnaire			
Variable	Spearman ρ coefficient	p	Spearman ρ coefficient p			
Disease severity (PASI)	0.05	0.62	0.17	0.11		
Quality of life (DLQI)	0.46	< 0.001	0.4	< 0.001		
Stigmatization						
Feelings of Stigmatization Questionnaire	0.22	0.04	0.36	< 0.001		
Anticipation of rejection	0.13	0.21	0.32	0.002		
Feeling of being flawed	0.31	0.003	0.4	< 0.001		
Sensitivity to other attitudes	0.21	0.05	0.31	0.003		
Guilt and shame	-0.03	0.74	0.16	0.13		
Positive attitudes	0.06	0.56	0.18	0.09		
Secretiveness	0.22	0.04	0.25	0.02		
6-item Stigmatization Scale	0.23	0.03	0.25	0.02		
Stress						
Holmes and Rahe Social Readjustment Scale	0.312	0.003	0.06	0.55		
Stress Self-assessment Scale	0.25	0.02	0.26	0.01		
Symptoms of depression (BDI)	0.29	< 0.01	0.43	< 0.001		

PASI: Psoriasis Area and Severity Index; DLQI: Dermatology Life Quality Index; BDI: Beck's Depression Inventory.

Table III. Influence of itch severity on patient's quality of life (QoL) (n = 91)

	QoL impairi	QoL impairment ^a				
	None	Small	Moderate	Very large	Extremely large	
Visual analogue scale	1.6 ± 0.9	3.2 ± 2.3	2.4 ± 1.9	4.7 ± 2.8	5.7 ± 2.3	< 0.001
4-item Itch Questionnaire	4.8 ± 1.8	10.0 ± 5.0	8.7 ± 4.0	11.2 ± 4.1	12.6 ± 4.1	0.001

^aAccording to translation of DLQI scoring by Hongbo et al. (27).

Using the MANOVA it was found that pruritus intensity was the only parameter significantly influencing the DLQI scoring in studied subjects (the VAS: F=3.77, p=0.06, the 4-item Itch Questionnaire: F=8.0, p<0.01). None of the other variables were observed to be an independent parameter significantly influencing the HRQoL: F values ranged from 0 for employment status (p=0.99) to 2.8 for joint involvement (p=0.1). Regarding multiple regression analysis, only the itch severity assessed both by VAS as well as by 4-item Itch Questionnaires were found to be important determinants of QoL level ($\beta=0.86\pm0.32, p<0.01$ and $\beta=0.42\pm0.16, p=0.01$, respectively).

Itch and feelings of stigmatization

The scoring of stigmatization in the analysed group of patients with psoriasis ranged between 26 and 127 points (mean 76.3 ± 19.2 points) according to the Feelings of Stigmatisation Questionnaire, and between 0 and 16 points (mean 5.0 ± 3.7 points) according to the 6-item Stigmatisation Scale (for details see (28)). No significant differences were found between subjects with and without pruritus regarding the level of stigmatization (Feelings of Stigmatisation Questionnaire: 76.7 ± 19.5 compared with 73.2 ± 16.5 points, respectively, p = 0.59; 6-item Stigmatisation Scale: 5.2 ± 3.8 compared with 3.0 ± 0.6 points, respectively, p = 0.08). However, the intensity of pruritus correlated significantly with the level of stigmatization (n=91) (Table II) and the domains "Feeling of being flawed", "Sensitivity to other attitudes" and "Secretiveness" of the Feelings of Stigmatization Questionnaire (5) seemed to be influenced by pruritus to the largest extent (Table II).

Analysing the level of stigmatization with MANOVA it was found that itch severity assessed according to the 4-item Itch Questionnaire was an independent variable significantly influencing the scoring of the Feelings of Stigmatisation Questionnaire (F=5.1, p=0.03). In addition, family history of psoriasis was another parameter significantly influencing the stigmatization level assessed by the Feelings of Stigmatisation Questionnaire (F=6.1, p=0.02), indicating that patients with negative family history of psoriasis were more stigmatized compared with subjects who confirmed that their relatives were suffering from psoriasis. Furthermore, duration of the current exacerbation of psoriasis, joint involvement, psoriasis duration, annual number of hospitalizations

and employment status were also independent parameters with significant impact on some domains of stigmatization feelings (data not shown). Interestingly, none of the studied parameters, including itch intensity, was found to be important independently for the 6-item Stigmatisation Scale scoring. On the other hand, multiple regression analysis only indicated itch severity according to the 4-item Itch Questionnaire as significantly influencing the stigmatization scoring according to the 6-item Stigmatisation Scale (β =0.22±0.09, p=0.02) as well as itch severity according to the 4-item Itch Questionnaire (β =1.5±0.42, p<0.001), and family history of psoriasis as important for the Feelings of Stigmatisation Questionnaire scoring (β =-10.8±4.0, p<0.01).

Itch and stress

Seventy-four patients (72.5%) experienced at least one stressful life event within one month prior to psoriasis exacerbation. According to the Holmes and Rahe Social Readjustment Scale stress severity ranged between 12 and 457 points (mean 121.8 ± 90.9 points). These live events were considered as causing no stress in 13 subjects (17.6%), mild stress in 13 (17.6%), moderate stress in 31 (41.9%), severe stress in 13 (17.6%) and extremely severe stress in 4 (5.4%) participants based on the Stress Self-assessment Scale. There was no difference in the presence of stress between patients with and without pruritus (72.8% compared with 70.0%, respectively; p=0.85). Moreover, patients who experienced at least one stressful life event within one month prior to disease exacerbation had similar itch severity compared with patients without stress (VAS: 3.6 ± 2.7 and 2.8 ± 2.6 points, respectively, p=0.15; 4-item Itch Questionnaire: 9.1 ± 4.9 and 9.0 ± 5.4 points, respectively, p=0.9). On the other hand, a significant correlation was found between itch intensity and degree of stress in most comparisons in pruritic patients (n=91) (for details see Table II).

Based on MANOVA, the itch severity assessed according to the 4-item Itch Questionnaire was the only independent variable significantly influencing the stress severity evaluated by the Stress Self-assessment Scale (F=4.49, p=0.04). On the other hand, none of the studied parameters independently influenced the scores of the Holmes and Rahe Social Readjustment Scale.

Multiple regression analysis revealed that none of the studied parameters significantly influenced the stress severity according to Stress Self-assessment

^bBased on analysis of variance.

Scale, while the scoring of the Holmes and Rahe Social Readjustment Scale was markedly modulated by PASI scores ($\beta = -2.6 \pm 1.28$, p = 0.04) and the number of hospitalizations per year ($\beta = 14.69 \pm 5.37$, p < 0.01).

Itch and depression

Regarding the presence of depressive symptoms in patients with psoriasis, the scoring of the BDI ranged between 0 and 36 points (mean 6.7 ± 6.6 points). Twentyone patients (20.6%) received more than 10 points in the BDI, suggesting a clinically relevant depression. Patients with pruritus seemed to be more depressive compared with subjects without itch (mean BDI 7.1 ± 6.8 compared with 2.9 ± 3.8 points, respectively, p = 0.02). In addition, all patients (n=21) with a BDI scoring over 10 points had pruritus during psoriasis exacerbation compared with 70 (76.9%) subjects with a BDI scoring equal or less than 10 points; however, this finding was not statistically significant (p=0.07). Significant correlations were found between itch intensity and BDI scoring (n=91) (Table II). In addition, the following parameters were found by MANOVA to be independent factors influencing the BDI: itch severity according to the 4-item Itch Questionnaire (F=11.51, p=0.001), joint involvement (F=4.63, p=0.04) and presence of lesions on visible skin areas (F=4.47, p=0.04); patients with more severe pruritus, with joint involvement and with psoriatic lesions on the face were more depressed. On the other hand, multiple regression analysis revealed the following covariates as significantly influencing the level of depression: itch severity according to the 4-item Itch Questionnaire ($\beta = 0.4 \pm 0.15$, p = 0.01), high school education ($\beta = 1.47 \pm 0.71$, p = 0.04) and employment ($\beta = -3.24 \pm 1.55$, p = 0.04).

DISCUSSION

A number of studies have demonstrated that itch is a frequent phenomenon in psoriatic subjects (3–10). It is even suggested, that the prevalence of itch among patients with psoriasis is comparable to that among subjects with prurigo or other forms of dermatitis (9). Chronic itch has also been described as negatively influencing patients' QoL (5, 15–17). This is related to a behavioural response to chronic itch, which usually causes patients to withdraw from activities (29).

A study by Verhoeven et al. (9), analysing various skin diseases (psoriasis constituted approximately 20% of included subjects), showed that itch correlated with QoL (measured by DLQI) to a greater extent (R=0.55) than pain (R=0.46) or fatigue (R=0.38). In accordance with these observations, our study also found that pruritus exerts a significant effect on QoL in patients with psoriasis. It was shown in 1988 that many patients consider itch to be the most troubling symptom of psoriasis

(4). Furthermore, pruritus was found to interfere with work ability among psoriatic subjects and nearly half of the analysed individuals (48.4%) reported pruritus to be the most troubling symptom during work activity (30). Many psoriatic individuals observed that pruritus was associated with difficulty in falling asleep and awakenings during the night (5). As a result of pruritus, 35% of the patients became more agitated, 24% became depressed, 30% had difficulty concentrating, and 23% changed their eating habits (5). In addition, we have documented previously that vulvar discomfort, such as itching or burning, in women with psoriasis frequently causes significant sexual problems, which is another important aspect of QoL (31).

Interestingly, itch severity was also related to the higher level of feelings of stigmatization. This is an interesting aspect of pruritus, because itch is not a visible symptom of the disease but rather a subjective, invisible sensation. However, scratching behaviour induced by itching in subjects with psoriasis may draw the attention of other people, and it is possible that they may notice psoriatic lesions more readily when somebody is scratching. This could be a probable explanation for the significant correlation between pruritus intensity and feelings of stigmatization.

Our results also suggest that the intensity of pruritus is related to stress experienced by the patients prior to psoriasis exacerbation; a finding that confirms our previous observations on this subject (3). This is also in agreement with studies demonstrating, as many patients with psoriasis have reported, that their disease is exacerbated by stress (32). It has even been suggested that patients who consider their psoriasis to be reactive to stressors have more disfiguring disease clinically and experience more psoriasis-related daily stress (13, 32). Remarkably, Verhoeven et al. (13) found, similarly to our group, that patients not only experienced more severe disease, but also more itch when they reported the highest level of daily stressors. Furthermore, these authors observed a significant correlation between level of daily stressors and scratching behaviour (13). Based on this observation it was hypothesized that the relationship between stressors and an increase in itch and disease severity 4 weeks later is present only in cases of relatively high levels of daily stressors (13). It seems that certain psychosocial interventions will probably decrease the morbidity associated with psoriasis among the high stress reactors, and may even result in a decline in the number of major flare-ups of psoriasis (13). On the other hand, it has been shown that greater severity of pruritus is responsible for greater psoriasis-related stress (33). Thus, a vicious circle can be easily found between stress, which can induce itch, and itch, which may provoke stress.

Depression can be found in approximately 15–30% of psoriatic individuals, and usually the majority of them suffered from reactive disorders (34, 35). It has been

reported that psychosocial comorbidity (e.g. depression) is high among patients with itch and that negative emotions can increase the level of itch (16, 36, 37). This finding also appears to be true for psoriasis, as it has been observed that the degree of depressive psychopathology discriminates between the mild, moderate and severe pruritus groups in patients with psoriasis on admission (4). Prospectively, the change in depression scores correlated with the change in pruritus (4). Thus, it was postulated that the depressed clinical state may reduce the threshold for pruritus (4). On the other hand, it was also suggested, that anxiety, depression and experiencing dissociative states are a consequence, rather than a cause, of having a chronic dermatological disorder accompanied by chronic itch (16). In line with this statement, we have shown previously that female patients with pruritus affecting the vulva were more depressed that those without itching (31). Here, it has also been demonstrated that patients with pruritus had higher depression scoring compared with subjects without itch. Verhoeven et al. (16) suggested that dissociative states could be a functional way of coping with chronic itch, as it may be a way to withdraw from the unpleasant itch experience. In addition, acceptance has been shown to be correlated with less itch intensity (38). Because psychological distress has been shown to be related to helplessness and less acceptance. these psychological cognitions may mediate the distress caused by itch in patients with chronic skin diseases (16, 38). Thus, similar to the situation with stress, a vicious circle can be found when analysing depression and itch in psoriasis. Depression may promote the sensation of itch, and chronic itch can provoke depression in susceptible

In conclusion, chronic pruritus is significantly associated with poorer psychosocial well-being of patients with psoriasis. It appears that itch may affect various aspects of patient's psychosocial status. However, prospective longitudinal studies are needed to better establish the degree of this influence and the exact relationship between pruritus and psoriatic patients' well-being. These findings emphasize the need for the development of effective anti-pruritic treatments for psoriatic subjects in order to improve their well-being.

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