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The psychological comorbidities of prurigo in European patients: A multi-centre study in 13 countries

Short title: Psychological impact of prurigo

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Abstract

Prurigo is defined by the presence of chronic pruritus and multiple localized or generalized pruriginous lesions. The aim of this study was to use an epidemiological approach to assess the psychological burden of patients with prurigo in European countries. In this multicentre European study, 3635 general dermatology outpatients[AF1] and 1959 controls were included. Socio-demographic data and answers to questionnaires (regarding quality of life, general health, anxiety and depression and suicidal ideation) were collected. There were 27 patients with prurigo; of these, 63% were men, and the mean age was 58.6 years old. Among patients with prurigo, 37.1[AF2]% suffered from anxiety and 29.6% from depression. Nineteen percent[AF3] of patients reported suicidal ideation, and for 80% of these patients, suicidal ideation concerned their skin disease. These frequencies were higher than in the 10 commonest dermatological diseases (including psoriasis, atopic dermatitis and leg ulcers for example). The impact on quality of life was severe, with a mean DLQI of 12.4, with an extreme impact on quality of life for 23% of patients and a very large impact for 27% of patients. The psychological comorbidities of prurigo are severe[AF4], greater than those of other dermatoses, and their impact on quality of life was significant. Thus, it is important to study this disease and to find new treatments.

Introduction

Prurigo occurs along with chronic pruritus and presents with symmetrically distributed papules, nodules and/or plaques (1). This disorder is characterized by intense pruritus as the dominant symptom (2,3). The skin between the nodules is usually normal. The term prurigo has been used for many decades without a clear definition. Recently, the European experts of the Task Force Pruritus of the European Academy of Dermatology and Venereology achieved a consensus regarding the definition, classification and terminology of prurigo (4). Prurigo is[AF5] a distinct disease that is defined by the presence of chronic pruritus and multiple localized or generalized pruriginous lesions (4). Prurigo is related to a neuronal sensitization to itch and development of an itch-scratch cycle. Prurigo can be associated with pruritus of dermatological, systemic, neurologic, psychiatric/psychosomatic, multifactorial or undetermined origin. It is still a matter of controversy whether prurigo represents a separate entity or is a reaction pattern due to the vicious circle of repeated itching and scratching. Little is known about the epidemiology and comorbidities associated with prurigo, particularly psychiatric disorders, such as anxiety and depression.

The aim of this study was to gather[AF6] data about prurigo from a large multicentre European study of general dermatology outpatients and to assess the psychological burden of these patients.

Patients and methods

Participants

A multicentre observational cross-sectional study was conducted in 13 European countries (5). Consecutive dermatology outpatients were invited to participate on random days. The inclusion criteria were age > 18 years, understanding the local language and not suffering from severe mental disease. Each centre recruited 250 patients; then, another 25 patients, increasing the number of participants. In total, 5442 individuals agreed to participate (79.9% of those invited). Of the initial 4026 patients, 16 were excluded: nine were too young and seven had missing data. A control group of healthy workers was invited to participate. Of the initial 1416 controls, 57 were excluded because they had a skin disease. Data were therefore used from 4010 patients and 1359 controls. Each patient was clinically examined by the dermatologist, who recorded the diagnosis, its severity, and comorbidities, including cardiovascular disease, chronic respiratory disease, diabetes mellitus, rheumatological disease and other conditions such as cancer. In our study, we identified cases of prurigo and compared their data to control patients and patients with other dermatological diseases.

Questionnaires

Each participant was asked to complete a two part document. The first part contained questions about socio-demographic variables: sex, age, ethnicity, marital status, education and self-reported socio-economic status. The second part contained several questionnaires:

-The Dermatologic Life Quality Index (DLQI) (6) consists of ten questions about symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex and treatment. Each question is scored from 0 to 3, giving a possible score range from 0 (no impact of skin disease on quality of life) to 30 (maximum impact on quality of life).

-The EuroQol 5 dimensions 3 levels (EQ-5D-3L) consists of 2 parts: the EQ-5D-3L descriptive system and the EQ Visual Analogue Scale (EQ VAS) (7). The EQ-5D-3L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems, some problems, and extreme problems. The EQ VAS records the respondent's self-rated health on a vertical, visual analogue scale where the endpoints are labelled "best imaginable health state" and "worst imaginable health state".

-The Hospital Anxiety and Depression Scale (HADS), a well-validated instrument that has good psychometric properties, has been used to assess the symptoms of anxiety disorders and depression in somatic, psychiatric, and primary care patients, as well as in the general population (8). The HADS includes seven items that assess anxiety and seven for depression, each with four possible answers.

For each dimension of anxiety and depression, a score from 0 to 7 is considered normal, from 8 to 10 is considered a borderline case, and from 11 to 21 is considered a case in need of further examination or treatment. This instrument was used in the validated translations relevant to the study countries[AF7].

- To assess suicidal ideation, the item “Have you ever thought of committing suicide?” with possible answers of "yes" or "no" was included. An additional question was given to the patient group: “Have you ever thought of committing suicide because of your skin?”

The dermatologist answered two questions: “Do you see depressive signs in the patient?” and “Do you see anxiety signs in the patient?” with the possible answers: “yes” or “no”.

Statistical analysis

All data were analysed using Microsoft Office Excel. The quantitative variables were described using the mean and standard deviation. The means of the two groups (prurigo patients and controls) were compared with Student’s T test[AF8]. The qualitative variables were described using the frequency and were compared between the two groups with a Chi square test or Fisher’s exact test in the case of small sample sizes. For all statistical analyses, the type 1 error was set at 5%. Data of prurigo patients were also compared with data of the 10 more frequent dermatoses (psoriasis, non-melanoma skin cancer, infections skin, eczema, acne, nevi, atopic eczema, benign skin tumours, hand eczema, leg ulcers) for the HADS score or with all dermatoses for DLQI in a descriptive way.

Results

The details of the participants' characteristics have been previously published (5). In this study, we included 27 patients with prurigo. The socio-demographic characteristics and comorbidities of patients with prurigo and controls are presented in Table 1.

	Patients with prurigo n=27	Controls n=1359	p-value
Countries, No (%)			
Belgium	2 (7.4)	131 (9.6)	
Denmark	3 (11.1)	122 (9.0)	
France	1 (3.7)	20 (1.5)	
Germany	2 (7.4)	133 (9.8)	
Hungary	0	134 (9.9)	
Italy	5 (18.5)	46 (3.4)	
Netherlands	4 (14.8)	0	
Norway	6 (22.2)	218 (16.0)	
Poland	2 (7.4)	125 (9.2)	
Russia	0	120 (8.8)	
Spain	0	116 (8.5)	
Turkey	1 (3.7)	109 (8.0)	
United Kingdom	1 (3.7)	85 (6.3)	
Age, years (MD=1/18)			
Range	28-84	18-89	
Mean +/- SD	58.6 +/-15.1	41.1 +/-13.6	<0.001
Sex, No (%) (MD=0/3)			
Female	10 (37.0)	903 (66.6)	0.001
Marital status, No (%) (MD=5/3)			
Single	2 (9.1)	362 (26.7)	
Married/partner	15 (68.2)	840 (62.0)	0.017
Separated/divorced	2 (9.1)	119 (8.8)	
Widowed	3 (13.6)	34 (2.5)	
Educational level, No (%) (MD=0/8)			
Low	8 (29.6)	375 (27.8)	
Higher	18 (66.7)	399 (29.5)	<0.001
University	1 (3.7)	577 (42.7)	
Stressful events during last 6 months, No (%) (MD=0 /13)	10 (37.0)	412 (30.6)	0.47
Symptoms of No (%)			
Depression (MD=4/7)	5 (21.7)	182 (13.5)	0.22
Anxiety (MD=4/9)	6 (26.1)	356 (26.4)	0.98
Comorbidities, No (%)			
Heart disease (MD=2/303)	5 (20.0)	78 (7.4)	0.037
Respiratory (MD=5/307)	3 (13.1)	47 (4.5)	0.078
Diabetes, (MD=2/305)	4 (16.0)	24 (2.3)	0.003
Rheumatological disease (MD=3/305)	1 (4.2)	48 (4.6)	1

Table 1. Socio-demographic characteristics and comorbidities of patients with prurigo and controls
MD: missing data

The severity of prurigo was evaluated by the doctor as slight in 20% of patients, mild in 50% and severe in 30%. Only 53.8% of patients claimed to know their diagnosis. Symptoms were present for more than one month in 96.2% of cases. To the question, "what is your level of concern about your skin disease?", 55.6% of patients answered "very much", 37.0% "middle" and 7.4% "little". Patients reported a flare-up of their skin disease every day in 57.7% of cases, every week in 11.5%, every month in 11.5% and several times a year in 19.2%. Approximately 50.0% of prurigo lesions were located on the torso, 46.1% on the hands, 26.9% on the scalp and 23.1% on the face[AF9]. Approximately 88.5% of patients presented with pruritus at the time of examination. The mean itch intensity was 6.6 +/- 3.1 and ranged from 0 to 10.

Data about anxiety, depression and suicidal ideation for patients with prurigo and controls are presented in Table 2.

	Patients with prurigo n=27	Controls n=1359	p-value
HADS anxiety			
Range	0-17	0-18	
Mean +/- SD	8.3 +/- 4.8	4.7+/-3.5	
≥ 11 (anxiety clinical case)	10 (37.1%)	150 (11.1%)	<0.001
HADS depression			
Range	1-16	0-16	
Mean + /- SD	7.6 +/- 4.1	4.3+/-3.2	
≥ 11 (depression clinical case)	8 (29.6%)	58 (4.3%)	<0.001
Suicidal ideation (MD=1)			
Suicidal ideation	5 (19.2%)	88 (8.3%)	0.03
Suicidal ideation concerning the skin disease (among those with suicidal ideation)	4 (80.0%)	N.A	
Suicidal ideation concerning the skin disease (in the whole sample)	4 (15.4%)	N.A	

Table 2. Anxiety, depression and suicidal ideation in patients with prurigo and controls
MD: missing data, N.A: not applicable

Approximately 37.1% of prurigo patients suffered from anxiety diagnosed with a HADS anxiety≥ 11, which was significantly higher[AF10][AF11] than that of the controls and more than that for the 10 more common dermatological conditions of the cohort of patients: 22.7% of patients with psoriasis, 21.0% of patients with hand eczema, 17.6% of patients with atopic eczema, 17.5% of patients with leg ulcers suffered from anxiety.

In the same manner, 29.6% of prurigo patients suffered from depression diagnosed with a HADS depression≥ 11, which was significantly greater[AF12] than that of the controls (4.3%) and higher than that of the 10 other more common dermatological conditions of the cohort of patients: 24.3% of

patients with leg ulcers, 15.1% of patients with hand eczema, 13.8% of patients with psoriasis and 10.1% of patients with atopic eczema suffered from depression.

Finally, 19.2% of prurigo patients reported past or present suicidal ideation, which was significantly higher[AF13] than that of controls (8.3%) and more than that of the 10 more common dermatological conditions of the cohort: in fact, 17.8% of patients with leg ulcers, 17.3% of patients with psoriasis, 15.4% of patients with atopic eczema and 14.2% of patients with hand eczema reported suicidal ideation.

We analysed the concordance of the diagnosis of anxiety and depression between the dermatologist and that suggested by the HADS questionnaire in the 27 prurigo patients: it was 75.0% when there was no depression and 78.6% when there was no anxiety. The true positive value was 50.0% for anxiety and 20.0% for depression, and the false negative value was 66.7% for depression and 64.7% for anxiety. The dermatologists underestimated depression and anxiety in 26.1% of consultations. On the other hand, dermatologists overestimated depression and anxiety in 17.4% and 13.0%, respectively, of consultations.

The mean DLQI was 12.4 +/- 8.6, with a range from 0 to 30. The distribution of the score categories of DLQI is presented in Figure 1. Compared to the 25 other dermatoses, prurigo had a large impact on quality of life, the same as hidradenitis suppurativa (DLQI=12.4) and greater than that of atopic dermatitis (DLQI=11.4) and pruritus (11.2). The values for all of the other dermatoses were under 10.

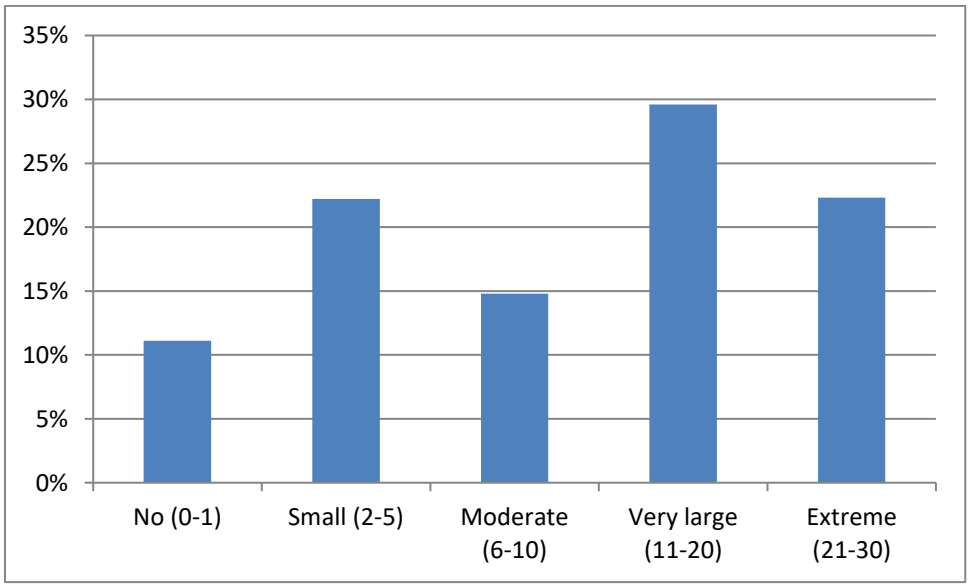

Figure 1: DLQI scores in patients with prurigo

The results of the EQ-5D-3L descriptive system are presented in Figure 2. The EQ VAS was 57.4 +/- 16.5. Among the dermatological diseases studied, prurigo had the third worst self-reported health, with a score of 57.4, behind leg ulcers (56.0) and hidradenitis suppurativa (56.9).

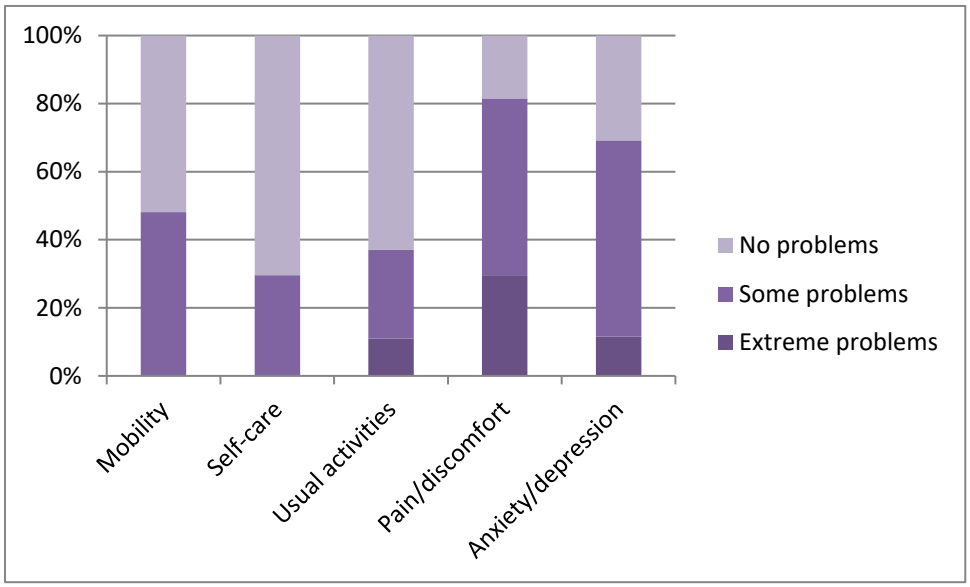

Figure 2. Results of the 5 dimensions of the EQ-5D-3L descriptive system for patients with prurigo.

Discussion

In our study, anxiety, depression and suicidal ideation were more common in patients with prurigo (37.1%, 29.6% and 19.2%, respectively) than in patients with the 10 other more common dermatological diseases (psoriasis, non-melanoma skin cancer, skin infections, eczema, acne, nevi, atopic eczema, benign skin tumours, hand eczema, and leg ulcers[AF14]). Studies on the psychological consequences of prurigo are scarce. A psychometric study from Dazzi et al. compared 20 patients with prurigo nodularis to 20 voluntary subjects (9). Specific questionnaires were used: the General Health Questionnaire, State Trait Anxiety Inventory-form Y, Beck Depression Inventory II and Eysenck Personality Questionnaire. Symptoms of T-anxiety [AF15] and depression were significantly more common in the group of patients with prurigo than in the control group (51.3% vs 39.5% and 19.2% vs 7.0%, respectively), but there was no significant difference for S-anxiety. A recent epidemiological study based on an analysis of a register included 877 patients with prurigo nodularis and ten times more controls (10). The frequencies of anxiety and depression and consumption of anxiolytics and antidepressants were significantly higher in patients with prurigo compared to controls, and there was no association between prurigo and suicide. Depression was found in 8.5% of patients with prurigo, and anxiety was only found in 2.1%. This result could be explained in several ways: the diagnosis was probably not always registered in the database, and there was probably an under-diagnosis. Another study compared the psychological comorbidities of 94 patients with prurigo not to controls but to 91 patients with psoriasis (11). There was no significant difference with regard to alexithymia, somatization symptoms, hypochondrias, anxiety (present in 18% of patients with prurigo vs. 11% with psoriasis) and depression (present in 22% of patients with prurigo and 21% with psoriasis). Psychological comorbidities can be considered to be a consequence of prurigo, but depression and anxiety can induce psychogenic pruritus and thereby lead to prurigo (12).

In a previously published study on the same cohort of patients, our patients with prurigo had one of the 3 lowest mean EQ-VAS scores (57.4) among the 10 most common dermatological diseases (13). This value was similar to that of rheumatoid pain (56.4)(14). In the linear regression of the EQ-VAS score (adjusted for age, sex, socio-economic status and comorbidities), patients with prurigo registered the lowest self-reported health (22.3 points lower than controls), after patients with hidradenitis suppurativa (24.2), compared to controls (13). Impairment for each of the five dimensions of the EQ5D for patients with prurigo compared to controls highlighted an increased odds ratio for all of the dimensions: 4.2 [1.7-10.6] for mobility, 7.35 [2.6-21.1] for self-care, 3.26 [1.3-8.2] for activity, 8.63 [2.8-26.5] for pain/discomfort and 4.90 [1.9-12.4] for depression/anxiety (13). Among the 35 dermatological diseases studied, for self-care, prurigo was the worst after blistering disease (9.73) [4.4-

21.6], and for pain/discomfort, prurigo was the worst after hidradenitis suppurativa (50.28) [12.0-211.0].

Among all of the dermatological diseases studied, prurigo had the second worst impact on quality of life, with a mean DLQI at 12.4, the same as hidradenitis suppurativa[AF16]. Impairment of quality of life is severe: for half of patients, it is considered to be a very or extremely large effect. These data are new; in fact, no study has evaluated quality of life in patients with prurigo before (15)[AF17].

Men were more numerous (59.3%) than women in our group of patients. Prurigo is usually considered to be more common in women. In a cohort of 108 prurigo nodularis patients, females represented 63.9% of the sample (16). Epidemiological data are lacking, so it is difficult to draw conclusions concerning the difference between sexes (17). The mean age of patients in our study was 57, and prurigo usually appears in middle age. The mean age was 61.5 years in Iking's study (16). A low level of education was significantly more common in patients with prurigo than in controls (60.9% vs 27.8%). Some comorbidities were significantly more common in patients with prurigo than in controls: heart disease and diabetes. These comorbidities or the drugs used to treat them could be a cause of prurigo. There is little information on comorbidities, but diabetes was present in 7.4% of patients in Iking's cohort (16).

This study has some limitations. The sample size is limited, but prurigo is a rare disease[AF18]. Prurigo was only defined very recently, so there is probably a heterogeneity of diseases named prurigo in our study because there was no consensual definition at the time of the study (4). Another limitation is that diagnoses of anxiety and depression were made with a questionnaire. Even if the HADS questionnaire has been validated[AF19], this method of diagnosis is censurable.

Prurigo remains relatively unexplored, but researchers are increasingly interested in this disease. In particular, the European experts of the Task Force Pruritus published an expert consensus on the definition, classification and terminology of chronic prurigo (4). The major criteria are: chronic pruritus (≥6weeks), history and/or signs of repeated scratching (e.g., excoriations and scars) and localized or generalized presence of multiple pruriginous lesions. These lesions occur due to a neuronal sensitization to itch and the development of an itch-scratch cycle (4). The treatment of prurigo remains challenging because data from randomized controlled trials are sparse (17–20). Some molecules are in development, such as neurokinin-1 receptor antagonists or antagonists for IL-31(21).

This study highlights prurigo's significant impact on quality of life, including the high frequency of anxiety, depression, and suicidal ideation. Thus, this disease should be further studied to find new approaches to management.

References[AF20][AF21]

1. Zeidler C, Ständer S. The pathogenesis of Prurigo nodularis--'Super-Itch' in exploration. Eur J Pain Lond Engl. janv 2016;20(1):37-40.

2. Wallengren J. Prurigo: diagnosis and management. Am J Clin Dermatol. 2004;5(2):85-95.

3. Accioly-Filho LW, Nogueira A, Ramos-e-Silva M. Prurigo nodularis of Hyde: an update. J Eur Acad Dermatol Venereol JEADV. mars 2000;14(2):75-82.

4. Pereira MP, Steinke S, Zeidler C, Forner C, Riepe C, Augustin M, et al. European academy of dermatology and venereology European prurigo project: expert consensus on the definition, classification and terminology of chronic prurigo. J Eur Acad Dermatol Venereol JEADV. 31 août 2017;

5. Dalgard FJ, Gieler U, Tomas-Aragones L, Lien L, Poot F, Jemec GBE, et al. The psychological burden of skin diseases: a cross-sectional multicenter study among dermatological out-patients in 13 European countries. J Invest Dermatol. avr 2015;135(4):984-91.

6. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol. mai 1994;19(3):210-6.

7. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. Health Policy Amst Neth. déc 1990;16(3):199-208.

8. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. juin 1983;67(6):361-70.

9. Dazzi C, Erma D, Piccinno R, Veraldi S, Caccialanza M. Psychological factors involved in prurigo nodularis: A pilot study. J Dermatol Treat. août 2011;22(4):211-4.

10. Jørgensen KM, Egeberg A, Gislason GH, Skov L, Thyssen JP. Anxiety, depression and suicide in patients with prurigo nodularis. J Eur Acad Dermatol Venereol JEADV. févr 2017;31(2):e106-7.

11. Schneider G, Hockmann J, Ständer S, Luger TA, Heuft G. Psychological factors in prurigo nodularis in comparison with psoriasis vulgaris: results of a case-control study. Br J Dermatol. janv 2006;154(1):61-6.

12. Ständer S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, et al. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. Acta Derm Venereol. 2007;87(4):291-4.

13. Balieva F, Kupfer J, Lien L, Gieler U, Finlay AY, Tomás-Aragonés L, et al. The burden of common skin diseases assessed with the EQ5D^{TM}: a European multicentre study in 13 countries. Br J Dermatol. mai 2017;176(5):1170-8.

14. Hunter DJ, Riordan EA. The impact of arthritis on pain and quality of life: an Australian survey. Int J Rheum Dis. févr 2014;17(2):149-55.

15. Basra MKA, Fenech R, Gatt RM, Salek MS, Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. Br J Dermatol. nov 2008;159(5):997-1035.

16. Iking A, Grundmann S, Chatzigeorgakidis E, Phan NQ, Klein D, Ständer S. Prurigo as a symptom of atopic and non-atopic diseases: aetiological survey in a consecutive cohort of 108 patients. J Eur Acad Dermatol Venereol JEADV. mai 2013;27(5):550-7.

17. Zeidler C, Tsianakas A, Pereira M, Ständer H, Yosipovitch G, Ständer S. Chronic Prurigo of Nodular Type: A Review. Acta Derm Venereol. 7 févr 2018;98(2):173-9.

18. Fostini AC, Girolomoni G, Tessari G. Prurigo nodularis: an update on etiopathogenesis and therapy. J Dermatol Treat. déc 2013;24(6):458-62.

19. Klejtman T, Beylot-Barry M, Joly P, Richard MA, Debarbieux S, Misery L, et al. Treatment of prurigo with methotrexate: a multicentre retrospective study of 39 cases. J Eur Acad Dermatol Venereol JEADV. 21 oct 2017;

20. Tsianakas A, Zeidler C, Ständer S. Prurigo Nodularis Management. Curr Probl Dermatol. 2016;50:94-101.

21. Pereira MP, Ständer S. Itch Management: Treatments under Development. Curr Probl Dermatol. 2016;50:71-6.