CLINICAL REPORT

Usability of Validated Sleep-assessment Questionnaires in Patients with Chronic Pruritus: An Interview-based Study

Theresa SUILMANN, Claudia ZEIDLER, Nani OSADA, Claudia RIEPE and Sonja STÄNDER
Center for Chronic Pruritus, Department of Dermatology, University Hospital Münster, Münster, Germany

Impaired sleep due to nocturnal pruritus is a common symptom in patients with chronic pruritus. However, there is no standardized, simplified instrument for assessing sleep-related problems in patients with chronic pruritus. After a literature search, we conducted 50 interviews with patients with chronic pruritus and tested 12 items most frequently used in routine sleep questionnaires. Afterwards, 2 sleep assessment questionnaires (Pittsburgh Sleep Quality Index; Regensburg Insomnia Scale) were selected for use in 88 patients with chronic pruritus with sleep impairment due to pruritus. They were completed twice; once before optimizing their individual pruritus therapy and once again after 4 weeks. During the latter survey, 21 patients reported that pruritus no longer negatively affected their sleep. These patients also achieved a significant improvement in their sleeping behaviour in the Regensburg Insomnia Scale. Therefore, the Regensburg Insomnia Scale appears to be well-suited to assessing sleep impairment in patients with chronic pruritus.

Key words: itch; nocturnal pruritus; sleep assessment; prurigo; clinical trial.

Accepted Apr 24, 2018; Epub ahead of print Apr 24, 2018

Acta Derm Venereol 2018; 98: 722–727.

Corr: Sonja Ständer, Department of Dermatology and Center for Chronic Pruritus, University Hospital Münster, Von-Esmarch-Str. 58, DE-48149 Münster, Germany. E-mail: sonja.staender@uni-muenster.de

SIGNIFICANCE

Chronic pruritus (CP) is a common symptom in the general population. In some patients the itching occurs predominantly at night. Accordingly, sleep patterns can be partly negatively affected. In this study, pruritus-related sleep impairments (especially waking up in the middle of the night or too early in the morning because of pruritus) were identified. In addition, we found that one already existing, validated sleep assessment questionnaire, the Regensburg Insomnia Scale, captures the specific sleep restrictions of patients with CP and detect any positive therapy effects on patients' sleep.

Chronic pruritus (CP), defined as pruritus persisting for more than 6 weeks (1), is a frequent subjective symptom in the general population, with an estimated lifetime prevalence between 22% and 25.5% (2, 3). Efforts are currently underway to standardize and validate instruments used to measure CP, especially due to its subjective nature (4). The documentation of the intensity of the pruritus and its influence on numerous aspects of quality of life (QoL) serve as the basis for an assessment of the efficacy of a treatment. One important aspect is the determination of sleep patterns, since CP often results in sleep disturbances. Up to 90% of patients with CP report impaired sleep due to nocturnal pruritus (5). Because sleep disturbances are only marginally addressed in current, standardized instruments for the QoL, assessments of sleep quality in patients with CP have thus far remained insufficient (6). A more detailed description of specific sleep-related problems could be useful for optimizing and adapting a therapy. The International Forum for the Study of Itch (IFSI) provides a general recommendation regarding which specific sleep instruments might be suitable (4). Several validated sleep assessment questionnaires described in the literature assess sleep impairment in a detailed manner; however, none of these instruments has been validated for use in patients with CP.

The aims of this study are to determine whether validated sleep questionnaires are able to detect specific sleep restrictions in patients with CP, and to attempt to define which questionnaire is most suitable to fulfil this task.

MATERIALS AND METHODS

This study was conducted at the Center for Chronic Pruritus in the Department of Dermatology at the University Hospital Münster from November 2014 to December 2016.

Literary research

To obtain an overview of current validated sleep questionnaires, literary research (step 1) was performed using databases such as PubMed (US National Institute of Health's National Library of Medicine) on 19 December 2014.

Interviews and testing the items most frequently asked in routine sleep questionnaires

For the next step, the informed consent of 50 patients (age ≥18 years) was obtained prior to conducting interviews regarding their sleep behaviour (step 2) and testing of 12 items most commonly used in routine sleep questionnaires (step 3). In this collective, all patients with CP were admitted, regardless of the existence of impaired sleep due to nocturnal pruritus, with the aim of gaining an overview of the prevalence of sleep impairment in patients with CP and to obtain a first impression of which sleep areas might be affected the most in this collective. Firstly, patients were prompted to describe, in their own words, their sleep patterns in the last 4 weeks, including any sleep problems. Post-interview, each patient was asked to complete an additional questionnaire comprised of the 12 items most frequently asked in examined sleep questionnaires, in order to increase the comparability of patients' statements.

doi: 10.2340/00015555-2947
Acta Derm Venereol 2018; 98: 722–727

Table I. Validated sleep questionnaires

Questionnaire	Year of publication	Items *n*	Description
Athens Insomnia Scale (AIS)	2000	8	Identification of sleep impairment by asking for: sleep induction, awakenings during the night, final awakening, total sleep duration, sleep quality, well-being during the day, functioning capacity, sleepiness during the day (15).
Bergen Insomnia Scale (BIS)	2008	6	These items refer to: sleep onset, maintenance and early morning wakening insomnia, feeling adequately rested, experiencing daytime impairment, being dissatisfied with current sleep (23).
Epworth Sleepiness Scale (ESS)	1991	8	Estimation of risk to fall asleep in 8 daily situations (24, 25).
Glasgow Sleep Effort Scale (GSES)	2005	7	Measuring sleep effort (26).
Insomnia Severity Index (ISI)	1993	7	Evaluation of the following aspects of sleep: problems with falling asleep, sleep maintenance and waking up too early in the morning, satisfaction with current sleep pattern, interference with daily functioning, impairment of quality of life, level of distress caused by the sleep problem (27).
Medical Outcomes Study Sleep Scale (MOS Sleep)	1992	12	These items concentrate on: sleep latency and maintenance, sleep adequacy and quantity, somnolence and respiratory impairments (28).
Munich Parasomnia Screening (MUPS)	2008	21	Captures parasomnia and nocturnal behaviours (29). No need for further examination, cause this questionnaire only deals with parasomnia and nocturnal behaviours. Therefore it is too specific for utilization in the collective.
Pittsburgh Sleep Quality Index (PSQI)	1989	24	Retrospective estimation of sleep quality and sleep disturbances in the last 4 weeks (12, 13).
Regensburg Insomnia Scale (RIS)	2013	10	Focus on psychological aspects, as well as on quantitative aspects of sleep (14).
Sleep Quality Index (SQI)	1991	8	Consists of the following items: time when falling asleep, insomnia, difficulties falling asleep, disturbed night time sleep, nocturnal awakening, tiredness in the morning, waking up too early in the morning, use of sedative drugs (30).
Stanford Sleepiness Scale (SSS)	1972	1	Assessing alertness (31).

Selection of the 2 questionnaires

In the 4th step, 2 of the investigated sleep questionnaires, containing the most relevant sleep items to patients with CP, were selected for testing in another collective (step 4).This selection was based on the results of the testing of the 12 most frequently asked items in routine sleep questionnaires (step 3).

Testing the 2 selected sleep questionnaires

A total of 88 patients (inclusion criteria: age ≥18 years with CP and thereby caused sleep disorders due to nocturnal pruritus) were included in this part of the study, for which their informed consent was obtained. The participating patients were asked to complete the 2 selected questionnaires twice, once during their visit (for the first time as well as repeatedly) at the Center for Chronic Pruritus and once more after 3–5 weeks (step 5). The aim was to prove whether one of the questionnaires is able to detect the specific sleep restrictions in patients with CP and associated sleep impairment. Moreover, we tried to verify whether one of them is able to determine any possible effects of changing or optimizing the individual anti-pruritic therapy on patients' sleep behaviour after 3–5 weeks. The intensity of pruritus was also assessed at both points in time via the visual analogue scale (VAS, 0–10) and numerical rating scale (NRS, 0–10) (7). Clinical and sociodemographic data were also collected during their visits to the Center for Chronic Pruritus. In addition, the patients were asked about possible diseases or health-related conditions that might have a negative impact on the quality of their sleep. They were asked to complete the Hospital Anxiety and Depression Scale (HADS) (8, 9), Dermatology Life Quality Index (DLQI) (10) and ItchyQol (6) during the first session of data collection. The type of medical treatment was not analysed further, since each patient received a standard topical or routine systemic therapy in accordance with the guidelines, but still experienced pruritus (11).

Statistical analysis

Statistical analysis was performed with software IBM SPSS Statistics for Windows Release 23 (2015; Chicago, IL, USA). The results were presented using descriptive statistics. The level of significance was found at $p<0.05$ and to be 2-sided. The differences between the non-normally distributed parameters were analysed between 2 independent groups using the Mann–Whitney *U* test. By means of a Wilcoxon test, the differences between the non-normalized parameters were able to be analysed between 2 dependent groups. The χ^2 test and the Fisher's exact test were used to compare the distribution of the categorical parameter between 2 independent groups.

The study was approved by the local ethics committee (2015-430-f-S) and registered in the DRKS (German Clinical Trials Register, DRKS-ID: DRKS00009767).

RESULTS

Literary research

A brief description and comparison of the validated questionnaires selected for examination, with regard to year of publication and number of items, are illustrated in **Table I** (step 1).

Interviews and testing the items most frequently asked in routine sleep questionnaires

A total of 50 patients with CP, irrespective of the presence of pruritus-caused sleep disturbances, were enrolled in this part of this study, including 25 women (mean ± standard deviation [SD] age 60 ± 14 years, range 36–83) and 25 men (mean age 57 ± 22 years, range 21–86). Asked about sleep-impacting comorbidities, 45 (90%) patients reported having no knowledge of having any pre-existing sleep

Table II. Results of the interviews (*n*= 50 with chronic pruritus)

Reported pruritus-related sleep impairments	Patients[a] *n* (%)
Nocturnal scratching	36 (72)
Awakening due to pruritus	22 (44)
Increased pruritus intensity due to warmth in bed	10 (20)
Reactions towards the occurrence of nocturnal pruritus	
Application of emollients	25 (50)
Intake of systemic antipruritic therapies	18 (36)
Scratching	17 (34)
Application of cooling agents to the skin	13 (26)
Attempting to remain calm	10 (20)
Alterations to their bedtime routine	8 (16)
Sleepiness during the day because of the adverse effects of a systemic antipruritic therapy	3 (6)
Pruritus while changing clothes prior to going to bed	3 (6)

[a]Number of patients who mentioned this kind of impairment in the interview.

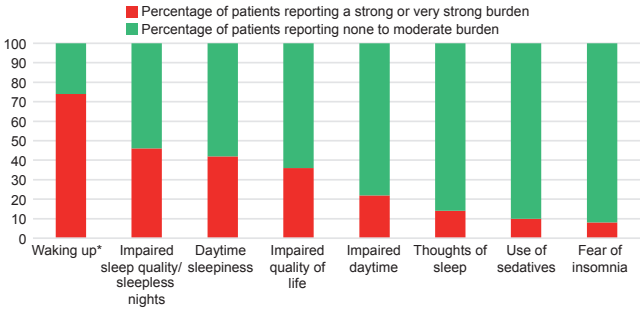

Fig. 1. Result of analysis of qualitative items of sleep questionnaires: relevance to patients with chronic pruritus ($n = 50$). *In the middle of the night or too early in the morning.

disorder unrelated to their pruritus. Four patients (2 men, 2 women) described sleep apnoea to be the cause of their sleep disturbances and one patient reported having nightmares unrelated to pruritus. The results of the interviews (step 2) are presented in **Table II**.

Testing the items most frequently used in the examined questionnaire (step 3) revealed the following results. In general, the 12 tested items were divided into 2 subgroups, 8 of which deal with qualitative aspects of sleep and the remaining 4 items concern quantitative statements.

The results of the qualitative items are described in **Fig. 1**. "Waking up in the middle of the night or too early in the morning" constitutes the single most relevant item of the questionnaire (74% of patients reported a strong or very strong burden). Thus, the detection of periods of awakening is a relevant component in the assessment of sleep behaviour in patients with CP due to its high prevalence in the examined collective, followed by "impaired sleep quality/sleepless nights" (46%) and "daytime sleepiness" (42%). The remaining 5 items "impaired quality of life" (36%), "impaired daytime" (22%), "thoughts of sleep" (14%), "use of sedatives" (10%) and "fear of insomnia" (8%) were less frequently mentioned and therefore less relevant to the assessment of sleep patterns in patients with CP. The last 4 items were utilized to assess the quantity of sleep and its impairment in order to provide an overview of their sleep behaviour. These could therefore be classified as being detrimental to the evaluation of patients' sleep. It was found that the mean ± SD time of retirement to bed was 22.56 ± 1 h 18 min, while the mean ± SD time to get up was 07.04 h ± 1 h 2 min. Most patients required 38 ± 39 min to fall asleep, while 6 h and 10 min ± 1 h 42 min was the mean duration of sleep.

Selection of the 2 questionnaires

The selection of the questionnaires (step 4) was based on the results of the testing of the most frequently asked items in routine sleep questionnaires (step 3). The Pittsburgh Sleep Quality Index (PSQI) (12, 13) and the Regensburg Insomnia Scale (RIS) (14) (Table SI[1]) were then selected based on the importance of 7 and 6 of their items, respectively (Table SII[1]). The Athens Insomnia Scale (15), a measuring tool recommended by the IFSI, also contains several important items (5 important items); however, there is currently no validated German language version available. Consequently, this questionnaire was not implemented into this study.

Testing the 2 selected sleep questionnaires

For the 5th step, 88 patients with CP and sleep disorders due to nocturnal pruritus completed the questionnaires on day 1 and after 4 weeks (3.94 weeks ± 0.7). Of these patients, 21

[1]https://doi.org/10.2340/00015555-2947

Table III. Description of the collective which completed the two selected questionnaires (n=88 with chronic pruritus (CP))

	Total collective $n = 88$	Sleepers $n = 21$	Non-sleepers $n = 67$	p*[a]
Demographics				
Sex, n (%)[b]				0.171
Women	45 (51.1)	8 (38.1)	37 (55.2)	
Men	43 (48.9)	13 (61.9)	30 (44.8)	
Age, years, mean ± SD (range)[c]	59 ± 17 (21–86)	57 ± 17 (21–76)	59 ± 17 (22–86)	0.622
Pruritus group, n (%)[b]				0.350
Chronic pruritus on inflamed skin	30 (34.1)	5 (23.8)	25 (37.3)	
Chronic pruritus on non-inflamed skin	31 (35.2)	10 (47.6%)	21 (31.3)	
Chronic pruritus, presenting with chronic scratch lesions	27 (30.7)	6 (28.6)	21 (31.3)	
Pruritus category, n (%)[d]				0.346
Dermatological diseases	39 (44.3)	6 (28.6)	33 (49.3)	
Systemic diseases	4 (4.5)	1 (4.8)	3 (4.5)	
Neurological disease	13 (14.8)	5 (23.8)	8 (11.9)	
Psychiatric diseases	3 (3.4)	0	3 (4.5)	
Mixed	28 (31.8)	9 (42.9)	19 (28.4)	
Others	1 (1.1)	0	1 (1.5)	
Duration of pruritus, years, mean ± SD[c]	9 ± 11 ($n = 80$)	9 ± 12 ($n = 20$)	9 ± 11 ($n = 60$)	0.505
Hospital Anxiety and Depression Scale (anxiety)[c]	7.7 ± 3.6 ($n = 73$)	5.8 ± 3.5 ($n = 16$)	8.2 ± 3.5 ($n = 57$)	**0.033**
Hospital Anxiety and Depression Scale (depression)[c]	6.8 ± 4.4 ($n = 72$)	4.6 ± 4.4 ($n = 16$)	7.4 ± 4.2 ($n = 56$)	**0.020**
Dermatology Life Quality Index[c]	10 ± 5.8 ($n = 70$)	7.6 ± 5.6 ($n = 15$)	10.6 ± 5.7 ($n = 55$)	0.060
ItchyQoL[c]	3.2 ± 0.7 ($n = 71$)	2.8 ± 0.7 ($n = 16$)	3.3 ± 0.7 ($n = 55$)	**0.010**

p*[a]: Level of significance: comparison between sleepers and non-sleepers day 1. [b]χ^2 test. [c]Mann–Whitney U test. [d]Fisher's exact test.
Sleepers: no sleep-related disturbances due to chronic pruritus after 4 weeks; Non-sleepers: sleep-related disturbances due to chronic pruritus after 4 weeks; SD: standard deviation. Significant difference is given in bold.

Table IV. Comparison of sleepers ($n=21$) and non-sleepers ($n=67$) according to pruritus intensity

	Total collective		Sleepers		Non-sleepers					
Pruritus intensity	Day 1 Mean±SD [median]	Day 28 Mean±SD [median]	Day1 Mean±SD [median]	Day 28 Mean±SD [median]	Day 1 Mean±SD [median]	Day 28 Mean±SD [median]	$p^{*a,e}$	$p^{*b,e}$	$p^{*c,f}$	$p^{*d,f}$
VAS average 24 h	5.9±2.3 [6.5] ($n=83$)	4.3±2.3 [4.0] ($n=84$)	5.9±2.1 [6.9] ($n=20$)	3.2±1.8 [3.0] ($n=21$)	5.9±2.4 [6.0] ($n=63$)	4.7±2.3 [4.5] ($n=63$)	0.868	**0.008**	**<0.001**	**0.001**
VAS worst 24 h	8.0±1.9 [8.4] ($n=83$)	6.8±2.4 [7.2] ($n=82$)	8.1±1.9 [8.8] ($n=20$)	5.6±2.7 [6.5] ($n=19$)	7.9±1.9 [8.2] ($n=63$)	7.2±2.2 [7.6] ($n=63$)	0.720	**0.015**	**0.001**	**0.010**
VAS today	5.1±2.7 [5.1] ($n=82$)	4.0±2.7 [3.8] ($n=84$)	4.7±2.6 [5.0] ($n=19$)	2.6±1.9 [2.0] ($n=20$)	5.2±2.7 [5.4] ($n=63$)	4.5±2.7 [4.5] ($n=64$)	0.532	**0.005**	**0.009**	0.245
NRS average 24 h	5.3±2.5 [6.0] ($n=83$)	4.4±2.6 [4.0] ($n=86$)	5.1±2.5 [5.0] ($n=19$)	2.8±1.8 [2.0] ($n=21$)	5.4±2.6 [6.0] ($n=64$)	4.9±2.7 [4.0] ($n=65$)	0.674	**0.001**	**0.007**	0.269

p^{*a}: Level of significance: comparison between sleepers and non-sleepers day 1; p^{*b}: Level of significance: comparison between sleepers and non-sleepers day 28; p^{*c}: Level of significance: comparison sleepers day 1/day 28; p^{*d}: Level of significance: comparison non-sleepers day 1/day 28. [e]Mann-Whitney *U* test. [f]Wilcoxon test. Sleepers: no sleep-related disturbances due to chronic pruritus (CP) after 4 weeks; Non-sleepers: sleep-related disturbances due to CP after 4 weeks. VAS: visual analogue scale; NRS: numerical rating scale; SD: Standard deviation. Significant difference is given in bold.

(23.86%) reported after 4 weeks (day 28) that pruritus no longer negatively influenced their sleep. The latter group was classified as "sleepers", whereas 67 (76.14%) patients were found to have persistent nocturnal pruritus following the second assessment. This group was thus classified as "non-sleepers" (**Tables III and IV**). All patients were asked about comorbidities that might influence their sleep, in addition to pruritus (Table SIII[1]). No significant differences between sleepers and non-sleepers were observed on day 1 ($p=0.874$; χ^2 test) and day 28 ($p=0.671$; χ^2 test). Furthermore, when comparing days 1 and 28, there was no noticeably significant difference between the groups due to comorbidities with a negative influence on sleep (Wilcoxon test, sleepers: $p=1.0$, non-sleepers: $p=0.317$).

Regensburg Insomnia Scale

As shown in **Table V**, sleepers were found to achieve values on the total scale on day 1 in the pathological range (>12) and values on day 28 that can be considered normal (≤12). In particular, the use of the items "early awakening", "easy awakening" and "sleepless nights" point to a significant reduction in sleep impairment in sleepers between days 1 and 28. Non-sleepers obtained higher values for each item, as well as for the total scale days 1 and 28, with no significant differences between the 2 measuring points. There were no significant differences between days 1 and 28 in the group of sleepers and non-sleepers regarding their bedtime and the time to get out of bed (Table SIV[1]).

Pittsburgh Sleep Quality Index

According to the overall index sleepers and non-sleepers both improved between days 1 and 28, without a significant distinction between the 2 groups. They both stayed in the pathological range (overall index higher than 5 points). In detail, sleepers experienced a significant improvement in their sleeping behaviour within the 4 weeks with regard to the components "sleep latency" and "sleep disorders", as well as to the items "sleep latency more than 30 min", "impaired sleep maintenance", "heat" and "pain". In contrast, non-sleepers achieved significant differences in the components "impaired sleep quality" and "sleep duration" and in the item "impaired sleep quality". Nevertheless, non-sleepers achieved higher values on days 1 and 28 for nearly each item, component and the overall index than the sleepers group (with 1 exception, "nightmares") (**Table VI**). The results of the items regarding patients' bedtime are shown in Table SV[1] ("time to go to bed", "time to fall asleep", "time to get up", "sleep duration").

DISCUSSION

Patients with CP frequently have nocturnal pruritus and associated sleep disturbances (5, 16). There is no vali-

Table V. Results of items from the Regensburg Insomnia Scale used by patients with chronic pruritus ($n=88$)

	Sleepers			Non-sleepers		
Items	Day 1 Mean±SD	Day 28 Mean±SD	$p^{*a,c}$	Day 1 Mean±SD	Day 28 Mean±SD	$p^{*b,c}$
1. Sleep latency	0.8±0.9 ($n=21$)	0.4±0.6 ($n=21$)	0.055	1.2±1.2 ($n=65$)	1.1±1.2 ($n=65$)	0.400
2. Sleep duration	1±0.8 ($n=20$)	0.7±0.6 ($n=20$)	0.266	1.2±0.8 ($n=63$)	1.2±0.9 ($n=63$)	0.602
3. Sleep continuity	2.4±1.2 ($n=21$)	2.1±1.2 ($n=21$)	0.441	2.3±1.4 ($n=66$)	2.5±1.3 ($n=66$)	0.537
4. Early awakening	2.1±1.2 ($n=21$)	1.6±1.1 ($n=21$)	**0.016**	2.3±1.2 ($n=65$)	2.3±1 ($n=65$)	0.880
5. Easy awakening	1.8±1.4 ($n=20$)	1.4±1.3 ($n=20$)	**0.035**	2.2±1.2 ($n=67$)	2.1±1.2 ($n=67$)	0.265
6. Sleepless nights	1.6±1 ($n=21$)	1.00±1.1 ($n=21$)	**0.033**	1.9±1.1 ($n=67$)	1.9±1 ($n=67$)	0.881
7. Thinking about sleep	1.2±0.9 ($n=21$)	0.9±0.9 ($n=21$)	0.183	1.9±1.1 ($n=67$)	1.8±1.1 ($n=67$)	0.611
8. Fear of insomnia	0.8±1.1 ($n=21$)	0.3±0.6 ($n=21$)	0.074	1.5±1.3 ($n=67$)	1.4±1.2 ($n=67$)	0.744
9. Impaired daytime	1.9±1.1 ($n=21$)	1.6±0.9 ($n=21$)	0.391	2.3±1.1 ($n=67$)	2.2±1.1 ($n=67$)	0.424
10. Sedative intake	0.3±0.6 ($n=21$)	0.3±0.7 ($n=21$)	1.0	1±1.5 ($n=67$)	0.9±1.3 ($n=67$)	0.355
Overall value of the scale Normal value: ≤12	13.3±5.7 ($n=19$)	10.4±5.9 ($n=19$)	**0.004**	17.8±6.2 ($n=59$)	17.0±5.5 ($n=59$)	0.146

p^{*a}: Level of significance: comparison sleepers day 1/day 28; p^{*b}: Level of significance: comparison non-sleepers day 1/day 28. [c]Wilcoxon test. Sleepers: no sleep-related disturbances due to chronic pruritus after 4 weeks; Non-sleepers: sleep-related disturbances due to chronic pruritus after 4 weeks. Significant difference is given in bold.

Table VI. Results of the Pittsburgh Sleep Quality Index (items, components, index) used by patients with chronic pruritus ($n = 88$)

	Sleepers			Non-sleepers		
	Day 1 Mean ± SD	Day 28 Mean ± SD	$p^{*a,c}$	Day 1 Mean ± SD	Day 28 Mean ± SD	$p^{*b,c}$
Items						
Sleep latency more than 30 min	2.8 ± 1.1 ($n = 21$)	2.1 ± 0.9 ($n = 21$)	**0.002**	3 ± 1.1 ($n = 67$)	2.8 ± 1.1 ($n = 67$)	0.246
Impaired sleep maintenance	3.2 ± 1.1 ($n = 21$)	2.5 ± 1.1 ($n = 21$)	**0.014**	3.5 ± 0.8 ($n = 67$)	3.4 ± 0.9 ($n = 67$)	0.289
Strangury	2.8 ± 1.3 ($n = 21$)	2.8 ± 1.2 ($n = 21$)	0.871	3 ± 1 ($n = 67$)	3.1 ± 1.1 ($n = 67$)	0.235
Breathing problems	1.1 ± 0.7 ($n = 21$)	1.1 ± 0.4 ($n = 21$)	1.0	1.5 ± 0.9 ($n = 67$)	1.5 ± 0.9 ($n = 67$)	0.802
Cough/snoring	1.5 ± 1 ($n = 21$)	1.6 ± 1 ($n = 21$)	1.0	1.6 ± 1 ($n = 67$)	1.8 ± 1 ($n = 67$)	0.137
Freezing	1.5 ± 0.8 ($n = 21$)	1.4 ± 0.7 ($n = 21$)	0.563	1.7 ± 1 ($n = 67$)	1.7 ± 1 ($n = 67$)	0.812
Heat	2 ± 1.1 ($n = 21$)	1.5 ± 0.8 ($n = 21$)	**0.039**	2.1 ± 1.1 ($n = 67$)	2.1 ± 1 ($n = 67$)	0.653
Nightmare	1.8 ± 0.9 ($n = 21$)	1.8 ± 1.1 ($n = 21$)	1.000	1.7 ± 0.9 ($n = 67$)	1.6 ± 0.9 ($n = 67$)	0.170
Pain	2.1 ± 1.2 ($n = 21$)	1.6 ± 0.9 ($n = 21$)	**0.023**	2.2 ± 1.2 ($n = 67$)	2.1 ± 1.2 ($n = 67$)	0.507
Other reasons for impaired sleep	2.6 ± 1.2 ($n = 12$)	2.2 ± 1 ($n = 12$)	0.398	3.2 ± 1.2 ($n = 38$)	3.2 ± 1.1 ($n = 38$)	0.738
Impaired sleep quality	2.5 ± 0.7 ($n = 20$)	2.4 ± 0.7 ($n = 20$)	0.465	2.9 ± 0.7 ($n = 66$)	2.7 ± 0.7 ($n = 66$)	**0.007**
Sedative intake	1.2 ± 0.4 ($n = 21$)	1.3 ± 0.6 ($n = 21$)	0.750	1.9 ± 1.3 ($n = 67$)	1.8 ± 1.2 ($n = 67$)	0.268
Daytime sleepiness	1.7 ± 1 ($n = 21$)	1.6 ± 0.9 ($n = 21$)	0.586	2 ± 1 ($n = 67$)	1.8 ± 1.1 ($n = 67$)	0.170
Everyday tasks	2.7 ± 1 ($n = 21$)	2.4 ± 0.7 ($n = 21$)	0.378	2.9 ± 0.8 ($n = 67$)	3 ± 0.8 ($n = 67$)	0.858
Components						
1. Impaired sleep quality	1.5 ± 0.7 ($n = 20$)	1.4 ± 0.7 ($n = 20$)	0.465	1.9 ± 0.7 ($n = 65$)	1.6 ± 0.7 ($n = 65$)	**0.004**
2. Sleep latency	1.6 ± 1 ($n = 20$)	1.1 ± 0.8 ($n = 20$)	**0.020**	1.9 ± 0.9 ($n = 66$)	1.8 ± 1 ($n = 66$)	0.123
3. Sleep duration	1.4 ± 1.2 ($n = 20$)	0.8 ± 1 ($n = 20$)	0.090	1.8 ± 1 ($n = 66$)	1.5 ± 1.1 ($n = 66$)	**0.022**
4. Sleep efficiency	1.3 ± 1.1 ($n = 20$)	0.8 ± 1.1 ($n = 20$)	0.114	1.9 ± 1.2 ($n = 66$)	1.8 ± 1.1 ($n = 66$)	0.417
5. Sleep disorders	1.6 ± 0.7 ($n = 20$)	1.2 ± 0.5 ($n = 20$)	**0.039**	1.6 ± 0.6 ($n = 66$)	1.6 ± 0.6 ($n = 66$)	0.819
6. Sedative intake	0.2 ± 0.4 ($n = 20$)	0.2 ± 0.6 ($n = 20$)	1.0	0.9 ± 1.3 ($n = 66$)	0.9 ± 1.2 ($n = 66$)	0.508
7. Daytime sleepiness	1.2 ± 0.9 ($n = 20$)	1.2 ± 0.7 ($n = 20$)	0.699	1.7 ± 0.8 ($n = 64$)	1.6 ± 0.8 ($n = 64$)	0.725
Index: Normal value: ≤5	8.6 ± 4.2 ($n = 20$)	6.6 ± 3.7 ($n = 20$)	**0.044**	11.7 ± 3.6 ($n = 65$)	10.8 ± 3.7 ($n = 65$)	**0.026**

p^{*a}: Level of significance: comparison sleepers day 1/day 28; p^{*b}: Level of significance: comparison non-sleepers day 1/day 28. [c]Wilcoxon test. Sleepers: no sleep-related disturbances due to chronic pruritus after 4 weeks; Non-sleepers: sleep-related disturbances due to chronic pruritus after 4 weeks. Significant difference is given in bold.

dated sleep questionnaire specifically designed for these patients. The current study demonstrates that some of the already existing validated sleep questionnaires, available in multiple languages, are appropriate for use in patients with CP.

In the open interviews, we gained an overview of the high degree of impaired sleeping behaviour in patients with CP due to scratching in the night (72%) and nocturnal awakening caused by pruritus (44%).

Based on comparison of the existing sleep questionnaires, we were able to identify the 12 most often asked items, which include 4 quantitative (hours of night sleep) and 8 qualitative (e.g. "waking up in the middle of the night or too early in the morning") aspects. Using these 12 items in patients with CP, we were able to demonstrate that several of them are relevant to this population. The most important aspects of an impaired sleep concern periods of waking up in the night or too early in the morning, reduced sleep quality or the experience of sleepless nights as well as daytime sleepiness.

An evaluation of the quantitative parameters is also essential. The mean ± SD sleep duration per night was 6 h 10 min ± 1 h 42 min, whereas the recommended (e.g. by the National Sleep Foundation) sleep duration for young adults/adults is 7–9 h and for elderly people 7–8 h (17).

In sum, patients with CP experience sleep interruption and disturbances during the night, resulting in reduced sleep quality and shortened sleeping time. The RIS and the PSQI were found to contain most of the relevant items and were therefore selected for testing.

Testing the RIS yielded the most interesting results. Patients classified as sleepers (no sleep-related disturbances due to pruritus at the second visit) achieved a significant reduction in their total RIS value, which was in the normal range by re-assessment after 4 weeks (total value ≤12) (14), whereas non-sleepers remained in the pathological range. The results of the PSQI are more ambiguous than the results of the RIS. Based on this data, we can conclude that the RIS is a useful instrument for assessing nocturnal pruritus in patients with CP.

In this study, a comparison of the general comorbidities with a negative influence on patients' sleep between both groups did not exhibit relevant differences. Previous studies have established a significant connection between sleep quality and psychiatric diseases, such as anxiety and depression (18, 19). Our data support this as non-sleepers have significant higher values for anxiety, depression and an impaired QoL. These factors might prevent improvements in quality of sleep and a positive response to a treatment and should be considered in the evaluation of the results. Anxiety and depression are also known to increase the intensity of pruritus (20). Interestingly, a significant difference in the pruritus intensity between sleepers and non-sleepers was not observed on day 1, whereas on day 28 a significant difference in pruritus intensity could be detected between these groups. Therefore, it could be assumed that an effective pruritus therapy with a significant reduction in pruritus intensity is the basis for sleep improvement in patients with CP. However, as shown in Table IV, the non-sleepers also achieved a significant reduction in VAS average in the last 24 h and in VAS worst in the last 24 h between both measuring points. This overall reduction in intensity is too slight to show a clinical improvement in sleep. However, future studies

should determine the influence and cut-off of the pruritus intensity leading to sleep disturbances.

Despite confirming the usability of sleep questionnaires for patients with CP, various issues associated with nocturnal pruritus, such as the influence of warmth in bed as mentioned in the interviews, are not assessed by current sleep questionnaires, which instead focus on the general aspects of sleep. The use of sleep questionnaires for patients with CP, such as the RIS, is unable to capture all dimensions of a disturbed sleep, but it is a feasible approach to assess many sleep problems in this population. Unless larger analyses focus on specific sleep-related problems due to pruritus, the development of a sleep questionnaire specific to CP is not pragmatic.

Although nocturnal pruritus is well-known in the context of limiting the QoL of patients with CP, its underlying pathophysiological mechanisms require more investigation in order to produce an effective therapy (16, 21, 22), which, without a more detailed measurement and evaluation is unfeasible. In this regard, a more comprehensive insight into the obstacles faced by patients with CP with nocturnal pruritus may be useful for further investigation into its pathophysiological mechanism and corresponding therapies.

The authors have no conflicts of interest to declare.

REFERENCES

1. 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: 291–294.
2. Matterne U, Apfelbacher C, Vogelgsang L, Loerbroks A, Weisshaar E. Incidence and determinants of chronic pruritus: a population-based cohort study. Acta Derm Venereol 2013; 93: 532–537.
3. Matterne U, Apfelbacher C, Loerbroks A, Schwarzer T, Büttner M, Ofenloch R, et al. Prevalence, correlates and characteristics of chronic pruritus: a population-based cross-sectional Study. Acta Derm Venereol 2011; 91: 674–679.
4. Ständer S, Augustin M, Reich A, Blome C, Ebata T, Phan NQ, et al. Pruritus assessment in clinical trials: consensus recommendations from the International Forum for the Study of Itch (IFSI) Special Interest Group Scoring Itch in Clinical Trials. Acta Derm Venereol 2013; 93: 509–514.
5. Lavery MJ, Stull C, Nattkemper LA, Sanders KM, Lee H, Sahu S, et al. Nocturnal pruritus: prevalence, characteristics, and impact on ItchyQoL in a chronic itch population. Acta Derm Venereol 2016; 96: 513–515.
6. Krause K, Kessler B, Weller K, Veidt J, Chen SC, Martus P, et al. German version of ItchyQoL: validation and initial clinical findings. Acta Derm Venereol 2013; 93: 562–568.
7. Reich A, Heisig M, Phan NQ, Taneda K, Takamori K, Takeuchi S, et al. Visual analogue scale: evaluation of the instrument for the assessment of pruritus. Acta Derm Venereol 2012; 92: 497–501.
8. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale – a review of validation data and clinical results. J Psychosom Res 1997; 42: 17–41.
9. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23: 56–62.
10. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. Clin Exp Dermatol 1994; 19: 210–216.
11. Ständer S, Zeidler C, Augustin M, Bayer G, Kremer AE, Legat FJ, et al. S2k Guidelines for the diagnosis and treatment of chronic pruritus – update – short version. J Dtsch Dermatol Ges 2017; 15: 860–872.
12. Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F. Test–retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. J Psychosom Res 2002; 53: 737–740.
13. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989; 28: 193–213.
14. Crönlein T, Langguth B, Popp R, Lukesch H, Pieh C, Hajak G, et al. Regensburg Insomnia Scale (RIS): a new short rating scale for the assessment of psychological symptoms and sleep in insomnia; Study design: development and validation of a new short self-rating scale in a sample of 218 patients suffering from insomnia and 94 healthy controls. Health Qual Life Outcomes 2013; 11: 65.
15. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. Athens Insomnia Scale: validation of an instrument based on ICD-10 criteria. J Psychosom Res 2000; 48: 555–560.
16. Lavery MJ, Stull C, Kinney MO, Yosipovitch G. Nocturnal pruritus: the battle for a peaceful night's sleep. Int J Mol Med Sci 2016; 17: 425.
17. Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. Sleep Health 2015; 1: 40–43.
18. Spira AP, Friedman L, Aulakh JS, Lee T, Sheikh JI, Yesavage JA. Subclinical anxiety symptoms, sleep, and daytime dysfunction in older adults with primary insomnia. J Geriatr Psychiatry Neurol 2008; 21: 149–153.
19. Lopresti AL, Hood SD, Drummond PD. A review of lifestyle factors that contribute to important pathways associated with major depression: diet, sleep and exercise. J Affect Disord 2013; 148: 12–27.
20. Krishnan A, Koo J. Psyche, opioids, and itch: therapeutic consequences. Dermatol Ther 2005; 18: 314–322.
21. Fishbein AB, Vitaterna O, Haugh IM, Bavishi AA, Zee PC, Turek FW, et al. Nocturnal eczema: review of sleep and circadian rhythms in children with atopic dermatitis and future research directions. J Allergy Clin Immun 2015; 136: 1170–1177.
22. Chang Y, Chiang B. Mechanism of sleep disturbance in children with atopic dermatitis and the role of the circadian rhythm and melatonin. Int J Mol Sci 2016; 17: 462.
23. Pallesen S, Bjorvatn B, Nordhus IH, Sivertsen B, Hjornevik M, Morin CM. A New scale for measuring insomnia: the Bergen Insomnia Scale. Percept Mot Skills 2008; 107: 691–706.
24. Kaminska M, Jobin V, Mayer P, Amyot R, Perraton-Brillon M, Bellemare F. The Epworth Sleepiness Scale: self-administration versus administration by the physician, and validation of a French version. Can Respir J 2010; 17: e27–34.
25. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991; 14: 540–545.
26. Broomfield NM, Espie CA. Towards a valid, reliable measure of sleep effort. J Sleep Res 2005; 14: 401–407.
27. Bastien C, Vallieres A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001; 2: 297–307.
28. Hays RD, Stewart AL. Sleep measures. In: Stewart AL, Ware JE, editors. Measuring functioning and well-being: the Medical Outcomes Study approach. Durham (NC): Duke University Press; 1992: p. 235–259.
29. Fulda S, Hornyak M, Müller K, Cerny L, Beitinger PA, Wetter TC. Development and validation of the Munich Parasomnia Screening (MUPS). Somnologie 2008; 12: 56–65.
30. Urponen H, Partinen M, Vuori I, Hasan J. Sleep Quality and Health: Description of the Sleep Quality Index. In: Peter JH, Penzel T, Podszus T, von Wichert P, editors. Sleep and health risk. Berlin: Springer; 1991: p. 555–558.
31. Hoddes E, Zarcone V, Smythe H, Phillips R, Dement WC. Quantification of sleepiness: a new approach. Psychophysiology 1973; 10: 431–436.