Invited review article

Assessment of severity and burden of pruritus

Manuel Pedro Pereira, Sonja Ständer

Department of Dermatology and Center for Chronic Pruritus, University Hospital Münster, Von-Esmarch-Str. 58, 48149 Münster, Germany

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BDI, Beck Depression Inventory;
DLQI, Dermatological Life Quality Index;
DRS, Dynamic Pruritus Score;
EADV, European Academy of Dermatology and Venereology;
HADS, Hospital Anxiety and Depression Scale; HRSD, Hamilton Rating Scale for Depression; IFD, Itch-Free Days; IFSI, International Forum for the Study of Itch; NRS, numerical rating scale; PBI-P, Patient Benefit Index-Pruritus; RCT, randomized controlled trial; SF-36, 36-item short form; SSS, Scratch Symptom Score; VAS, visual analogue scale; VRS, verbal rating scale

ABSTRACT

Chronic pruritus is a complex multifactorial symptom associated with many different diseases that represents a diagnostic and therapeutic challenge for physicians. In order to better manage chronic pruritus, a detailed medical history, individualized diagnostic procedures and treatment approaches are necessary. Treatment should not only take itch into consideration, but also scratching-induced skin lesions and accompanying disorders such as anxiety, depression and insomnia. Various standardized questionnaires and scales have been developed to assist in the characterization and assessment of these parameters. Monodimensional scales (e.g. the visual analogue scale) represent a simple method for assessing pruritus intensity and are frequently used; however, they can easily be confounded and may indicate the level of satisfaction regarding the medical care provided rather than the itch course. The Dynamic Pruritus Score and Itch-Free Days questionnaire enable a closer assessment of patient responses to treatment. Because chronic pruritus has the potential to greatly impact the quality of life, it is important that physicians recognize it as a major issue. The Dermatology Quality of Life Index is an instrument that is used in a variety of dermatological conditions, but may be unsuitable for measuring pruritus of extracutaneous origin. The ItchyQol is a tool designed specifically for those suffering from pruritus. Additional tools, such as the Hospital Anxiety and Depression Scale, take psychiatric comorbidities into consideration. Recommendations from European (EADV-based Task Force Pruritus) and international (International Forum for the Study of Itch) expert groups focusing on assessment instruments for chronic pruritus are also provided in this article.

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Introduction

Pruritus is the most common symptom in dermatology with estimates showing that more than one-third of the patients attending dermatological practices suffer from this symptom, a majority of those chronically. The Global Burden of Disease project listed pruritus as one of the 50 most common inter disciplinary symptoms leading to high burden levels. Chronic pruritus, i.e. pruritus lasting longer than 6 weeks, affects almost one fifth of the general population leading to great impairment of quality of life. It should be thoroughly investigated, since not only dermatological conditions cause chronic itch, but also systemic, neurologic or psychiatric diseases. Furthermore, different diseases may be present simultaneously or, in some instances, the cause may remain unknown.

Since pruritus is a subjective symptom of multifactorial nature, its assessment may be challenging. The International Forum for the Study of Itch (IFSI) established a classification system dividing chronic pruritus into one of three categories upon physical examination: i) chronic pruritus on inflamed skin; ii) chronic pruritus on normal skin and iii) chronic pruritus with severe scratch lesions. This classification helps the attending physician to direct the diagnostic efforts in order to determine the underlying cause. Many factors, such as location, duration of the disease, intensity and accompanying sensory symptoms (e.g. burning, tingling or stinging sensations), should be taken into account. Moreover psychiatric comorbidities (e.g. depression and anxiety), current mood or stress levels may affect the pruritus perception and appraisal and thereby confound the assessment of the symptom. In order to enable a
comprehensive view on the symptom and current level of confounders, multiple instruments are recommended in the assessment of chronic pruritus.5

Only a minority of patients suffering from chronic pruritus has access to specialized centers. As a result the underlying causes are often not comprehensively investigated and patients may receive sub-standard care. Additionally treatment costs may be high and some of the available therapy options are not covered by national health systems or by health insurances. A higher awareness of the societal burden is thus necessary in order to achieve a better standardized care. Measuring itch is essential not only for the proper care of the individual patients but also to raise awareness of the relevance of chronic pruritus in health care. Furthermore, in randomized clinical trials (RCT) measurement of pruritus should be performed in a standardized manner to allow comparisons between studies and ensure the highest medical and professional standards.

This review article aims to give an overview of the available instruments for the measurement of itch (Table 1) and to give recommendations for their use in patient care and in RCTs.

Pruritus intensity

An assortment of scales has been developed in order to better assist physicians in assessing pruritus intensity. The intensity can be quickly measured with monodimensional scales that are routinely used in clinical care and RCTs. Patients can be asked to rate their itch intensity from 0 (“no itch”) to 10 (“worst imaginable itch”) with the numerical rating scale (NRS; Fig. 1). Another monodimensional scale, the visual analogue scale (VAS), provides patients with the opportunity to indicate the intensity of their itch by marking on a 10 cm long, ruler-shaped scale. Both endpoints are marked with a number corresponding to the intensity, with 0 representing “no itch” and 10 the “worst imaginable itch” (Fig. 2). A variation of this scale demonstrates to patients that at one-third of the length corresponding to 3.3 cm, they would normally feel the urge to scratch. However, this biases the patient and should not be used in RCTs. Scores below 3.0 VAS/NRS points are generally associated with mild itch, whereas scores higher than 6.9 illustrate severe itch. Scores above 9.0 represent a very severe itch.6 The verbal rating scale (VRS) is a further monodimensional scale that allows patients to describe their itch intensity by means of gradually rising adjectives (0 — no itch, 4 — worst imaginable itch).7 The NRS, VAS and VRS have been validated in large-scale studies consisting of chronic pruritus patients with pruritic dermatoses or pruritus of various origins. These instruments have high reproducibility and there was a high correlation between scales.6–8 There is still no consensus on the best recall period (12 h, 24 h, 3 or 7 days). In RCTs it is common to address the past 24 h. However, these scales only provide the itch intensity at a specific point in time, being susceptible to confounders such as current mood, stress and comorbidities. Multidimensional scales, such as the Itch Severity Scale,1 a self-reported seven-item scale, can be alternatively used but are not routinely established in clinical care. They combine itch intensity, sleep disturbance and burden by the symptom aiming to give a comprehensive rating of the itch impact. However, patients may face difficulties in unequivocal selection of a category. Thus, these instruments are not recommended to be used in RCTs until more research describes their validity in chronic pruritus assessment.

Scratch lesions and scratching activity

Scratch lesions may be an indirect sign indicating the severity of a pruritic condition (Fig. 3). The Scratch Symptom Score (SSS) and the Prurigo Activity Score are descriptive tools that have been constructed for use in monitoring scratch lesions over time.9 However, they are not validated yet limiting their use in RCTs. Alternatively, wrist actigraphy, a non-invasive method of monitoring motor activity, can be utilized to assess scratching behavior in humans.11 Accelertometers are devices that measure proper acceleration and can be used for similar purposes. Both methods of objectively measuring scratch activity are mainly used for research purposes or RCTs but not in daily practice. However, scratch lesions and scratching activity do not necessarily demonstrate the severity of the pruritus. To prevent the development of lesions, some patients refrain from scratching despite intense pruritus, while others wear gloves, apply ice or cold water to the affected areas, or adopt other various strategies to cope with the pruritus and hamper the urge to scratch.12 In some cases, such as in hydroxyethyl starch-induced pruritus, scratching enhances the itch sensations and thus patients avoid to scratch and usually do not develop scratching lesions. On the other hand, patients with an automatic scratching behavior may present with extensive lesions in spite of an absence

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of itch. Data gathered from instruments measuring scratching behavior or lesions should therefore be cautiously interpreted as it is more suitable for monitoring the progress of the pruritic condition rather than assessing its severity.5

Instruments for assessing the course of pruritus

Several instruments that monitor the course of itch have been developed by researchers. The Dynamic Pruritus Score (DPS) is a practical tool that can be utilized for follow-up visits of patients with chronic pruritus. Patients are asked to rate their current level of pruritus in comparison to their previous visit. This instrument could be recently validated, showing high reliability and validity.13 While monodimensional scales as the VAS or NRS assess itch intensity at one specific point in time, the DPS provides information on the direction of the itch development, i.e. whether it is getting better or worse with treatment.

Another option is the multidimensional 5-D itching scale, which was designed to evaluate several components of chronic pruritus, including the affected areas of the body, itch intensity, course of itch through the day, disability induced by the pruritus and whether or not the symptom has changed in the past few weeks, and if so, how (5-D’s: degree, duration, direction, disability and distribution).14 Alternatively, the Itch-Free Days (IFD) questionnaire is both simple and useful for observing improvements during treatment. This questionnaire was recently validated and will be available soon. It is composed of a set of questions, which describe several parameters related to the itch course. A score calculation enables a comparison of different time-points of assessment.

Other additional instruments, such as the pruritus-specific Patient Benefit Index (PBI-P), have been developed to determine the benefits gained from treatment and the degree of global satisfaction.15 This questionnaire assesses the relevance of 27 possible therapeutic benefits for the patient prior to treatment and the extent to which they were met post-treatment. A weighted score is then determined based on the therapeutic benefits relevant to the individual patient. Furthermore, the PBI-P has been validated for chronic pruritus patients and has proven a high correlation with scores from the VAS and Dermatological Life Quality Index (DLQI).16

In recent years, there has been an increasing interest in modern technologies as instruments for monitoring pruritus. A patient-oriented, mobile software application for Android, ItchApp®, was recently developed and validated for use as a computerized diary. It can be utilized by patients to store self-reported data regarding the course of their itch. The app was developed with a user-friendly design in mind and is consequently viewed as a helpful tool for both the clinical trials and the clinical monitorship of chronic pruritus patients.17

Psychiatric comorbidities

Psychiatric comorbidities such as anxiety and depression often accompany chronic pruritus, particularly in patients with long-standing symptoms and unresponsive to treatment. It is crucial to address this issue in order to extensively assess pruritus patients. The Hospital Anxiety and Depression Scale (HADS) is the most widely used instrument and is comprised of two scales that analyze anxiety and depression. It can also conveniently be used to observe the development of these aspects over time. A high score in either scale signals a possible pathological finding to the attending clinician, who consequently discusses the possibility of a concomitant psychiatric treatment with the patient.18,19 The Beck Depression Inventory (BDI)20,21 and the Hamilton Rating Scale for Depression (HRSD)22 are other valuable tools that can be used to screen for depression in patients with somatic disorders.

Quality of life

Chronic pruritus can greatly reduce patient quality of life.23 For this reason, there are a variety of tools available that assess the quality of life of affected patients. The ItchyQol was developed specifically for pruritic conditions and focuses not only on the impact of pruritus on daily activities, but also on the characteristics of the symptoms and on the level of psychological strain.24,25 The DLQI constitutes an alternative instrument for both pruritus (in the context of dermatoses or severe scratch lesions) and other dermatological conditions.26 The DLQI is widely used and has already been validated. Furthermore, its usefulness has been established for patients with pruritic conditions of cutaneous

Fig. 3. Scratch lesions. Pruritus of different origins may lead to scratch lesions. Two examples of chronic pruritus patients with scratching lesions are seen. A: a patient with atopic dermatitis exhibits excoriations; B: prurigo nodularis can be seen in a patient with diabetogenic pruritus.

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Assessment of chronic pruritus in clinical trials

The multifactorial nature of chronic pruritus contributes to its refractoriness and need for comprehensive diagnostic procedures and lengthy therapies. A detailed medical history and individualized diagnostic procedures and approaches to treatment are thus required. It is important to treat visible scratch lesions and accompanying disorders, including psychiatric comorbidities and sleep disorders, in addition to the itch itself. In order to adequately manage chronic itch, it is necessary to adopt a multidisciplinary approach to treatment.29,30

A detailed medical history and individualized diagnostic procedures and approaches to treatment are required due to the complex multifactorial nature of chronic pruritus. Standardized questionnaires provide attending physicians with the opportunity to gain valuable information during each visit. Although no international standardized questionnaire has been developed yet, a few options such as the American31 or German Itch Questionnaire (“APG-Questionnaire”), the Eppendorf Itch Questionnaire and the Münster Neuroderm Questionnaire, are currently available.32,33 These questionnaires provide various information on the pruritic disease, for instance regarding the intensity, quality and location of pruritus, the duration of the disease and alleviating and aggravating factors.

At each visit to the doctor’s office, patients may be asked to complete questionnaires on various topics, including the characteristics of the itch, psychiatric comorbidities (e.g. HADS), itch intensity (e.g. NRS or VAS), impairment of the quality of life (e.g. DLQI) and benefits achieved by treatment from the patients’ point of view (PBI-P).34 The first questionnaire on the characteristics of itch should only be completed during the initial visit, while the subsequent questionnaires serve as convenient follow-up tools. The attending physician can thus quickly obtain the relevant information, determine any new developments in these parameters during follow-up visits and examine how they have been influenced by the therapies. A European network of itch experts reached an agreement that pruritus intensity and impact on quality of life are the most relevant parameters to assess in the clinical care.35 The need for a detailed and methodical, physician-obtained, pruritus-specific medical history is another essential aspect to consider. The affected locations, comorbidities, co-medications and alleviating measures should be documented during the initial visit. Previous therapeutic attempts and their side effects, current medications and comorbidities should also be assessed.34

Chronic pruritus presents a therapeutic challenge due to its complexity and multidisciplinary nature. Management of the symptom can be difficult in a general practice or a dermatological office. Centers specializing in pruritus are thus vital in providing specialist and multifactorial treatment. Many also offer inpatient care to patients, as well as extensive diagnostics (e.g. imagiology to exclude a neoplastic cause, food intolerance tests) and acute treatment with off-label substances (e.g. aprepitant, a neurokinin-1 receptor antagonist) or intravenous drugs (e.g. naloxone for cholestatic pruritus).34

Assessment of chronic pruritus in clinical trials

It is recommended to include patient-reported outcomes in RCTs in order to demonstrate the therapeutic success from the patient’s point of view.7 Therapeutic benefits, overall satisfaction and the impairment of quality of life are associated parameters that are important to assess. These aspects can be assessed as single-point (e.g. symptom intensity; NRS) or two-point (e.g. DPS) assessment during the trial (e.g. before and after treatment).

Global initiatives such as the special interest group “Scoring itch in clinical trials” of the IFSI or the “Task Force Pruritus”, a network of experts of the European Academy of Dermatology and Venereology (EADV), are currently focused on reaching an international consensus regarding outcome proposals for RCTs. Monodimensional scales that evaluate pruritus intensity are the most widely adopted outcome tools (e.g. the VAS or NRS). These scales, however, produce subjective data that may reflect satisfaction rather than the itch intensity. Physicians are therefore urged to explain the purpose of the scale, as well as perform a test run, prior to beginning the study. There are also methodological aspects to consider. A consensus regarding the frequency with which this outcome should be assessed throughout a RCT (daily journal or only during study visits) or per day (once per day or several times per day) has yet to be reached. The outcomes themselves may vary between RCTs and depending on the study. Some studies focus on the mean itch intensity, while others concentrate on the most intense itch as the primary outcome.

The IFSI recommends that RCTs also include, in addition to data taken from the VAS, additional patient-reported outcomes such as those regarding quality of life, resulting psychiatric comorbidities and sleep disorders.

Outcomes on the course of the symptom may provide more sensitive data compared to static scales assessing symptom intensity.36 Therefore newly developed tools evaluating the course of the pruritus may be in foreground in future RCTs. Monitoring instruments (e.g. the DPS, IFD) are still infrequently used in RCTs and require swift validation. Evaluating the benefits from treatment from the patients’ point of view provides indispensable information. The PBI should thus be implemented for use in RCTs. Scales that examine psychiatric comorbidities (e.g. the HADS and BD urgency) also function as a screening tool for unsuitable study patients and contribute with vital information on study participants’ well-being during RCTs. Scales developed for determining sleep impairment (e.g. the Stanford and Epworth Sleepiness Scales and the Athens Insomnia Scale) may also be adopted for use in providing supporting information. Other scales are important for the insight they provide through determining the impact on patients’ quality of life. Although the ItchyQol comprises a valid alternative, the DLQI remains the most widely used tool.34

A general agreement of international medical communities on which instruments are best suited for use in RCTs on chronic pruritus would allow for comparisons between studies and ensure the highest medical and professional standards. The IFSI (www.itchforum.org) and EADV (http://www.eadv.org/scientific/task-forces/) created a platform, which enables a discussion of these issues.

Conclusion

Chronic pruritus is a complex condition characterized by a multifactorial nature. It is thus necessary to adopt a standardized
approach for the management of affected patients. Scales utilized to measure itch intensity are frequently used in clinical practice; however, additional instruments assessing the itch intensity, psychiatric comorbidities, impact on patient quality of life and patient satisfaction should also be integrated into the routine care of chronic pruritus. A consensus on which instruments to use for assessments in RCTs should be reached in order to ensure the highest standards.

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Conflict of interest

The authors have no conflict of interest to declare.

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