

Urticaria and Quality of Life

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Abstract

The common perspective of physicians on chronic urticaria (CU) refers to a benign disorder with no pain and no threat to function or life. Health-related quality-of-life (HRQOL) tools have demonstrated the extent to which physicians underestimate the impact of this disorder. From the patient perspective, CU affects as many dimensions of the HRQOL as some life-threatening diseases or well-recognized disabling chronic skin disorders, such as psoriasis or atopic dermatitis. Pruritus as well as swelling and wheals triggered by unavoidable events, such as pressure or sweating, greatly contribute to HRQOL impairment. Recent trials have suggested that dermatology-specific HRQOL instruments could be more relevant than more objective severity scores when studying and comparing the benefit of various therapeutic strategies in chronic idiopathic urticaria.

Index Entries

Urticaria; angioedema; quality of life; severity; therapeutic trials; antihistamines.

Introduction

Health-related quality of life (HRQOL) can be defined as the way an individual perceives and reacts to health status and other nonmedical aspects of his or her life (1), including physical and emotional well-being and satisfaction with social function (2). In its chronic form, urticaria can interfere with HRQOL in a way that is often underestimated.

How Relevant Is the Measure of QOL in a Skin Disorder Like Chronic Urticaria?

Because the skin is the most visible organ of the human body and the face and hands are very important in communication, skin that appears healthy is essential for positive self-perception and social life. Because it is the best-

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equipped organ in sensitive receptors, any disturbance can have a great impact on physical and mental well-being. One can easily understand that skin diseases—even those with a benign course—can alter the QOL in the same way as more debilitating and life-threatening diseases (3,4). The impact of a disorder on the QOL reflects the patient's perspective on the consequences of this disorder, which can be very different from the physician's perspective. The physician usually focuses his or her estimation of the severity on the threat to life and on functional disabilities, whereas the patient may value different factors that could interfere with daily life, social relationships, comfort, and image. The HRQOL measures are more or less linked to the so-called objective measures of lesions (size, number, thickness, erythema, etc.) of skin disorders, but there are great discrepancies between the two assessments, making HRQOL assessments meaningful and valuable. HRQOL measures are not only important for evaluating the burden of a disease but also for assessing the therapeutic efficacy. In this regard, HRQOL assessment combines both the advantages and the drawbacks of a therapeutic strategy in a single measure and, therefore, is likely a good reflection of the benefit to the patient.

Urticaria is a frequent dermatological disease characterized by the occurrence of transient itching wheals. Chronic urticaria (CU) is defined by the recurrence of the lesions over a time period exceeding 6 wk. When an etiological factor is identified and eradicated, the course of lesions can be controlled. However, most CU stay undocumented and, therefore, are referred to as chronic idiopathic urticaria (CIU), which in practice, should be considered as an autonomous disorder of unknown etiology, rather than as an allergic disorder in which the allergen has not yet been detected. Because of the chronic discomfort induced by pruritus, the anxiety induced by relapsing course, and the lack of specific cause and because

the impairment of the social life is linked to unpredictable attacks of pruritus and swelling, one can expect that CIU effects the QOL of patients. However, few studies have focused on the impact of CIU on HRQOL.

How is QOL Measured?

HRQOL tools with good metrological properties have been developed, assessed, and validated. The most commonly used tools are psychometric self-questionnaires. Responses to these questions aggregate into domains or dimensions that explore different components of QOL, such as physical dimension (physical abilities and their consequences in everyday life), psychological dimension (self-perception, anxiety, depression, etc.), social relationships (family, relatives, sexual, work, etc.), and somatic dimension relative to symptoms such as pain. There are different types of instruments to measure HRQOL, all of which can be used in CIU. Some provide overall scores, whereas others provide multidimensional profiles. Generic tools, such as Nottingham Health Profile (NHP; ref. 5) and Medical Outcome Study Short Form 36 (6), can be applied to any disorder and are useful to compare HRQOL impairment in patients suffering from different conditions. However, they may have a low reactivity to particular impairment on the QOL observed in skin disorders. Specific tools relative to a defined group of disorders, such as skin diseases, are more sensitive to changes and, therefore, are useful in evaluating the impact of a therapeutic strategy. The Dermatology Life Quality Index (DLQI; ref. 7) is the oldest dermatology-specific tool, but a few performing instruments have been developed more recently in agreement with a now well-defined methodology (Skindex, VQ-Dermato) (8,9). Finally, hyperspecific tools dedicated to a single disorder are extremely sensitive to change but may lose part of their meaning regarding overall QOL. In this regard, Baiardini et al.

(10) recently developed an urticaria-specific HRQOL instrument called CU-QOL.

What Effect Does CU Have on QOL?

Answering this question requires a reference system to compare the impact of CIU on QOL in other dermatological and nondermatological disorders. A study by O'Donnel et al. (3) used a generic HRQOL tool to compare CIU with cardiac disease. Overall scores of NHP showed that patients with urticaria suffered from considerable loss of energy, sleep disturbance, and emotional upset and that between 38.5 and 56% experienced difficulties in daily life. Comparison of the scores to those of patients with cardiac disease (i.e., patients awaiting coronary artery bypass grafting) showed almost identical scores for energy, social isolation, and emotional reaction, suggesting that patients with CIU felt a similar lack in this domain as patients with heart disease. As expected, patients with CIU perceived less restriction in physical mobility and had lower pain scores, but their scores for sleep disturbance were higher. Unexpectedly, from the patient perspective represented by NHP, the overall impact of CIU was rated as severe as a cardiac or respiratory disorder with a potential life threat. This highlights how much doctors' opinions can differ from patients' opinions.

Another way of rating the severity of the impact of CIU on the QOL is to compare CIU with other dermatological conditions; the impact of these dermatological conditions on the QOL is already well recognized by dermatologists. Poon et al. (4) studied patients with deep pressure urticaria and cholinergic urticaria and found similar mean DLQI scores to those previously reported in patients with severe atopic dermatitis and higher scores than those of patients with psoriasis, acne, Behçet's syndrome, Darier's disease, Hailey-Hailey disease, and vitiligo. In a prospective trial, we recently compared the impact of CIU on

HRQOL with that of psoriasis and atopic dermatitis using VQ-Dermato (11), a dermatology-specific tool. This study showed that impairment of HRQOL is significantly lower in CIU and psoriasis than in atopic dermatitis ($p < 0.0001$), even after adjustment for the severity of the disease. However, this impairment is not significantly lower in CIU than in psoriasis. Therefore, the impact of CIU on HRQOL is similar to, or even higher than, those of other dermatological diseases usually considered as severe and disabling, suggesting that the consequences of CIU are underestimated.

What Domains of the QOL Are Most Impaired in Patients With CIU?

The profile of the impact of QOL on a skin disorder can be deduced from the clinical profile and the treatment profile. In our study comparing CIU, atopic dermatitis, and psoriasis (11), the "physical discomfort" dimension was more degraded in atopic dermatitis and CIU than in psoriasis ($p < 0.001$) and the "leisure activities" dimension was more degraded in psoriasis than in CIU ($p < 0.001$). "Self-perception" and "treatment-induced restrictions" dimensions were much less affected in CIU than in psoriasis and atopic dermatitis ($p < 0.001$). The "daily living activities" dimension was much less impaired in psoriasis than in CIU and atopic dermatitis ($p < 0.001$).

Finally, because CIU is a highly pruritic disorder, it mainly affects the symptom dimension and, subsequently, impairs common daily activities. Conversely, because CIU is a non-permanent disorder and is rarely visible on the face, it does not induce as great an alteration of one's image as a permanent and often visible disorder like psoriasis. The characteristics of the urticaria determine the type of impact. For example, the most restricted HRQOL dimensions in patients with cholinergic urticaria are in the subdomains of sport and sexual activities (3). Notably, the treatment of CIU by oral

antihistamines, which are usually well tolerated, impairs the QOL much less than topical treatment used in other disorders (11).

Which Characteristics of Urticaria Have the Greatest Contribution to the Severity of Impact on the QOL?

Two studies have suggested that physical triggering factors, such as pressure or sweating, greatly contribute to this impact. Indeed, O'Donnel (3) found significantly more problems with mobility, choice of clothing, work, and hobbies in delayed pressure urticaria than in other CIUs.

In the study by Poon (4), patients with delayed pressure urticaria had greater impairment of HRQOL than patients suffering from CIU without physical triggering factors (mean DLQI: $43 \pm 23\%$ vs $25 \pm 24\%$). Differences were most notable in the subdomains of symptoms/feelings, leisure, and work. Among patients suffering from physical urticaria, patients with cholinergic urticaria had the highest mean total DLQI scores ($50 \pm 34\%$). Unexpectedly, DLQI scores were less affected in patients with intermittent angioedema manifestations or symptomatic dermatographism. These data suggest that the triggering of multiple urticaria wheals by any effort (cholinergic urticaria) or occurrence of painful swelling at any mobilization (pressure urticaria) are probably more restrictive for QOL than for the pruritus or the fear of severe attacks of angioedema. One must also account for the fact that the antihistamines are much more efficacious on the pruritus of common CIU than on the handicap of urticaria induced by pressure or sweating.

Is HRQOL a Meaningful and Relevant Outcome Measure for Therapeutic Trials in CIU?

The objective measure of transient lesions (dimensions, erythema, thickness, number of wheals), which change hourly, is not relevant.

There is no direct function impairment to measure in CIU, with the exception of specific forms, such as pressure urticaria. The semiquantitative assessment of pruritus by a visual analogical scale does not cover all the aspect of the restrictions in the patient's life. Urticaria treatment may also interfere with the patient's comfort by inducing effects, such as somnolence. Finally, the most meaningful target of any treatment for CIU should be to preserve the QOL. However, the HRQOL measures often are considered insensitive and unreliable outcome measures because of their "subjectivity." Remember that it is possible to "objectively" measure "subjective" feelings. In two multicenter, placebo-controlled studies using DLQI and the Work Productivity and Activity Impairment (WPAI) instrument, Thompson et al. (12) evaluated the effect of 60 mg of fexofenadine administered twice daily vs placebo on HRQOL and productivity (at work, at school, and in daily activities). Overall improvement in DLQI scores was statistically significant in the fexofenadine group ($p \leq 0.0002$). Improvement was also significant in work productivity ($p \leq 0.0152$) and in performance of daily activities ($p \leq 0.0002$), as reflected by WPAI. In two recent trials of CIU, QOL was chosen as the main objective for the first time (13,14). The first study was a 6-wk, double-blind, placebo-controlled trial testing 5 mg of desloratadine (administered once daily) vs placebo (13). DLQI and VQ-Dermato improvement from baseline were significantly greater in the desloratadine group than in placebo group ($p \leq 0.001$ for DLQI and $p = 0.009$ for VQ-Dermato). Using the same HRQOL instruments in another randomized study comparing desloratadine as a continuous treatment and desloratadine as a PRN "as needed" treatment only at the time of flare-up, we were able to show that a continuous treatment with antihistamines better preserved QOL than an "as-needed" treatment (14). Mean VQ-Dermato scores improved by 71% between days 1 and 90 in the daily desloratadine group compared

with a 54% improvement in the PRN group. Overall DLQI scores also showed differences favoring daily desloratadine, although the scale proved to be less sensitive to changes than VQ-Dermato.

Finally, Shikiar et al. (15) recently analyzed data from two phase III clinical studies of patients treated with a range of fexofenadine doses vs placebo (16,17) to estimate the minimal important difference in the DLQI for patients with CIU. This concept refers to the smallest difference in a score that can be considered meaningful (18). They estimated that a change in the DLQI score in the range of 2.24 to 3.10 could be considered clinically relevant in patients with CIU.

Despite a very low mortality, a usually effective treatment, an absence of functional impairment and sequelae, and a reputation of low-severity disorder among the doctors, the impact of CIU on the HRQOL of patients is rated by the patients at similar or higher levels than other life-threatening diseases and chronic skin disorders, such as psoriasis or atopic dermatitis. Beside pruritus, unavoidable triggering factors, such as pressure or sweating, greatly contribute to this HRQOL impairment. Therefore, dermatology-specific HRQOL instruments are a meaningful way to measure the severity of CIU, and several recent trials have shown that they are particularly relevant in assessing the therapeutic strategies in CIU.

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