Original Article

Psychometric Field Study of Hereditary Angioedema Quality of Life Questionnaire for Adults: HAE-QoL

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What is already known about this topic? Although there has been an increasing interest in health-related quality of life (HRQoL) in hereditary angioedema due to C1 inhibitor deficiency (C1-INH-HAE) in recent years, only generic questionnaires (eg, SF-36) have been used, as no disease-specific HRQoL questionnaire was available.

What does this article add to our knowledge? This is the first disease-specific HRQoL questionnaire in C1-INH-HAE. It has been developed in an international setting following published guidelines regarding development and cross-cultural adaptation. It shows good reliability and validity evidence.

How does this study impact current management guidelines? C1-INH-HAE experts recommend measuring HRQoL annually and specially when assessing the need for long-term prophylaxis. The measurement of HRQoL with a disease-specific questionnaire allows assessing specific concerns and indicators related to the disease in contrast with generic ones available.

BACKGROUND: Hereditary angioedema due to C1 inhibitor deficiency (C1-INH-HAE) may affect health-related quality of life (HRQoL). A specific HRQoL questionnaire for adult patients with C1-INH-HAE, the HAE-QoL, has recently been developed in Spain.

OBJECTIVE: The objective of this study was to perform a cross-cultural validation and psychometric study of the HAE-QoL in an international setting.

METHODS: Cross-cultural adaptation of the Spanish HAE-QoL draft version and an international rating phase with experts were performed. The resultant version of the HAE-QoL, a clinical questionnaire, and Short Form 36-item Health Survey Version 2.0 (SF-36v2) were pilot tested internationally. Item reduction was based on both descriptive and exploratory factor analysis. Psychometric properties were assessed.

RESULTS: Cross-cultural adaptation of the HAE-QoL was performed in 18 countries. The draft version of the HAE-QoL was pilot tested in 332 patients, and accurate data were obtained from 290 patients from 11 countries. The reduction process resulted in a new version with 25 items and 7 dimensions (treatment difficulties, physical functioning and health, disease-related stigma, emotional role and social functioning, concern about offspring, perceived control over illness, and mental health). Strong psychometric properties were observed (Cronbach's α 0.92; test-retest reliability 0.87). Convergent validity showed mild to moderate correlations with SF-36v2 physical and mental component summaries (0.45 and 0.64, respectively) and with SF-36v2 dimensions ($P < .004$). HAE-QoL scores discriminated significantly among severity groups (median: asymptomatic 133.5 vs severe 84.0; $P < .001$); between patients with and without long-term prophylaxis (median: 101 vs 90; $P = .001$); and between patients with and without psychiatric and/or psychological care (median: 74 vs 103; $P \leq .001$).

CONCLUSIONS: The HAE-QoL, currently available in 18 languages, showed good reliability and validity evidence. **(J Allergy Clin Immunol Pract 2016;4:464-73)**

Key words: *Disease-specific; Quality of life; Hereditary angioedema; C1 inhibitor; Questionnaire; Validation studies; Psychometric; Adults; HAE-QoL; SF-36v2*

Hereditary angioedema due to C1 inhibitor deficiency (C1-INH-HAE) is a rare autosomal dominant disorder characterized by recurrent episodes of subcutaneous and submucosal angioedema affecting various body sites, most frequently

Abbreviations used

AE-QoL- Angioedema quality of life questionnaire
C1-INH-HAE- Hereditary angioedema due to C1 inhibitor deficiency
CHI- Corrected homogeneity index
CQ- Clinical questionnaire
EFA- Exploratory factor analysis
GLS- Generalized least squares
HRQoL- Health-related quality of life
ICC- Intraclass correlation coefficient
LTP- Long-term prophylaxis
PAF- Principal axis factoring
SF-36v2- Short Form 36-item Health Survey Version 2.0

gastrointestinal mucosa, face, limbs, and larynx.[1,2] Its estimated prevalence is 1:50,000-1:100,000 inhabitants.[3-5]

This disease is associated with a significant and multifaceted disease burden.[6] Several aspects of C1-INH-HAE can significantly impair a patient's health-related quality of life (HRQoL), such as unpredictability of attacks, which are frequently disabling, disfiguring, painful, and even potentially fatal.[1,7-9] Other factors found to burden patients include delay in diagnosis,[3,4] unnecessary medical procedures, treatment with ineffective drugs,[2,10] and severe side effects from some medications administered as maintenance therapy.[11,12] It is currently well recognized that the effect of disease on HRQoL is an important facet to consider when assessing the general burden of disease and measuring the response to treatment.[13,14] Evidence of the effect of C1-INH-HAE or its treatment on HRQoL has been documented using generic instruments.[15-20]

In this report, we describe the development and psychometric evaluation of HAE-QoL, a multidimensional and specific HRQoL questionnaire for adult patients with C1-INH-HAE. The purpose is to provide a discriminant and evaluative tool to complement evaluations based on generic measures, thereby focusing on aspects that are both relevant and specific to patients living with C1-INH-HAE who are not covered by generic questionnaires.

METHODS

Process validation was performed according to methodologies described in published guidelines and previous HRQoL studies.[21-29] An outline of the development process is shown in Figure E1, available in this article's Online Repository at www.jaci-inpractice.org.

Development of draft version (phase I)

The development of the initial version of the HAE-QoL included a national multicenter study performed in Spain. After review of published medical literature and semistructured interviews with

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