

Portuguese version of Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q): assessment of reliability and validity

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Background: Drug hypersensitivity in children impacts the quality of life of the patients and their caregivers. The parent-reported drug hypersensitivity quality of life questionnaire (P-DrHy-Q), the first disease-specific quality-of-life questionnaire for caregivers who have children with drug hypersensitivity, was recently developed. The aim of this study was to assess the validity and reliability of the portuguese version of the P-DrHy-Q.

Method: A translation of the Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q) to the Portuguese population was performed, assessing its applicability in 74 caregivers from two allergy departments. The analyses included internal consistency (Cronbach's alpha) and test-retest reliability: 14 caregivers completed the P-DrHy-Q without any intervention one week after answering the first questionnaire.

Results: The 12-item scale assessed the mental health and social activity. The internal consistency of the scale was good (Cronbach's alpha = 0.824) and the test-retest associations were excellent (Intra-class correlation coefficient = 0.985; $p < 0.001$). The mean value of the questionnaire was (37.01 SD, 18.57) with Mental Health being more affected than Social Activity. Employed caregivers had a significant higher score ($p < 0.001$). No other factor was statistically significant.

Conclusion: The Portuguese version of the P-DrHy-Q is valid for evaluating quality of life impairment in Portuguese caregivers of children with drug hypersensitivity. Its application might be relevant for future research and provide clinicians and researchers with a tool to define which psychosocial support is required to provide more comprehensive care in drug hypersensitivity.

Key words: drug hypersensitivity; quality-of-life questionnaire for caregivers; validity and reliability; P-DrHy-Q.

Introduction

Measurement of health-related quality of life (HRQoL) is critical in the global evaluation of the impacts of the diseases and their therapies^{1,2}. HRQoL scales are widely

used in allergic diseases as well as other chronic illnesses as an endpoint in clinical trials and in routine clinical practice.

These assessment measures, increasingly used, are most of the times formulated in English, targeted for its use only in the English-speaking population. Translation and cultural adaptation of health questionnaires published and applied in other cultures is important in the international setting, as they provide the use of the tool in clinical practice and in research, provide greater accuracy in measuring health aspects related to the population in question, comparison of results between different samples, as well as the cross-cultural studies.

Hypersensitivity reactions to drugs in children have a parent-reported prevalence of around 10%, with a much lower real prevalence, and a lower prevalence of confirmed DH as compared to adults⁴. DHRs are considered a public health problem due to associated morbidity and socioeconomic costs.

Drug hypersensitivity may also affect the mental health and quality of life of patients and family members. The Drug Hypersensitivity Quality of Life Questionnaire was initially created by *Baiardini I et al.* and the results showed good validity, internal consistency, and reliability⁵. However, measuring the quality of life in children is different from adults. Later, *Yuenyongviwat A et al.*, develop and validate a questionnaire for the assessment of the specific burden of drug hypersensitivity from the caregiver's perspective, using a multi-dimensional concept to examine the impact of the health status on the quality of life of caregivers who have children with a history of drug hypersensitivity the Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q),

Given the absence of specific assessment tools designed for evaluating the quality of life in caregivers who have children with drug hypersensitivity in Portugal, the main objective of this study was to develop and assess the validity and reliability of a Portuguese version of Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q). The secondary objectives were to evaluate P-DrHy-Q in different caregivers and patients subgroups (drug hypersensitivity, type of reaction, age, single or multiple drug hypersensitivity reactions and sociodemographic of the caregivers).

Methods

Ethics

The research project was approved by the Ethics Committee and carried out in accordance with the Declaration of Helsinki. All participants gave their oral informed consent to participate.

Study design and Subject

Study participants were prospectively recruited from two different Allergy and Clinical Immunology Department located in tertiary healthcare centers in North of Portugal between June to July 2020. The inclusion criteria were an age under 18 years and having objective symptoms compatible with drug hypersensitivity suspicion. Medical records were scrutinized by the investigators, to determine eligibility. Parents of eligible children were invited to participate. Parents were asked to fulfill the questionnaire, and instructions were given by the investigators on how to proceed. Sociodemographic and clinical characteristics of the children and caregivers were recorded.

Parent-reported Drug Hypersensitivity Quality of Life Questionnaire (P-DrHy-Q)

P-DrHy-Q which was originally developed in Thailand includes 12 items evaluated on a ten-point Likert scale [from 1 (not at all) to 10 (very)], investigating two different domains: Mental Health and Social Activity⁶. It was designed to be completed by the caregiver, is easy to administer, is easy to score and requires a few minutes to complete. Questions and scores were formulated so that higher scores reflected worse HRQoL.

Translation and cross-cultural adaptation methods

The process of linguistic equivalence was initiated by contacting the authors of the original questionnaire to ask for authorization to use it in the present study. Cross-cultural translation was performed according to guidelines⁷. Linguistic validation consisted in 3 steps: forward translation, backward translation and comprehensibility testing. Forward translation was performed by two independent translators that had no previous knowledge of the questionnaire. Both were native speakers in the target language. Supported by an experienced specialist in drug allergy diagnosis and treatment, a combined version was obtained. Agreement was achieved through unanimity on a single reconciled version with all elements (translators and physician). The consensual version was tested in caregivers of children with a history of drug hypersensitivity. No comments, doubts or suggestions were posed, showed that the questions were easily understandable and do not require explanation.

Reliability

Reliability measures were of two types: 1. Internal consistency was evaluated using Cronbach's alpha calculated for each scale and 2. Test-retest reliability (reproducibility): P-DrHy-Q was administered twice to 14 caregivers separated by 7 days interval in the absence of any significant clinical or personal change; intraclass correlation coefficients quantified reproducibility of scores over 7 days.

Statistical analysis

SPSS version 22 (SPSS-Inc, Chicago, IL) was used for statistical analysis. Quantitative variables were expressed as means \pm standard deviations, with 95 % confidence intervals. Qualitative variables were compared using χ^2 test and Fisher's exact test. The normality was verified using the Shapiro-Wilk test. For all variables, significance was set at $p < 0.05$ for two tails. The internal consistency of the scale was evaluated using Cronbach's alpha coefficient. It is accepted crossways that alpha > 0.7 is acceptable, > 0.8 is good, and > 0.9 is excellent. Intra-class correlation coefficient was performed to assess the discriminative reliability of the test-retest associations.

Results

In the cognitive debriefing no comments, doubts or suggestions were done.

Characteristics of the participants

There were no refusals to participate in the study. A total of 74 caregivers with a child with a reliable history of drug hypersensitivity were included in this study.

Demographic characteristics of the patients were shown in (Table 1): 48.6% (n=36) of the children were females and 51.4% (n=38) were males. Ages ranged from 1-15 years with an average of 5.08 ± 3.64 years. Mild reactions in 85.1% (n=63) of cases, moderate 9.5% (n=7) and severe 5.4% (n=4), were observed. The most common implicated drugs to hypersensitivity reactions were antibiotics (65/74 patients, 87.8 %) and non-steroidal anti-inflammatory drugs (5/14 patients, 6.8 %) and 2 (2.7 %) had a history of drug hypersensitivity reaction to more than one drug.

Demographic characteristics of the caregivers were shown in (Table 2): 86.5% (n=64) were female and 13.5% (n=10) were male. Their ages were ranged from 30-45 years in 74.3% (n=55), 20-30 years in 16.2% (n=12) and over 45 years in 9.5% (n=7). 47.3% (n=35) had basic education, 27.0% (n=20) university graduation. 78.4% (58) were employed and 21.7 % (16) unemployed. 89.2% (66) were married and 98.6% were the main caregiver. Most of the family income was above 600 euros (€)/month. None of them have previous experienced in care of children with drug hypersensitivity.

The average global score was 37.01 [0-120], mean Mental Health 27.92 ± 13.66 [0-50; questions 1-5] and Social Activity 9.09 ± 6.34 [0-70; questions 6-12] (Table 3). The Mental Health presented higher scores than social that indicate that is the domain more affected in the caregivers.

There were no statistically significant differences in the Scores between the clinical characteristics of the patients (sex, age, severity of the reaction or number of drugs involved). However, in regard to sociodemographic characteristics of the caregivers it was found that when the caregiver is employed, the Social Activity Score is higher compared to unemployed cases.

Reliability

The P-DrHy-Q showed adequate internal consistency, as demonstrated by the very strong Cronbach's alpha coefficient ($C = 0.884$). In table 5, the values represented are the Cronbach's alpha coefficient of the scale if that question were excluded. Mental Health and Social Activity subscales were also adequate: $C = 0.983$; $p < 0.001$ and $C = 0.997$; $p < 0.001$ respectively (Table 6).

Test-retest reliability was assessed on 14 caregivers and was excellent: ICC 0.985; $p < 0.001$ (Table 6) for scales but also in Mental Health and Social Activity subscales: ICC 0.978; $p < 0.001$ and ICC 0.992; $p < 0.001$ respectively (Table 6).

Discussion

Evaluation of patient-reported outcomes by validated tools, either disease-specific when

available or generic ones, in clinical trials for allergic diseases are very important. An original questionnaire allowing the assessment of impact of biopsychosocial factors on drug allergy in caregivers of drug hypersensitivity pediatric patients entitled P-DrHy-Q has recently been developed and validated⁶. The original version was primarily developed in English language. In the present study this tool was translated and culturally adapted to Portuguese speaking population. To our best knowledge, our study is the first that validated P-DrHy-Q for another language and culture after development of the original questionnaire. Cross-cultural adaptation is relevant because, currently, there is no other measure for quality of life of caregivers with drug hypersensitivity children in Portugal. The decision to culturally adapt the P-DrHy-Q, rather than to develop a new measure, was based on the fact that the adaptation of a previously described and validated measure, which has been translated and validated to other languages, makes it possible to compare results across studies conducted in different countries. This present study contributes to attain this gap, both in clinical trials and in routine practice.

The results of the study showed that the P-DrHy-Q is a self-applied psychosocial impact scale in drug allergy. Furthermore, it is a brief and low-cost way to assemble data that may guide the clinician to decide which factors should be included in a

multidisciplinary approach to the caregivers. The factor analysis demonstrated that the scale may be used to measure two types of parental burden: mental health and social activity. Both of these domains had excellent internal reliability in both versions of the scale. The statistical analyses provided evidence that Portuguese version of the P-DrHy-Q met the standards for good internal consistency reliability with a Cronbach's alpha of $R=0.884$; $p < 0.001$ along with excellent test-retest reliability, $ICC= 0.985$ (Tand version: Cronbach's alpha = 0.897 and the test-retest reliability, $ICC= 0.9439$; $p < 0.001$). Therefore, it may be possible to adapt the scale to incorporate two sub-scale scores as well as an overall score to provide more information on the type of parental burden that is most salient.

The average score of P-DrHy-Q in our 74 for caregivers of patients who had suffered an allergic reaction with a drug were 37.01 ± 18.57 . Its application demonstrated negative impact on mental health and social activity in the caregivers of affected children. In our study we found higher score in the mental score than the social.

We believe that our study had some strengths. The study was performed in two different Allergy and Clinical Immunology Department and includes patients with different types of drug allergy.

Second, we had opportunity to observe relationship of the P-DrHy-Q scores to other clinical factors of the patients and sociodemographic characteristics of the caregivers. In the process of validating the DrHy-Q questionnaire, *Baiardini et al* found that the highest score (and therefore worse QoL) occurred in patients who had suffered anaphylaxis⁵. Results of our study showed that in the group of caregiver employed, had significantly higher P-DrHy-Q scores in particular Social Activity Score, indicating a worse HRQoL compared to unemployed individuals which can be explain, due to a more stressful life in the employed caregivers and less time available to control situation to less control in child diary activity. No others statistically significant were found.

This study has also several limitations. Our study has a small sample size; the analysis of a greater number of cases may reveal more robust results.

Other limitation of the study was that it does not takes into account the influence of a drug allergy evaluation and does not analyze if the quality of life improved significantly after completing a drug allergy evaluation. *Gatamintza et al.* conducted a prospective multicenter study in Spain to evaluate the quality of life of patients who suffered a possible allergic drug reaction, and analyzed the effect of a drug allergy evaluation⁸. A total of 340 adult's patients answered the specific questionnaire twice: before the drug allergy evaluation, and 1 month after it was completed. The quality of life was found to be significantly improved after completing a drug allergy evaluation.

Conclusion

The Portuguese version of the P-DrHy-Q has been developed and culturally adapted for use in Portuguese speaking population. This is the first parent-reported health-related quality of life instrument for drug allergy. This study demonstrated that the Portuguese version of the P-DrHy-Q can be a tool to evaluate interaction of biopsychosocial factors in caregivers of drug hypersensitivity patients. It shows good internal consistency and reliability. The questionnaire may be used both in research and in routine practice in Portugal. Gaining information on which type of parental burden is more salient provide more comprehensive care in drug hypersensitivity and may be useful in determining appropriate support for the caregivers.

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