

Turkish version of the Drug Hypersensitivity Quality of Life Questionnaire: assessment of reliability and validity

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Accepted: 10 June 2015 / Published online: 20 June 2015
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Abstract

Purpose The first disease-specific quality-of-life questionnaire in patients with drug hypersensitivity, Drug Hypersensitivity Quality of Life Questionnaire (DrHy-Q), was developed and validated recently. The aim of this study was to assess validity, reliability and responsiveness to interventions of the Turkish version of the DrHy-Q.

Methods The Turkish version of the DrHy-Q was administered to prospectively enrolled 736 patients with drug hypersensitivity from ten allergy units. To assess validity, all patients completed the validated Turkish version of Psychological General Well-Being Index (PGWBI). For test–retest reliability, 182 patients completed the DrHy-Q 1 week after the first questionnaire administration

without any intervention. Responsiveness was assessed on 97 patients who had a DrHy-Q recorded at a follow-up visit after the intervention.

Results The internal consistency and test–retest reliability of the scale were adequate (Cronbach's $\alpha = 0.934$, intra-class correlation coefficient = 0.783). The DrHy-Q scores showed weak negative correlations with the PGWBI total and domain scores ($r = -0.378$ to -0.254 , $p < 0.001$). DrHy-Q was able to discriminate the patients with one drug hypersensitivity reaction from the patients with two and above two reactions ($p = 0.012$ and $p < 0.001$, respectively), and the patients who experienced a respiratory reaction from the patients who did not ($p = 0.018$). However, it did not discriminate the patients

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with comorbid disease including psychiatric comorbidity ($p > 0.05$). The baseline DrHy-Q scores were significantly higher than the post-intervention scores ($p = 0.008$).

Conclusion The Turkish version of DrHy-Q is reliable and valid for evaluating quality of life in patients with drug hypersensitivity, and it appeared responsive to interventions.

Keywords Disease-specific questionnaires · Drug allergy · Drug hypersensitivity · Quality of life

Introduction

Measurement of health-related quality of life (HRQoL) is critical in the global evaluation of the impacts of the diseases and their therapies. 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. Two types of tools are used in the evaluation of HRQoL: generic and disease-specific questionnaires. Generic questionnaires can be used to assess patients suffering from different diseases. Disease-specific questionnaires are targeted to a specific disease and are more sensitive than the generic ones [1].

Hypersensitivity reactions to drugs are common in adults, and the prevalence varies according to the characteristics of the population such as age, gender and comorbidities. Drug hypersensitivity reactions affect more than 7 % of the general population and therefore represent an important public health problem [2, 3]. The self-reported prevalence of drug hypersensitivity has been reported as 4.7–13.4 % in young adults in our country [4, 5]. Although patients with drug hypersensitivity experience symptoms only intermittently, the impact of the disease on emotional aspects of life is not negligible. A certain level of fear, aggression, anxiety or depression should be expected in patients with drug allergies, as they could experience symptoms ranging from mild to life-threatening reactions following consumption of drug [6]. Trying to avoid exposure to drugs which the patient has hypersensitivity, anxiety and fear of the recurrence of the allergic reaction and concerns about using other drugs may adversely affect quality of life. As drug hypersensitivity causes symptoms only after exposure to the offending drug, it is generally not adequate to evaluate the burden of drug hypersensitivity with generic HRQoL questionnaires. These generic scales may fail in detecting the impacts of relatively mild diseases and diseases with short-lived symptoms. Therefore, disease-specific quality-of-life scales are needed in drug hypersensitivity and they are important for estimating the burden of drug hypersensitivity.

The only specific tool measuring HRQoL in patients with drug hypersensitivity was developed by an Italian group

(DrHy-Q: Drug Hypersensitivity Quality of Life Questionnaire) [7]. It has been validated and found to be appropriate for use alone or in combination with other patient-reported outcome questionnaires to explore the subjective experiences of patients with drug hypersensitivity [7].

However, the DrHy-Q has not been translated yet into different languages and has not been validated in various cultural settings including Turkey. Further, the original version has not been designed to assess the potential differences between different patient subgroups (i.e., patients with single or recurrent drug hypersensitivity reactions and patients with comorbid diseases) and to assess the responsiveness of the tool to interventions such as diagnostic tests (skin test and/or oral provocation test), and provocation test for finding safe alternative drug or desensitization with culprit drug. Therefore, the main objective of this study was to assess the validity and reliability of the Turkish version of DrHy-Q in subjects with drug hypersensitivity. The secondary objectives were to evaluate DrHy-Q use in different patient subgroups (patients with drug hypersensitivity reactions of different severity, patients with single or recurrent drug hypersensitivity reactions and patients with comorbid diseases) and the sensitivity of DrHy-Q to changes after interventions.

Methods

Drug Hypersensitivity Quality of Life Questionnaire

DrHy-Q which was originally developed in Italy [7] includes 15 items evaluated on a five-point Likert scale [from 1 (not at all) to 5 (very much)]. It was designed to be completed by the patient, 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 of the questionnaire

The DrHy-Q was translated into Turkish using forward- and back-translation procedures. The original Italian version of DrHy-Q was translated into Turkish by an independent professional Italian translator. The Turkish draft of the DrHy-Q was back-translated by another independent professional Italian translator. The back-translated version was reviewed by the Italian and Turkish authors, and the final version was approved by both. This version was applied to 40 patients with drug hypersensitivity to test the wording of the questions. Almost all did understand the questionnaire and wording of the questions. This pretesting phase showed that the questions were easily understandable and do not require explanation.

Patients

The Department of Allergy and Clinical Immunology of Ankara University was the coordinator center. Study participants were prospectively drawn from ten different allergy units located in tertiary healthcare centers in Turkey between June 2013 and July 2014. The inclusion criteria were an age of at least 18 years and having objective symptoms compatible with drug hypersensitivity and the diagnosis of drug hypersensitivity made by an allergist experienced in drug hypersensitivity. All patients gave their written/oral informed consent, and the Local Ethics Committee at the Ankara University, Ankara, Turkey, approved the protocol. Sociodemographic and clinical characteristics of the patients were recorded.

Validation procedure

The psychometric properties of the Turkish version of the DrHy-Q were evaluated in accordance with current guidelines [8]. The statistical analyses have been performed on raw scores.

Reliability

It measures the homogeneity of a scale. The reliability of DrHy-Q was tested by Cronbach's alpha coefficient in terms of internal consistency [9]. Usually, a reliability of ≥ 0.70 and ≥ 0.85 is considered adequate for group-level and individual comparisons, respectively [10]. The test-retest reliability of DrHy-Q was evaluated by administering the questionnaire to randomly selected 182 patients on two occasions 1 week apart without any intervention and in the absence of any clinical or personal significant change and by using intra-class correlation coefficient (ICC). More specifically, the ICC (3,1) type based on the Shrout and Fleiss classification was employed, that is, a two-way mixed-effects model. This ICC model indicates the proportion of variance that is due to between-subject variability relative to the sum of between-subject variability and measurement error. The ICC will be large when there is little variation in the measurements obtained for the same subject between two sessions compared to the variation of measurements obtained between different subjects. We denote ICC values <0.4 as poor, 0.4 – 0.59 as fair, 0.60 – 0.74 as good and >0.75 as excellent [11].

Validity

In order to assess validity, all patients completed the validated Turkish version of Psychological General Well-Being Index (PGWBI) [12]. PGWBI is a 22-item self-administered questionnaire, consisting of six mood states

(anxiety, depressed, positive well-being, self-control, general health and vitality) [13]. Each item is scored on a six-point Likert scale (from 0 (most distress) to 5 (highest level of well-being), leading to a total score between 0 and 110 points, with higher values indicating better well-being [13]. The PGWBI has been extensively used as an indicator of HRQoL in patients with chronic conditions [14, 15]. Three validation analyses were designed to assess validity.

In order to evaluate how well the unidimensional model obtained for the original Italian version of the instrument fits our data, *confirmatory factor analysis (CFA)* was performed. A first-order CFA for categorical data was applied with a weighted least (WLSM) Chi-square estimation with robust standard errors and mean and variance-adjusted statistics. Items with factor loadings below 0.40 were planned to be eliminated. The following goodness-of-fit indices were used to assess the degree of fit between the model and the sample: Comparative Fit Index (CFI; >0.90 : acceptable, >0.95 : excellent), Tucker–Lewis Index (TLI; >0.90 : acceptable, >0.95 : excellent) and root mean square error of approximation (RMSEA; <0.08 : acceptable, <0.05 : excellent) [16].

Divergent validity was assessed with Spearman correlation coefficients between the DrHy-Q scores and the PGWBI total and domain scores and the times elapsed since the first and last drug hypersensitivity reactions. We denoted -0.25 to 0 or 0 to 0.25 = little or no relationship; -0.50 to -0.25 or 0.25 to 0.50 = fair relationship; -0.75 to 0.50 or 0.50 to 0.75 = moderate-to-good relationship; -1.0 to -0.75 or 0.75 to 1.0 = good-to-excellent relationship. Our hypothesis is that quality of life specifically related to drug hypersensitivity is poorly associated with general well-being.

Number of the experienced drug hypersensitivity reactions, presence/absence of psychiatric comorbidity or other comorbid diseases and different clinical presentations of the drug hypersensitivity reaction may cause potential differences in DrHy-Q. Therefore, we used these parameters in order to assess the *discriminant validity*, the instrument's ability to differentiate between populations that are expected to be different. We grouped the patients according to the number of the experienced drug hypersensitivity reactions as one, two and above two. Evaluation of the discriminant validity of the questionnaire with respect to the number of the experienced drug hypersensitivity reactions was performed using Kruskal–Wallis variance analysis (with its post hoc test for pair-wise comparisons). We compared the DrHy-Q scores of the patients with different clinical presentation of drug hypersensitivity to assess whether the DrHy-Q could distinguish patients with different clinical presentations. Comparisons between groups with respect to clinical characteristics (presence/absence of psychiatric comorbidity or other

comorbid diseases, type of symptoms of the drug hypersensitivity reaction) were performed using the Mann–Whitney U test.

Responsiveness

Responsiveness was assessed on randomly selected 97 patients with a second DrHy-Q recorded at a follow-up visit just after the intervention such as diagnostic interventions (skin tests and/or oral provocation test), oral provocation test for finding safe alternative drug or oral/IV drug desensitization. These interventions were completed within 2 ± 1 days, and the second DrHy-Q was applied at the end of this time period. Second DrHy-Q was recorded just after interventions in order to understand immediately the impact of intervention on the patient without interfering factors that the patient may expose later. Effect size (ES) was used as responsiveness measure [17]. The ES is defined as the mean change in score (effect) divided by the standard deviation of the baseline scores. Thresholds to interpret the ES values are given by Cohen, J. as 0.2 is small, 0.5 is moderate, and 0.8 is large [18]. Wilcoxon test was also used to demonstrate the responsiveness of the DrHy-Q by evaluating mean changes between the baseline and post-intervention DrHy-Q scores.

P values <0.05 were considered statistically significant. All analyses were performed using the SPSS version 15.0 for Windows and MPlus [19].

Results

Characteristics of the patients

A total of 736 patients with a reliable history of drug hypersensitivity were included in this study. There are some missing data regarding demographic characteristics of patients as shown in Table 1. Seven hundred and eleven patients completed the DrHy-Q. Mean DrHy-Q score was 32.87 ± 10.94 (with median 32.49 minimum: 2.72, maximum: 56.23). The most common implicated drugs to hypersensitivity reactions were non-steroidal anti-inflammatory drugs (485/736 patients, 65.9 %) and antibiotics (285/736 patients, 38.7 %). Three hundred and ninety patients (53 %) had a history of drug hypersensitivity reaction to more than one drug. The clinical symptoms were urticaria and/or angioedema in 483 (65.6 %), anaphylaxis in 191 (26.0 %), respiratory reaction in 150 (20.4 %) and delayed-type cutaneous reaction in 69 patients (9.4 %). Clinical characteristics of the patients are detailed in Table 2.

Reliability

The internal consistency reliability of the scale was adequate with a Cronbach's alpha of 0.934. Test–retest reliability was assessed on 182 patients (median (min–max) age 42 (18–78) years; female/male (%) 72.0/27.5). The ICC for test–retest reliability was 0.783 (95 % confidence interval 0.720–0.834), thereby indicating excellent reliability.

Validity

Fifteen items of the DrHy-Q were subjected to first-order CFA to confirm the unidimensional structure obtained for the original Italian version of the instrument. According to factor loadings and goodness-of-fit statistics, this unidimensional structure was confirmed for the Turkish version of the DrHy-Q (χ^2 748.359, *df* 90). The data showed a reasonable fit to the model (CFI = 0.961, TLI = 0.955 and RMSEA = 0.101). Items and factor loadings are shown in Table 3. All items had a factor loading above 0.40; therefore, none of the items were excluded.

Divergent validity was confirmed by fair negative correlations between the DrHy-Q scores and the PGWBI domain scores and the PGWBI total scores ($r = -0.378$ to -0.254 , $p < 0.001$ for all correlations) (Table 4). There was no correlation between the DrHy-Q scores and the time intervals since the first and last drug hypersensitivity reactions ($r = 0.032$, $p = 0.414$, $r = 0.06$, $p = 0.113$, respectively).

The *discriminant validity* of the questionnaire was confirmed. DrHy-Q scores of the patients with two and above two drug hypersensitivity reactions were significantly higher, indicating more impairment in HRQoL than

Table 1 Demographic characteristics of the patients

Age (years), median (min–max), $n = 717^a$	42 (18–78)
Female/male, n (%) ^a	542 (73.6)/187 (25.7)
Education, n (%) ^a	
Primary school	225 (33.1)
High school	264 (38.8)
University	191 (28.1)
Occupation, n (%) ^a	
Housewife	262 (40.1)
Worker	101 (15.5)
Officer	107 (16.4)
Independent business owner	86 (13.2)
Retired	62 (9.5)
Student	35 (5.4)

^a There were some missing data regarding demographic characteristics of the patients as seen on the table

Table 2 Clinical characteristics of the patients (*n*#736)

	<i>n</i> (%)
Implicated drugs	
Non-steroidal anti-inflammatory drugs	485 (65.9)
Antibiotics	285 (38.7)
General Anesthetics	9 (1.2)
Radiocontrast media	18 (2.4)
Local Anesthetics	19 (2.6)
Others	97 (13.2)
Diagnostic methods (missing cases = 71)	
Reliable history only	589 (80)
Reliable history and in vivo methods	21 (2.9)
Reliable history, in vivo and in vitro methods	2 (0.3)
Reliable history and in vitro methods	7 (1)
Reliable history and provocation tests	46 (6.3)
Number of the implicated drugs (missing cases = 20)	
1	326 (44.3)
2	167 (22.7)
>2	223 (30.3)
Time elapsed since the first drug hypersensitivity reaction (months), median (min–max), <i>n</i> = 666	36 (0–528)
Time elapsed since the last drug hypersensitivity reaction (months), median (min–max), <i>n</i> = 624	7 (0–486)
Type of symptoms of the drug hypersensitivity reaction	
Urticaria and/or angioedema	483 (65.6)
Respiratory reaction	150 (20.4)
Delayed-type cutaneous reaction	69 (9.4)
Anaphylaxis	191 (26)
Number of the experienced drug hypersensitivity reactions (missing cases = 3)	
1	117 (16)
2	178 (24.3)
>2	438 (59.7)
Concomitant allergic diseases	
Rhinitis	177 (24)
Asthma	179 (24.3)
Rhinitis and asthma	89 (12.1)
Venom hypersensitivity	22 (3)
Other	119 (16.2)
Familial history of drug hypersensitivity (yes/no)	96 (13.2)/630 (86.8)
Comorbid diseases (yes/no)	265 (36.5)/461 (63.5)
Comorbid diseases	
Cardiovascular diseases	76 (28.7)
Gastrointestinal diseases	43 (16.2)
Respiratory diseases	10 (3.8)
Endocrine disease	72 (27.2)
Other	136 (51.3)
Familial history of psychiatric diseases (yes/no)	93 (12.8)/631 (87.2)
Psychiatric comorbidity, (yes/no), <i>n</i> (%)	(123/603), (16.9/81.9)
Psychiatric comorbidity	
Depression	89 (72.4)
Anxiety disorder	35 (28.5)
Bipolar affective disease	1 (0.8)

Table 2 continued

	<i>n</i> (%)
Somatization disorder	4 (3.3)
Psychotic disorder	2 (1.6)
Other	10 (8.1)

Table 3 Items and factor loadings of the items in the Turkish version of DrHy-Q

Items	Factor loadings
Since I am unable to take drugs every illness limits me more than other people	0.641
I am afraid of being administered a drug during an emergency to which I am allergic	0.726
I feel frightened due to my problem of allergy reaction	0.750
The problem of adverse reaction to drugs affects my life	0.773
I would like the allergist's opinion before taking drugs prescribed by other specialists	0.614
Even a little discomfort for me is a problem	0.804
I feel different from others	0.813
I feel anxious due to my problem of allergy reaction	0.852
For each disease I would be confident that there is a drug that I can safely take	0.639
I am afraid I could not deal with the pain	0.713
I feel anguished due to my problem of allergy reaction	0.831
I worry every time I take a drug different from ones that cause my allergic reactions	0.788
I give up leisure activities (sport, vacations, trips) because of my problem	0.685
I'm in a bad mood due to my problem of allergy reaction	0.838
The idea of taking a medicine makes me feel anxious	0.779

the DrHy-Q scores of the patients with one drug hypersensitivity reaction ($p = 0.012$ and $p < 0.001$, respectively, Table 5). DrHy-Q scores of the patients who experienced two and above two drug hypersensitivity reactions were found to be similar ($p = 0.196$). When we compared the DrHy-Q scores of the patients with different clinical presentation of drug hypersensitivity, the only significant difference was detected in comparison with patients with and without a respiratory reaction ($p = 0.018$) (Table 5). The DrHy-Q scores of the patients who experienced or did not experience other type of hypersensitivity reaction to drugs were not statistically significant (Table 5). We also compared the DrHy-Q scores for patients who had a psychiatric comorbidity versus patients who had not, and for patients who had other comorbid diseases versus patients who had not, to evaluate the effect of these comorbidities to the disease-specific HRQoL. The impairment of HRQoL did not differ significantly between patients either with or without a psychiatric comorbidity ($p = 0.261$) or in patients with or without another comorbid disease ($p = 0.383$, Table 5).

Responsiveness

Responsiveness was assessed on 97 patients (median (min–max) age 45 (18–78) years; female/male (%) 76.3/23.7). The

Table 4 Spearman correlation coefficients between DrHy-Q and PGWBI total and subscores

PGWBI domain	Spearman correlation coefficient, <i>p</i> value
Anxiety	$r = -0.327, p < 0.001$
Depressed mood	$r = -0.337, p < 0.001$
Positive well-being	$r = -0.254, p < 0.001$
Self-control	$r = -0.327, p < 0.001$
General health	$r = -0.362, p < 0.001$
Vitality	$r = -0.310, p < 0.001$
Total	$r = -0.378, p < 0.001$

baseline DrHy-Q scores (mean $\pm$ SD, median [min–max]) (32.9 ± 10.9 , 32.5 [2.7–56.2]) were significantly higher than the post-intervention DrHy-Q scores (29 ± 10.4 , 27.4 [11.5–54.9]) ($p = 0.008$). The ES was 0.36, which can be considered as a small magnitude of effect.

Discussion

The present study showed that the Turkish version of DrHy-Q is a reliable and valid instrument for evaluating quality of life in patients with drug hypersensitivity. It can discriminate the patients with one drug hypersensitivity

Table 5 DrHy-Q scores in patients with different clinical characteristics

		DrHy-Q Score mean $\pm$ SD median (min- max)	Cohen's <i>d</i> (effect size)	<i>p</i> value
Number of the experienced drug hypersensitivity reactions	1 (<i>n</i> = 112)	28.5 $\pm$ 11.1 27 [9.3–53.2] ^{¥,§}	1 versus 2: −0.36	<0.001 ^a
	2 (<i>n</i> = 174)	32.5 $\pm$ 11 32 [12–56.2] [¥]	1 versus >2: −0.53	
	>2 (<i>n</i> = 423)	34.2 $\pm$ 10.6 34.7 [2.7–56.2] [§]	2 versus >2: −0.16	
Comorbid diseases	Yes (<i>n</i> = 258)	32.34 $\pm$ 10.83 32.26 (7.57–55.55)	Yes versus no: −0.08	0.383 ^b
	No (<i>n</i> = 446)	33.24 $\pm$ 11.02 32.78 (2.72–56.23)		
Psychiatric comorbidity	Yes (<i>n</i> = 119)	33.83 $\pm$ 10.66 35.85 (12.47–53.45)	Yes versus no: 0.10	0.261 ^b
	No (<i>n</i> = 585)	32.72 $\pm$ 11.00 31.80 (2.72–56.23)		
Clinical presentation of the drug hypersensitivity reaction				
Urticaria/angioedema	Yes (<i>n</i> = 470)	32.88 $\pm$ 10.73 32.36 (2.72–55.55)	Yes versus no: −0.003	0.967 ^b
	No (<i>n</i> = 225)	32.91 $\pm$ 11.41 33.30 (11.25–56.23)		
Respiratory reaction	Yes (<i>n</i> = 147)	34.90 $\pm$ 10.72 34.86 (11.25–55.55)	Yes versus no: 0.23	0.018^b
	No (<i>n</i> = 551)	32.38 $\pm$ 10.95 31.93 (2.72–56.23)		
Delayed cutaneous reaction	Yes (<i>n</i> = 41)	31.15 $\pm$ 10.69 29.44 (12.52–51.91)	Yes versus no: −0.18	0.197 ^b
	No (<i>n</i> = 657)	33.10 $\pm$ 10.96 33.02 (2.72–56.23)		
Anaphylaxis	Yes (<i>n</i> = 183)	33.86 $\pm$ 10.93 34.74 (11.25–56.23)	Yes versus no: 0.12	0.200 ^b
	No (<i>n</i> = 515)	32.57 $\pm$ 10.94 31.94 (2.72–55.55)		

^a Kruskal–Wallis test, ^b Mann Whitney U test[¥], [§] Groups differ statistically significant based on post hoc comparisons of Kruskal–Wallis test

reaction than patients with two or more drug hypersensitivity reactions, and it can distinguish patients with drug-induced respiratory reactions than without respiratory reactions. Additionally, the tool appeared to be responsive to interventions including diagnostic tests, oral provocation and desensitization.

HRQoL is often measured as a patient-reported outcome and is incorporated into clinical trials as an outcome measurement beyond morbidity and mortality [20]. Evaluation of patient-reported outcomes by validated tools, either disease-specific when available or generic ones, in

clinical trials for allergic diseases has been recommended by the recent position paper [21]. A new questionnaire specific for the assessment of quality of life in patients with drug hypersensitivity entitled DrHy-Q has recently been developed and validated [7]. To our best knowledge, our study is the first study that validates DrHy-Q for another language and culture after development of the original questionnaire. The statistical analyses provided evidence that Turkish version of the DrHy-Q met the standards for good internal consistency reliability with a Cronbach's alpha of 0.934. (Italian version 0.928) along with adequate

test–retest reliability (ICC 0.783). Further, Turkish version of the DrHy-Q showed a reasonable fit to the original Italian version of the instrument (CFI = 0.961, TLI = 0.955 and RMSEA = 0.101).

It is already well known that assessing the patient's subjective point of view via disease-specific questionnaire offers a more comprehensive description of the impact of the disease on patient's everyday life [22]. Therefore, in parallel to the development of the tool, clinical trials will be performed to verify the impact of drug hypersensitivity on HRQoL. Having a validated instrument for such patients will allow to understand the specific subjective experience of drug hypersensitivity. Further, we will have an opportunity to evaluate the same patients at different times (e.g., before and after establishment of diagnosis, after finding a safe alternative or before and after desensitization to culprit drug) or to evaluate the impact of different clinical presentation of drug hypersensitivity varying from mild to severe on HRQoL. Assessing subjective side of drug hypersensitivity reactions will lead to personalized approach, resulting in better patient management.

As expected, our results showed that correlation of the DrHy-Q scores with the PGWBI total and domain scores were weak and negative, which was in agreement with the original Italian version of the DrHy-Q [7]. Contrary to the fact that the DrHy-Q is a disease-specific questionnaire with higher scores indicating worse HRQoL, the PGWBI is a generic quality-of-life questionnaire and evaluates self-perceived psychological and general well-being with higher scored indicating better well-being. Therefore, negative and weak correlation is expected and suggests that the DrHy-Q can have capacity to measure the subjective experiences of patients with drug hypersensitivity that are difficult to measure with generic instruments.

We believe that our study had some advantages. The large sample size with 736 patients, larger than the number of patients in Italian version (485 patients), was one of them. Second, we had opportunity to observe relationship of the DrHy-Q scores to other clinical factors such as number of reaction and presence of comorbid diseases including psychiatric morbidity. This relationship had been considered as the topic of future studies in the Italian version of the DrHy-Q [7]. Our results showed that patients with two or more drug hypersensitivity reactions had significantly higher DrHy-Q scores indicating a worse HRQoL. Contrary to expectation, any comorbid diseases including psychiatric comorbidity did not affect HRQoL as shown by similar DrHy-Q scores on each group. In the original questionnaire, it was reported that the tool was able to distinguish patients with reactions of different severity since the DrHy-Q scores from patients with anaphylactic shock were significantly higher than those from patients with other reactions [7]. However, the Turkish

version of DrHy-Q could not distinguish patients with different clinical presentations except patients with or without respiratory reaction. We defined anaphylaxis based on the recent WAO guideline, and shock was not the only criteria for anaphylaxis [23]. This may also explain the difference between these two versions. In fact, it has been demonstrated that HRQoL is at least in part independent of specific symptoms of a disease [22] which may be the other explanation of the difference between two studies.

The measurement of responsiveness, which was not performed in the original version, to interventions such as diagnostics tests, oral provocation test for finding safe alternative or desensitization, was the other advantage of the study. This effort showed that the tool was sensitive to interventions although we did not systematically evaluate which interventions specifically influence responsiveness. This was the limitation of the study. However, a national multicenter study was already planned regarding responsiveness of the Turkish version of the DrHy-Q to drug desensitization and is going to examine the responsiveness of the instrument in a more comprehensive manner in this specific population. We had to discuss our data comparing the only one available study in this area [7], and that was the another limitation of the study. Additionally, the majority of the patients included in this study had non-steroidal anti-inflammatory drug and/or antibiotic hypersensitivity; this fact might limit the possible generalization of our findings to patients with drug hypersensitivity to other drugs.

In conclusion, Turkish version of DrHy-Q has sufficient reliability, validity and responsiveness, and it can be used in patients with drug hypersensitivity for both determining the subjective experiences and response to interventions.

Conflict of interest The authors have no conflict of interest with any commercial or other associations in connection with the submitted article.

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