How much drug allergies affect quality of life?

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ABSTRACT

Background: Drug hypersensitivity reactions are considered public health problems due to associated morbidity and socioeconomic costs. The evaluation of health-related quality of life in patients with drug hypersensitivity is still a widely unconsidered topic. The aim of our study is to reveal the effects of drug allergy on the quality of life of patients who apply to our outpatient clinic with the complaint of drug allergy.

Methods: This study is prospective a questionnaire study under supervision. Patients who applied to the University of Health Sciences, Bursa Postgraduate Research and Training Hospital Department of Allergy outpatient clinic between August 2019 and May 2020 with the complaint of drug allergy filled out the quality of life questionnaire (DrHy-Q), and short questionnaire of psychological well-being index (PGWBI) under the supervision of a specialist physician before the diagnostic procedures.

Results: The study was conducted with 150 cases and 73.3 % (n=110) of the cases were female and 26.7% (n=40) were male. No significant correlation was found between the demographic characteristics of the patients, the observed symptoms, the culprit drugs, familial and individual comorbid and psychological diseases, and DrHY-Q (p>0.05). DrHY-Q was only affected from the type of allergic reaction. A negative statistically significant weak correlation was also detected between the total DrHY-Q score and the PGWBI total score (r: -0.283; p<0.01).

Conclusions: We found that DrHY-Q is sensitive to reaction type and able to discriminative type 1 and type 2 reactions (p=0.017; p<0.05). We think that more comprehensive studies are needed on this subject.

Keywords: Drug allergy, Drug hypersensitivity, Quality of life

INTRODUCTION

Drug hypersensitivity is directed against any adverse reaction to the drug and immunological mechanisms are responsible for its occurrence.¹² Drug hypersensitivity reactions (DHRs) are side effects of drugs given at a normally tolerated dose. DHRs have been identified as one-third of adverse drug reactions and affect more than 7% of the general population.³

Hypersensitivity reactions to drugs affect 10% to 20% of hospitalized patients.⁴⁵ Epidemiological studies have shown that more than 5% of the population have experienced least a times DHR in their lives. DHRs are considered public health problems due to associated morbidity and socioeconomic costs in the world wide.⁶ In our country, prevalence of drug hypersensitivity has been reported as 4.7-13.4 % in young adults.⁷

Risk factors for DHR include females’ sex, age, presence of allergic diseases, ethnicity, and genetics.⁸⁹

Patients with drug hypersensitivity experience sensation of anxiety, fear, tension and these symptoms are closely related to drug intake for present or future health problems. These emotions can influence life and also disrupt daily performance.
Health related quality of life (HRQoL) scales are widely used in allergic diseases as well as other chronic illnesses. HRQoL has become an important outcome measure in the treatment of allergic diseases but the evaluation of HRQoL in patients with drug hypersensitivity is still a widely unconsidered topic.\textsuperscript{10,11}

Validity and reliability studies of the Turkish version were conducted by Bavbek et al in their study. HRQoL was evaluated before and after diagnostic intervention in patients with DHR. They also expressed the improvement of drug allergy in the quality of questionnaire (DrHy-Q) filled out by the patients, after desensitization with a provoked test or suspected drug to find safe alternative drugs.\textsuperscript{12}

The aim of our study is to reveal the effects of drug allergy on the quality of life of patients who apply to our outpatient clinic with the complaint of drug allergy, and to contribute to this neglected and controversial issue to some extent.

**METHODS**

This study was a prospective questionnaire study under supervision, taking into account the patient archive. Patients who applied to the University of Health Sciences, Bursa Postgraduate Research and Training Hospital Department of Allergy outpatient clinic between August 2019 and May 2020 with the complaint of DrHy-Q, and short questionnaire of psychological well-being index (PGWBIs) under the supervision of a specialist physician before the diagnostic procedures. All patients gave written informed consent. This study was approved by University of Health Sciences, Bursa Postgraduate Research and Training Hospital, Ethics Committee.

Patients aged 18 years and over with drug allergy were enrolled in the study randomly. The DrHy-Q questionnaire with 15 questions developed by the Italians and validated in Turkish by Bavbek et al was used. It consists of 15 items evaluated on a five-point Likert scale [From 1 (not at all) to 5 (many)].

The psychometric properties of the Turkish version of the DrHy-Q were evaluated in accordance with current guidelines.\textsuperscript{13} The questionnaire PGWB1 consists of 22 items, investigating six different domains: anxiety, depression, positive and well-being, self-control, general health, and vitality. In our study, we used the short form of PBGWB1 (containing questions 5, 6, 7, 18, 21 and 22). It consists of 6 items evaluated on a five-point Likert scale [From 1 (worst) to 5 (best)].

**Statistical analysis**

NCSS (number cruncher statistical system) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used while evaluating the study data. The suitability of the quantitative data to normal distribution was tested by Kolmogorov-Smirnov, Shapiro-Wilk test and graphical evaluations. Student t Test was used for comparing two groups of quantitative data with normal distribution. One-way Anova Test was used for comparisons of three or more normally distributed groups, and Bonferroni test was used for paired comparisons. In evaluating the relations between variables, Pearson correlation analysis was used for variables with normal distribution and Sperman Correlation Analysis for variables that did not show normal distribution. Significance was assessed at least at the p<0.05 level. The evaluation of the Cohen alpha coefficient is made according to the following criteria: 0.0≤α<0.40, the scale is not reliable, 0.40≤α<0.60, the scale has low reliability, 0.60≤α<0.80 it is very reliable, 0.80≤α<1.00, the scale is a highly reliable scale. The evaluation of the Correlation coefficient (r) is made according to the following criterion: 0.0-0.25 very poor, 0.25-0.49 poor, 0.50-0.69 medium, 0.70-0.89 good, 0.90-1.00 very good).

**RESULTS**

This research included the patients having drug allergy who were admitted to the allergy and clinical immunology outpatient clinics between October 2019 and May 2020. The study was conducted with 150 cases and 73.3 % (n=110) of the cases were female and 26.7% (n=40) were male. Their ages were ranged from 18 to 72 years with an average of 42.41±13.16 years. Evaluation of descriptive properties of patients were shown in (Table 1).

| Properties | N   | %    |
|------------|-----|------|
| Age (year) | Min-max (Median) | 18-72 (40.5) |
|            | Median±SD       | 42.41±13,16 |
| Sex        | Female          | 110   | 73.3 |
|            | Male            | 40    | 26.7 |
| Education status | Primary school | 88   | 58.7 |
|            | High school     | 32    | 21.3 |
|            | University      | 30    | 20.0 |
|            | Housewife       | 69    | 46.0 |
|            | Worker          | 42    | 28.0 |
|            | Officer         | 8     | 5.3  |
| Job        | Independent business owner | 8 | 5.3 |
|            | Retired         | 18    | 12.0 |
|            | Student         | 5     | 3.3  |

Demographic characteristics of the patients; 58.7% (n=88) of the cases were primary school graduates, 21.3% (n=32) high school graduates, 20.0% (n=30) university graduates, 46.0% and (n=69) housewives, 28.0% (n=42) workers, 5.3% (n=8) civil servants, 5.3% (n=8) independent business owners, 12.0% (n=18)
retired, 3.3% (n=5) students. Clinical characteristics of the patients were shown in (Table 2).

Skin symptoms in 81.3% (n=122) of cases, anaphylaxis 16.7% (n=25), gastrointestinal symptoms 18.0% (n=27), respiratory symptoms 47.3% (n=71) and cardiovascular symptoms 24.0% (n=71) n=36) were observed. Concomitant diseases 44.7% (n=67) of cases, family history of drug hypersensitivity 18.7% (n=28), comorbid disease 37.3% (n=56), history of psychiatric illness 14.0% (n=21) and psychiatric comorbidity 19.3% (n=29) were observed.

Table 2: Clinical characteristics of the patients.

| Clinical characteristics | Min-Max (Median) | N  | %   |
|--------------------------|------------------|----|-----|
| Number of the implicated drugs | 1-7 (2) | 1 drug | 49 | 32.7 |
|                          | Median ±SD       | 2.29±1.27 |
|                          | 2 drugs          | 47  | 31.3 |
|                          | 3 drugs          | 28  | 18.7 |
|                          | ≥4 drugs         | 26  | 17.3 |
| Implicated drugs         | Non-steroid anti inflammatory drugs (NSAID) | 54 | 36.0 |
|                          | Antibiotics      | 57  | 38.0 |
|                          | NSAID+Proton pump inhibitors (PPI) | 7  | 4.7 |
|                          | NSAID+Antibiotics | 30  | 20.0 |
|                          | NSAID+Antibiotics +PPI | 2  | 1.3 |
| Number of the experienced drug hypersensitivity reactions | Min-max (median) | 1-20 (2) |
| HOW MANY MONTHS HAVE PASSED SINCE THE FIRST REACTION? | Median ±SD | 3.11±2.95 |
| HOW MANY MONTHS HAVE PASSED SINCE THE LAST REACTION? | Min-max (median) | 1-324 (24) |
|                          | Median ±SD       | 49.13±64.36 |
| Type of symptoms of the drug hypersensitivity reaction | Type 1 | 133 | 88.7 |
|                          | Type 2           | 17  | 11.3 |
| Symptoms type            | Skin             | 122 | 81.3 |
|                          | Anaphylaxis      | 25  | 16.7 |
|                          | Gastrointestinal | 27  | 18.0 |
|                          | Respiratory      | 71  | 47.3 |
|                          | Cardiovascular   | 36  | 24.0 |
| Concomitant allergic diseases | No | 83  | 55.3 |
|                          | Yes              | 67  | 44.7 |
| Familial history of drug hypersensitivity | No | 122 | 81.3 |
|                          | Yes              | 28  | 18.7 |
| Comorbid diseases        | No               | 94  | 62.7 |
|                          | Yes              | 56  | 37.3 |
| Familial history of psychiatric diseases | No | 129 | 86.0 |
|                          | Yes              | 21  | 14.0 |
| Psychiatric comorbidity  | No               | 121 | 80.7 |
|                          | Yes              | 29  | 19.3 |

Distribution of scores and internal consistency values for PGWBI and DrHY-Q Scales were shown in (Table 3).

PGWBI total score range from 14 to 30, with an average of 21.71±3.45. DrHY-Q total score range from 15 to 75, with an average of 51.03±12.44. When Cronbach's alpha values showing the internal consistency of the scale questions are examined; 0.853 for the PGWBI scale and 0.805 for the DrHY-Q scale are observed. Accordingly, our PGWBI and DrHY-Q scales are highly reliable. Relationship between DrHY-Q and PGWBI Scale Scores were shown in (Tables 4).

A negative statistically significant weak correlation was found between the total DrHY-Q score and anxious, depressive, positive and energetic mood scores (r:-0.333; r: -0.253; r: -0.223; r:-0.260; p<0.01 ). No statistically significant relationship between the total DrHY-Q score and self-control and general health scores were found.
A negative statistically significant weak correlation was also found between the total DrHY-Q score and the PGWBI total score (r: -0.283; p<0.01). Evaluation of PGWBI and DrHY-Q scale scores according to descriptive features were shown in (Table 5).

### Table 3: Distribution of scores and internal consistency values for PGWBI and DrHY-Q scales.

|                  | Min-Max (Median) | Med±SD | Cronbach’s alpha |
|------------------|------------------|--------|------------------|
| Anxious          | 2-5 (3)          | 3.17±0.72 |                  |
| Depression       | 2-5 (4)          | 3.49±0.82 |                  |
| Positive well being | 2-5 (4)        | 3.57±0.71 |                  |
| Self-control     | 2-5 (4)          | 3.88±0.64 |                  |
| General health   | 2-5 (4)          | 3.99±0.74 |                  |
| Vitality         | 2-5 (4)          | 3.62±0.92 |                  |
| Total PGWBI      | 14-30 (22)       | 21.71±3.45 | 0.853            |
| Total DrHY-Q     | 15-75 (51)       | 51.03±12.44 | 0.805            |

### Table 4: Relationship between DrHY-Q and PGWBI scale scores.

|                  | DrHY-Q total score |
|------------------|--------------------|
|                  | r                  | P value   |
| Anxious          | -0.333             | 0.001**   |
| Depression       | -0.253             | 0.002**   |
| Positive well being | -0.223           | 0.006**   |
| Self-control     | -0.147             | 0.073     |
| General health   | -0.048             | 0.560     |
| Vitality         | -0.260             | 0.001**   |
| Total PGWBI      | -0.283             | 0.001**   |

A negative statistically significant very weak correlation was found between age and PGWBI total score (r: -0.161; p=0.05). No statistically significant relationship between age and the total DrHY-Q score was found (p<0.05). A statistically significant difference was found between the PGWBI total scores of the cases according to gender (p=0.008; p<0.01) and PGWBI total scores of male subjects were higher than women.

### Table 5: Evaluation of PGWBI and DrHY-Q scale scores according to descriptive features.

| Parameters               | PGWBI total score | DrHY-Q total score | Cohen’s d (effect size) |
|--------------------------|-------------------|--------------------|-------------------------|
|                          | N | Med±SD | Med±SD |                      |
| Age (year)               | r | -0.161 | -0.072 | 0.07                  |
|                          | p | 0.049* | 0.380  |                       |
| Sex                      |    | Kadin  | 21.26±3.36 | 51.96±12.40 | 0.28                |
|                          |    | Erkek  | 22.95±3.43 | 48.48±12.34 |                   |
|                          | p | 0.008** | 0.129  |                       |
| Education status         |    | İlköğretim | 21.08±3.29 | 52.47±12.90 | 1-2: 0.45           |
|                          |    | Lise    | 22.63±3.65 | 46.88±10.68 | 1-3: 0.09           |
|                          |    | Üniversite | 22.60±3.39 | 51.27±12.21 | 2-3: 0.38           |
|                          | p | 0.027* | 0.092  |                       |
| Implicated drugs         |    | 1 ilaç   | 21.71±3.13 | 48.29±13.39 | 1-2: 0.31           |
|                          |    | 2 ilaç   | 22.26±3.58 | 51.98±10.36 | 1-3: 0.30           |
|                          |    | 3 ilaç   | 20.43±3.49 | 52.18±12.72 | 1-4: 0.37           |
|                          |    | ≥4 ilaç  | 22.12±3.59 | 53.27±13.53 | 2-3: 0.02           |
|                          | p | 0.145  | 0.293  |                       |
|Reaction type             |    | Type 1  | 21.47±3.44 | 51.89±11.79 | 0.62                |
|                          |    | Type 2  | 23.65±2.96 | 44.29±15.52 |                   |
|                          | p | 0.014* | 0.017* |                       |
| Skin                     |    | No      | 20.64±3.59 | 52.82±9.87 | 0.18                |
|                          |    | Yes     | 21.96±3.39 | 50.62±12.96 |                   |
|                          | p | 0.069  | 0.401  |                       |
| Anaphylaxis              |    | No      | 21.97±3.35 | 50.62±12.84 | 0.20                |
|                          |    | Yes     | 20.44±3.73 | 53.08±10.17 |                   |
|                          | p | 0.043* | 0.369  |                       |
| Gastrointestinal Symptoms|    | No      | 21.99±3.37 | 51.15±12.76 | 0.05                |
|                          |    | Yes     | 20.44±3.61 | 50.48±11.10 |                   |
|                          | p | 0.034* | 0.800  |                       |
| Respiratory              |    | No      | 22.11±3.43 | 50.29±13.16 | 0.13                |
|                          | p | 0.034* | 0.800  |                       |

Continued.
No statistically significant difference was found between the total DrHY-Q scores of the cases according to gender (p>0.05) and also total DrHY-Q scores of the subjects according to their educational status (p>0.05). A statistically significant difference was found between the PGWBI total scores of the cases according to their educational status (p=0.027; p<0.05) and also between PGWBI total scores of high school and university graduates were higher than primary school graduates (p=0.017; p=0.029; p<0.05, respectively). No statistically significant difference was found between the PGWBI total scores of the high school and university graduates (p>0.05).

No statistically significant relationship was found between the PGWBI total score and the number of drug reactions of the patients, the time elapsed after the first reaction, the time after the last reaction (p>0.05).

A positive statistically significant and very weak correlation was found between the total DrHY-Q score and the number of drug reactions (r=0.179; p<0.05). No statistically significant correlation was found between the total DrHY-Q score and the time elapsed after the first reaction and the last reaction (p>0.05).

PGWBI and DrY-Q total scores of the cases were not found statistically significant difference according to the number of drugs implicated (p>0.05).

A statistically significant difference was found between the PGWBI total scores of the cases according to the type of reaction (p=0.014; p<0.05); and PGWBI total scores of patients with Type 2 reaction were higher than those with type 1.

A statistically significant difference was found between the total DrHY-Q scores of the cases according to the reaction type (p=0.017; p<0.05); and patients with type 1 reaction had higher DrHY-Q total scores than those with type 2.

There was no statistically significant difference was found between PGWBI total scores according to the presence of skin, respiratory and cardiovascular symptoms in the cases (p>0.05). A statistically significant difference was found between the PGWBI total scores according to the presence of gastrointestinal symptoms in the cases (p=0.034; p<0.05); patients with gastrointestinal symptoms had lower PGWBI total scores. A statistically significant difference was found between the total PGWBI scores according to presence the anaphylaxis symptom of cases (p=0.043; p<0.05); and patients with symptoms of anaphylaxis had lower PGWBI total scores. There was no statistically significant difference between the total DrHY-Q scores according to the presence of skin, anaphylaxis, respiratory, gastrointestinal and cardiovascular symptoms (p>0.05). There was no statistically significant difference between PGWBI and DrY-Q total scores of the cases according to the presence of accompanying disease (p>0.05). There was no statistically significant difference between the PGWBI and DrY-Q total scores of the patients according to the presence of familial drug hypersensitivity history (p>0.05).

A statistically significant difference was found between the PGWBI total scores of the cases according to the presence of comorbid diseases (p=0.007; p<0.01) and PGWBI total scores of patients with comorbid diseases were lower. Patients with gastrointestinal symptoms

| Parameters | PGWBI total score | DrHY-Q total score | Cohen’s d |
|------------|-------------------|--------------------|-----------|
| Symptoms   |                   |                    |           |
| Cardiovascular Symptoms | Yes | 21.27±3.45 | 51.86±11.62 |           |
|           | p                 | 0.134              | 4.43      |
|           | No                | 21.94±3.45         | 51.18±12.87 | 0.05     |
|           | p                 | 0.156              | 8.04      |
| Concomitant allergic diseases | No | 22.06±3.79 | 52.22±11.91 | 0.21     |
|           | p                 | 0.160              | 1.96      |
| Familial history of drug hypersensitivity | No | 21.9±3.48 | 50.87±12.64 | 0.07     |
|           | p                 | 0.146              | 0.737     |
| Comorbid diseases | No | 22.30±3.38 | 52.11±12.42 | 0.23     |
|           | p                 | 0.172              |           |
| Familial history of psychiatric diseases | No | 22.04±3.35 | 51.55±12.45 | 0.30     |
|           | p                 | 0.208              |           |
| Psychiatric comorbidity | Yes | 22.77±2.85 | 50.21±12.11 | 0.34     |
|           | p                 | 0.100              |           |

*P= Pearson Korelasyon katsısyi, a= student t test, b= One way ANOVA test, **p<0.01, p<0.05
and/or anaphylaxis having lower PGWBI total scores were statistically significant (p=0.034; p<0.05), (p=0.043; p<0.05). A statistically significant difference was found between the total DrHY-Q scores of the cases according to the presence of comorbid diseases (p>0.05) and also between the PGWBI total scores of the cases according to the presence of familial psychiatric disease history (p=0.004; p<0.01). PGWBI total scores of patients with a familial history of psychiatric disease were lower. A statistically significant difference was not found between the total DrHY-Q scores of the cases according to the presence of familial psychiatric disease history (p>0.05).

DISCUSSION

The DrHy-Q can easily be added to other descriptive survey studies while investigating the impact of drug allergy on people's lives. The DrHY-Q tool was first developed as a tool that is easy to apply, not affected by suspected drugs, compatible with similar procedures, and can capture the health-related quality of life (HRQoL) effect by Baiardini et al in Italy. As PGWBI was widely used as an indicator of HRQoL in patients with chronic conditions, it was administered in addition with DrHY-Q to patients. They stated that the weak correlation detected between PGWBI and DrHY-Q reflected the patient experiences optimally. In our study; a negative statistically significant weak correlation was also found between the total DrHY-Q score and the PGWBI total score (r=-0.283; p<0.01).

After this first validation study in Italy, and this study was also done in Turkey and Netherlands. Based on this tool, we determined the reflections of the allergic process on our patients' lives and reported the results. In our study; PGWBI and DrHY-Q scales are highly reliable, and when Cronbach's alpha values showing the internal consistency of the scale questions are examined; 0.853 for the PGWBI scale and 0.805 for the DrHY-Q scale were found in our study.

In our drug allergies questionnaire, women were in majority among our patients who participated in this study. A statistically significant difference was found between the total DrHY-Q scores of the cases according to the type of reaction (p=0.017; p<0.05); and patients with type 1 reactions had higher DrHY-Q total scores than those with type 2 reactions. This is also the only common point between DrHY-Q and PGWBI in our study, but, PGWBI total scores of patients with type 2 reaction were higher than those with type 1 (p=0.014; p<0.05). This condition can be explained by the vital effects of the type 1 reaction on the psychology of the patients.

Patients with gastrointestinal symptoms and/or anaphylaxis had lower PGWBI total scores and statistically significant (p=0.034; p<0.05), (p=0.043; p<0.05). There was no statistically significant difference between the total DrHY-Q scores according to the presence of skin, anaphylaxis, respiratory, gastrointestinal and cardiovascular symptoms (p>0.05).

Our study is similar to the study of Gastaminza et al. There was no control group in both studies. If people have experience even once an allergic reaction to the drug, they are emotionally affected due to severity of the reaction and a drug taking fear effect develops. Baiardini and Bavbek et al also revealed this approach in their study. This approach may explain the absence of control group. In the study of Moayeri et al, the Dutch DrHy-Q can discriminate between patients with one or more than one implicated drug hypersensitivity reaction. DrHY-Q total scores of the cases did not differ statistically significant according to the number of drugs implicated in our study (p>0.05).

In the Turkish study, a discriminative ability with respect to the presence of respiratory symptoms was also observed, but it was not confirmed in our study and Moayeri et al study. The discriminative ability between severity of reactions (anaphylaxis, other reactions) reported in the Italian validation, could also not be seen in Moayeri et al and our study. In our study; there was no statistically significant difference between the total DrHY-Q scores according to the presence of skin, anaphylaxis, respiratory, gastrointestinal and cardiovascular symptoms (p>0.05).

CONCLUSION

In our study, we found that DrHY-Q is sensitive to reaction type and can be discriminative between type 1 and type 2 reactions (p=0.017; p<0.05). No significant correlation was found between the demographic characteristics of the patients, the observed symptoms, the culprit drugs, familial and individual comorbid and psychological diseases, and DrHY-Q (p>0.05). DrHY-Q was only affected from the type of allergic reaction. A negative statistically significant weak correlation was also detected between the total DrHY-Q score and the PGWBI total score (r=-0.283; p<0.01). We think that more comprehensive studies are needed on this subject.

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