Food allergy–related quality of life after double-blind, placebo-controlled food challenges in adults, adolescents, and children

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Background: Currently, the longitudinal validity (validity over time) and responsiveness (ability to measure change over time) of the Food Allergy Quality of Life Questionnaire–Adult Form (FAQLQ-AF), the Food Allergy Quality of Life Questionnaire–Teenager Form (FAQLQ-TF), and the Food Allergy Quality of Life Questionnaire–Child Form (FAQLQ-CF) are unknown. Additionally, the self-reported impact of a double-blind, placebo-controlled food challenge (DBPCFC) on health-related quality of life (HRQL) in adults (≥18 years of age), adolescents (13-17 years of age), and children (8-12 years of age) is unknown.
Objective: The aims of this study were to assess the longitudinal validity and responsiveness of the FAQLQ-AF, FAQLQ-TF, and FAQLQ-CF and to assess the impact of a DBPCFC on HRQL.
Methods: Two hundred twenty-one participants suspected of food allergy were included from Dutch allergy centers. Participants undergoing a DBPCFC (experimental group) completed the FAQLQ and Food Allergy Independent Measure (FAIM) 1 month before (baseline) and 6 months after (follow-up) a DBPCFC. Participants not undergoing a DBPCFC (control group) completed the questionnaire package twice with a 7-month interval.
Results: HRQL scores improved after a DBPCFC, with greater improvements in HRQL scores after a negative outcome (food allergy ruled out) than a positive outcome (food allergy confirmed), demonstrating responsiveness of the FAQLQs. Significant correlations were shown between the change (follow-up minus baseline) in FAQLQ and FAIM scores supporting longitudinal validity of these questionnaires: FAQLQ-AF (Pearson correlation coefficient = 0.71, $P < .001$), FAQLQ-TF (Pearson correlation coefficient = 0.35, $P = .018$), and FAQLQ-CF (Pearson correlation coefficient = 0.51, $P < .001$).
Conclusions: Our findings demonstrate the longitudinal validity and responsiveness of the FAQLQs. Greater improvements in HRQL scores were shown after a negative outcome than after a positive outcome. (J Allergy Clin Immunol 2012;130:1136-43.)

Key words: *Double-blind, placebo-controlled food challenge, food allergy, health-related quality of life, longitudinal validation, responsiveness*

Food is essential for life and important in social activities. Consequently, living with food allergy might seriously disrupt the daily life of patients with food allergy.[1] They are often afraid of allergic reactions on accidental exposure and are continuously faced with dietary and social restrictions.[2] Health-related quality of life (HRQL) instruments can be used as outcome measures to evaluate this impact of food allergy and its subsequent interventions on HRQL.[3] HRQL is of particular interest as an outcome measure for food allergy because symptoms of this disease are infrequent and mortality is low.

Recently, the self-administered Food Allergy Quality of Life Questionnaire–Adult Form (FAQLQ-AF), Food Allergy Quality of Life Questionnaire–Teenager Form (FAQLQ-TF), and Food Allergy Quality of Life Questionnaire–Child Form (FAQLQ-CF) were developed for measuring HRQL in patients with food allergy.[2,4,5] The FAQLQ-AF, FAQLQ-TF, and FAQLQ-CF were shown to be valid, reliable, and discriminative instruments.[2,4-6] However, HRQL instruments that will be used as outcome measures in clinical trials must correlate over time with other relevant measures (longitudinally validity) and must be able to measure small but relevant HRQL changes over time (responsiveness).[3,7] Currently, the longitudinal validity and responsiveness of the FAQLQ-AF, FAQLQ-TF, and FAQLQ-CF are unknown.

A double-blind, placebo-controlled food challenge (DBPCFC), which is the gold standard for diagnosing food allergy, is likely to cause HRQL changes over time, especially if the test result is negative (food allergy ruled out). Until now, only 1 study has been published on the impact of food challenges on HRQL. This study showed that parent-proxy–reported HRQL of children with food allergy (0-12 years) improves after a food challenge.[3] Thus far, no studies have been published on the impact of a DBPCFC on HRQL in adolescents (13-17 years of age) and adults (≥18 years of age). Because these age groups are developmentally different, the experience of food allergy and its subsequent interventions might differ for each group. Additionally, no studies have been published on the impact of a DBPCFC on HRQL scores in children (8-12 years of age) from the child's perspective, whereas it is well known that there generally is child-parent disagreement on the child's HRQL.[8,9] Finally, no studies have been published

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Abbreviations used

DBPCFC: Double-blind, placebo-controlled food challenge
FAIM: Food Allergy Independent Measure
FAQLQ-AF: Food Allergy Quality of Life Questionnaire–Adult Form
FAQLQ-CF: Food Allergy Quality of Life Questionnaire–Child Form
FAQLQ-TF: Food Allergy Quality of Life Questionnaire–Teenager Form
HRQL: Health-related quality of life
MID: Minimal important difference
NNT: Number needed to treat
SEM: Standard error of measurement

comparing HRQL in participants who undergo a DBPCFC with control participants.

Therefore, the aims of this study were to investigate the longitudinal validity and responsiveness of the FAQLQs and to investigate the self-reported impact of a DBPCFC on HRQL of adults, adolescents, and children with food allergy.

METHODS

Participants and procedures

Adults (≥18 years of age), adolescents (13-17 years of age), and children (8-12 years of age) who were awaiting a clinically indicated DBPCFC were included from Dutch allergy centers in Groningen and Voorburg between May 2007 and January 2011. The only criterion used for referral for a DBPCFC was a clinical suspicion of food allergy. IgE measurements, skin prick tests, or prior history of anaphylaxis were not routinely used in our decision to refer for a DBPCFC. The 2 centers collaborate on uniform methodology of DBPCFC procedures.[10,11] A DBPCFC consists of a placebo and an active challenge, which were randomly administered on separate days with at least a 2-week interval. Participants and any subjects with patient contact were blinded to the sequence of the 2 challenges.

All patients visiting the clinic with suspected food allergy were placed on the waiting list for a DBPCFC on a first-come, first-served basis. Participants were included in the experimental group or control group based on the expected duration of time spent on the waiting list for a DBPCFC. Participants who were expected to have a DBPCFC within 6 months were included in the experimental group and completed the questionnaire package at home 1 month before (baseline) and 6 months after (follow-up) a DBPCFC (placebo and active challenge) was performed. Participants who were not expected to have a DBPCFC within 6 months were included in the control group and completed the questionnaire package twice with a 7-month interval without undergoing a DBPCFC (no placebo or active challenge). Additionally, participants recruited through Dutch food allergy support organizations were included in the control group when they reported a physician-diagnosed food allergy (skin prick test, IgE).

Participants were excluded from the study if diagnostic/therapeutic interventions or accidental ingestions resulting in clinical allergic reactions (Mueller classification grade III/IV) had taken place between baseline and follow-up measurement or when less than 85% of the questions were completed. Possible differences between descriptive characteristics of participants (Table I) recruited in the participating centers and between participants from the control and experimental groups were examined by using χ^2 (nominal data) and Mann-Whitney (ordinal, continuous data) tests.

This study was approved by the local medical ethics review commission, who deemed that permission from the commission was not required.

Questionnaires

FAQLQs. The Dutch FAQLQ-AF, FAQLQ-TF, and FAQLQ-CF are self-reported, disease-specific instruments for measuring the effect of food allergy on the adult's (≥18 years of age),[2] adolescent's (13-17 years of age),[5] and child's (8-12 years of age) HRQL,[4] respectively. The FAQLQ-AF contains 29 items and 4 domains (Risk of Accidental Exposure, Emotional Impact, Allergen Avoidance and Dietary Restrictions, and Food Allergy–related Health). The FAQLQ-TF contains 23 items and 3 domains (Allergen Avoidance and Dietary Restrictions, Risk of Accidental Exposure, and Emotional impact). The FAQLQ-CF contains 24 items and 4 domains (Risk of Accidental Exposure, Emotional Impact, Allergen Avoidance, and Dietary Restrictions). Each item is scored on a 7-point scale. The total FAQLQ score of each questionnaire is the mean of all items and ranges from 1 (minimal impairment in HRQL) to 7 (maximal impairment in HRQL).

Food Allergy Independent Measure. The Food Allergy Independent Measure (FAIM),[12] a self-report instrument, reflects the participant's perceived food allergy severity and food allergy–related risk. The FAIM consists of 4 expectation-of-outcome questions, which capture the participants' perceived expectation of the chance of accidental exposure and of what will happen after accidental exposure. These expectations are likely to be the source/predictors of HRQL changes in patients with anaphylactic disorders.[13] Additionally, the FAIM contains 2 questions that reflect disease severity. Each question was scored on a 7-point scale. The total FAIM score is the mean of all items and ranges from 1 (limited severity perception) to 7 (greatest severity perception). Instruments based on the method of expectation-of-outcome questions have proved to be useful independent measures for evaluating the construct validity of HRQL instruments[2,4,5,14-16] and are used in this study to evaluate the longitudinal validity of the FAQLQs.

Statistical analysis

Data were analyzed with SPSS software for Windows (version 18.0; SPSS, Chicago, Ill).

Change in HRQL and perceived disease severity after DBPCFC. Changes in HRQL (follow-up minus baseline FAQLQ scores) were tested for significance (Wilcoxon signed-rank test). *P* values of .05 or less were considered statistically significant. The overall difference in HRQL changes was calculated as follows:

HRQL change for the experimental group −HRQL change for the control group.

After the outcome of the DBPCFC, participants in the experimental group (Exp_total) were split into 3 groups: (1) positive outcome (ie, food allergy in question confirmed [Exp_pos]); (2) negative outcome (ie, food allergy in question ruled out [Exp_neg]); and (3) questionable outcome (ie, food allergy not confirmed/not ruled out [Exp_quest]). Additionally, a subgroup analysis was performed on participants with a negative outcome and no remaining other food allergy (Exp_neg_NRFA). Changes in perceived disease severity (follow-up minus baseline FAIM scores) were analyzed in the same way.

Relevance of changes in HRQL after DBPCFCs. Both a statistical and clinical method were used to evaluate whether a change in HRQL was considered relevant.

First, the smallest change in HRQL that is considered statistically important is called the standard error of measurement (SEM) and is calculated as follows:

$$\text{SEM} = \sigma_x \sqrt{1 - r_{xx}}.^{17,18}$$

σ_x represents the SD of the FAQLQ baseline measurement, and r_{xx} represents the reliability or the intraclass correlation coefficient of the FAQLQs.[6,14]

Second, the smallest change in HRQL that is considered clinically important by participants is called the minimal important difference (MID).[19] The MID has been estimated to be approximately 0.5 in several HRQL questionnaires using a 7-point scale[3,17,19,20] and can be used to calculate the therapeutic value of an intervention. The therapeutic value of an intervention is defined as the number of participants who need to undergo the intervention for 1 participant to have a clinically important improvement over and above that which he or she would have experienced with the control intervention. The therapeutic value of a DBPCFC was calculated by using the methodology of number needed to treat (NNT).[21]