

The psychological impact of food allergy and undergoing a food challenge test in adult age

INTRODUCTION

Food allergies are an abnormal response of the body to otherwise harmless food proteins involving the immune system (1). The prevalence of food allergy has increased in recent decades and is now recognised as a substantial public health burden in developed countries with up to 10% affected (2, 3). Symptoms vary and can involve the skin, oropharyngeal tract, gastrointestinal tract, respiratory and cardiovascular systems, with the most severe and sometimes fatal manifestation being anaphylactic shock. Food allergy has an unpredictable nature and individuals with only mild reactions may have a severe and life-threatening reaction on re-exposure.

Although research into possible treatments for food allergy including immunotherapy is being carried out, there is currently no cure. Food allergic individuals must carefully avoid the causal foods on a daily basis and carry emergency treatment such as adrenaline in case they have a reaction. Thus, living with food allergies constitutes a unique stressor that is both chronic and acute, i.e. facing a daily threat of accidental allergen ingestion compounded by acute stress during allergic reactions (4).

Diagnosis of food allergy involves taking a detailed clinical history to guide the requirement for skin prick and/or serum specific immunoglobulin E (sIgE) testing. When the clinical history and tests alone cannot provide a definitive diagnosis, or when the possibility of having outgrown an allergy exists, an oral food challenge is essential (5). A food challenge involves the graded administration of the potential culprit food in order to identify if an individual is allergic or tolerant, thereby confirming or excluding a diagnosis of food allergy.

There is evidence that food allergy can lead to increased anxiety about food safety, social isolation and exclusion, and emotional pressure related to constant vigilance; impacting well-being, mental health and quality of life (6-8). While some quantitative studies have examined the effect of food challenge tests on HRQoL (9-14), the majority have been on children/adolescents or their carers. To our knowledge, only one study has included adults and was done in the context of a double-blind, placebo-controlled food challenge (DBPCFC) (14). It found that HRQoL scores improved significantly after a DBPCFC when all outcomes of the test were combined compared to a control group with greater improvements after a negative outcome when a food allergy was ruled out than a positive outcome (food allergy confirmed). However, there is a need to assess whether this is the case for open food challenges which are the type of food challenges more commonly performed in clinical practice rather than DBPCFC.

Another aspect that has received little attention in the context of food allergies is the role of health anxiety. People who are anxious about their health are more likely to misinterpret health information as personally threatening (15, 16); show adverse emotional reactions to ambiguous diagnostic test results, and are less reassured following the medical investigation of symptoms, even when there is no evidence of disease (e.g. 17, 18). Based on these findings, people with high health anxiety may be less reassured by a negative allergy test than people low on health anxiety.

The present study was designed to assess the psychological impact of food allergy and open food challenges on HRQoL, emotional distress, health anxiety and negative mood in an adult population. Based on previous research we predicted that: 1) there would be better HRQoL and lower emotional distress, health anxiety and negative mood in people who test negative following a food challenge test. 2) 'HRQoL' would improve among all people undergoing a food challenge test, but to a greater extent among people testing negative. 3) People higher on health anxiety would be less likely to be reassured by a negative food challenge.

MATERIALS & METHODS

Design

This research consisted of two studies: 1) a cross-sectional study that compared HRQoL and psychological measures among adults with clinician confirmed food allergy diagnosis (based on clinical history, skin prick and/or serum IgE testing) vs. adults who had undergone a food challenge test and 2) a prospective study that examined changes among people undergoing a food challenge test.

A negative challenge was defined as tolerating the food without any evidence of allergic symptoms, thus allergy to the food tested was excluded while a positive outcome required the presence of symptoms and objective signs consistent with IgE mediated food allergy.

Ethical considerations

The North East-Sunderland National Research Ethics Service (NRES) Committee approved this research project in September 2013 (REC reference: 13/NE/0271). Following this, Research and Development approval was sought from the Royal Brompton and Harefield NHS Foundation Trust and was granted (2013AT007B). The research was conducted in accordance with the ethical standards established in the Declaration of Helsinki and informed consent was obtained from all participants before enrolment in the studies.

Recruitment and participants

Study 1

Individuals that had previously attended the Allergy Department at Royal Brompton & Harefield NHS Foundation Trust, London and were diagnosed with food allergy based on clinical history, skin prick and/or IgE tests (Group 1 FA-No challenge) or who had previously undergone a clinically indicated food challenge (Group 2-Food Challenge) were identified from the medical records. The inclusion criteria for participating in this study were aged 18 or older, clinician confirmed IgE mediated food allergy or previous food challenge. Individuals could not participate if they were considered adults with incapacity.

Study 2

All individuals who were waiting to have a food challenge test between October 2013 to March 2015 were invited to participate in the study. Fifty-six individuals were eligible to participate.

Measures

Demographic characteristics

Participants were asked to record their age, gender, ethnicity and educational qualifications.

Food allergy characteristics

Specifically designed questions were used to assess the foods that previously caused allergic symptoms, age when first experienced a reaction, treatment received, investigations for food allergy and adrenaline auto-injector possession. Participants who had undergone a food challenge test were asked about the number and type of food/s they had tested, time between the initial reaction and the food challenge test to the suspect food and outcome of the challenge.

Health-related quality of life

The FAQLQ-Adult Form was used in this study as this is the only disease-specific HRQoL questionnaire for food allergic adults (19), using a 5-point Likert scale with response options: 0-not at all, 1-slightly, 2-moderately, 3-very and 4-extremely. It has four subscales which can be combined to generate a total HRQoL score: Allergen Avoidance and Dietary Restrictions (AADR), example item 'How troublesome do you find it that you have to be alert to what you are eating?'; Emotional Impact (EI), example item 'How frightened are you of accidentally eating the wrong food?'; Risk of Accidental Exposure (RAE), example item 'How troublesome is it that labels are incomplete?'; Food Allergy-related Health (FAH), example item 'How worried are you that it is unclear to which foods you are allergic?'. In Study 1, participants who had undergone a food allergy challenge test were asked to complete this in relation to their perceived quality of life now and prior to completing the challenge test. In Study 2, participants completed the questionnaire before the food challenge and three months after.

Emotional distress

Emotional distress was measured using the 12-item version of the General Health Questionnaire (GHQ-12) (20). Responses were scored 0-3 and were summed to produce a scale from 0 to 36, with higher scores indicating greater distress.

State anxiety

State anxiety was assessed with the validated 6-item version of the Spielberger State Trait Anxiety Inventory (STAII) with response options on a 6 point scale (21). Responses were totalled giving a score of between 6 and 24, with higher scores indicating higher anxiety.

Positive and Negative Affect was measured using the Positive and Negative Affect Schedule (PANAS) (22). Participants were asked how they feel 'right now'. Participants were asked to rate the extent to which they experienced each of the emotions on a 5-point Likert scale ranging from "very slightly or not at all" to "extremely". Both subscales range from 10 (low) to 50 (high).

Health anxiety

A shortened version of the Health Anxiety Questionnaire (HAQ) (23, 17) was used in this study in order to assess the presence of health anxiety in our study population. Participants responded using a 4-point Likert scale 'not at all' or rarely', 'sometimes', 'often', 'most of the time', with responses averaged to give scores from 1 to 4, with higher scores indicating higher levels of health anxiety.

Co-morbidities

Participants were asked whether they suffered from any other allergic conditions or any other medical conditions.

Reassurance following a negative test was assessed with the following items: 'If your test to any food was NEGATIVE (i.e. no symptoms) how reassured are you that you are not allergic to that food?'. Response options were: 'Not at all', 'Slightly', 'Moderately', 'Very' and 'Extremely'.

Food re-introduction. Participants were also asked if they had re-introduced the food back into their diet if their food challenge test was negative (response options: 'Yes, small amounts', 'Yes, normal amounts', 'No, still avoiding' or 'No, haven't re-introduced but not avoiding'). If they had not re-introduced it, what were the reasons (response options: 'Fear of reaction', 'Not convinced of negative test', 'Reaction on eating food after challenge', 'Not confident to try alone', 'Other').

If your challenge was negative, does this mean that you no longer need to carry any emergency medication? 'Yes' 'No, I have other allergies'

Procedure

All potential participants were provided with an information sheet including details about the study and a copy of the questionnaire. They were informed that participation was voluntary and that they had the right to withdraw at any time during the study. Furthermore, declining to take part in the study would have no impact on their care. They were also provided with the researchers contact details in case they had any questions about the research. If they wished to take part, they had to give written informed consent and complete the questionnaire provided with the information sheet and return in the enclosed stamped self-addressed envelope.

Data analyses

Statistical analyses were performed using SPSS software (IBM SPSS Statistics for Windows, Version 23.0, Armonk, NY: IBM Corp). Differences between groups were assessed using either General linear model (GLM) for continuous data or chi-square/ Fisher's exact test for categorical data. Linear regression was used to assess differences between the groups on measures of HRQoL, emotional distress, health anxiety and mood. GLM was used to assess change in HRQoL between the two food challenge groups. The percentage of missing data was less than 5%.

The sample size was calculated to detect a medium effect size (Cohen's $f^2=0.15$ / Cohen's $f=0.25$) at 80% power and 5% significance level. For linear regression, assuming ten predictors, the sample size was 118. For GLM to detect changes in pre and post-challenge HRQoL scores for 2 groups (food challenge positive or negative) across two time points (before and three months after the test), the total sample size was 34 (G*Power, version 3.1.7) (14).

RESULTS

Study 1

In total 276 individuals participated. Group 1 (FA-No challenge) consisted of adults with clinician confirmed food allergy but who had not undergone a food challenge test. The response rate for Group 1 was 83.2% with 208 adults (69.7% female- n=145) consenting to participate out of 250 eligible individuals. Group 2 (Food Challenge) included 68 adults who had previously undergone a food challenge test. All challenge tests were clinically indicated either for diagnostic purposes i.e. inconclusive skin prick/sIgE tests or to assess if individuals had outgrown an allergy i.e. suspected to no longer be allergic. The response rate for this group was 59.1% (68 out of eligible 115 individuals participated). Fifty percent of the 68 participants (n=34) had a negative challenge outcome i.e. allergy to tested food excluded (FC-Negative) and 50% (n=34) had a positive challenge test to a food (FC-Positive) i.e. allergy confirmed.

In the total study sample (n=267), the majority were female (69.2% n=191), had educational qualifications (97.8%, n=261), and identified their ethnicity as White (73.6%, n=203). There were significant differences between the groups in age ($F(2,273) = 4.138$; $p=0.017$); post-hoc comparisons showed the FC-Positive group were significantly older than Group 1 ($p=0.024$), but there was no difference in age between the FC-Positive and FC-Negative subgroups ($p=1.000$). There were no significant differences between the groups in terms of gender, ethnic group, or educational level (Table I).

As is common in individuals with food allergies, many of the participants suffered with other allergic conditions. These included: asthma 59.1% (n=163) and allergic rhinitis 68.8% (n=190), although prevalence of other comorbidities such as heart disease was low. The FC-Positive group were more likely to have asthma than Group 1 (OR: 3.559, 95% CIs: 1.414 to 8.962, $p<0.007$), and the FC-Negative group (OR: 4.667, 95% CIs 1.540 to 14.143, $p=0.006$) with no difference between the FC-Negative group and Group 1 (OR: 1.311, 95% CIs: 0.634 to 2.710, $p=0.465$). There were no differences between the groups on other allergies or comorbidities.

Food allergy profile, diagnosis and treatment

Food allergy profiles across the groups are shown in detail in Table II. Forty-nine percent (n=112) reported that they had previously experienced symptoms consistent with anaphylaxis.

There were no significant differences between the groups in terms of age of allergy onset, food type, anaphylaxis and treatment received. There was a significant difference in gastrointestinal (GI) symptoms between groups, with the FC-Negative less likely to report GI symptoms than Group 1 ($p=0.017$), but no differences between the other comparisons (FC-Negative vs. FC-Positive; FC-Positive vs Group 1). There were no significant differences between the groups on the other symptoms.

Among participants who underwent a food challenge, the mean length of time between first experiencing symptoms to the suspect food and undergoing a food challenge to that food was 12.47 years, ranging from one month to 50 years.

Adrenaline auto-injector possession

65.2% (n=180) of all participants reported that they were advised to and were carrying adrenaline auto-injector devices. There was a significant reduction in the proportion of people who reported carrying an adrenaline autoinjector who tested negative in the food challenge, (85.3%, n=29 pre-challenge vs. 61.8%, n=21 post-challenge; $p=0.021$). In the FC-Positive group there was no significant change (52.9 %, n=18 pre-challenge vs. 67.6%, n=13 post-challenge; $p=0.227$).

Health-related quality of life

The FC-Negative group reported better HRQoL than Group 1, even after adjusting for age, presence of asthma and GI symptoms (factors that had differed across the three allergy groups). There was no difference in total HRQoL scores between the two groups with confirmed food allergy (FC-Positive vs Group 1) in both unadjusted and adjusted analyses (Table III). Presence of both asthma and GI symptoms were predictive of poorer HRQoL ($p=0.006$ and $p<0.001$ respectively). The same pattern of significant results was seen in the HRQoL sub-scales AADR and FAH. No differences were observed between the FC-Positive or FC-Negative groups in comparison with Group 1 once the Bonferroni correction had been applied.

Emotional distress and mood

There were no differences between the three groups on emotional distress, state anxiety, or positive and negative affect. The FC-Positive group reported lower levels of health anxiety than Group 1 in both unadjusted and adjusted analyses, although this was no longer significant following a Bonferroni correction (Table III).

Change in HRQoL in food challenge group

The GLM analysis showed a significant effect of time, with improvements in HRQoL ($F(1,65) = 44.40$, $p<0.001$). There was a non-significant trend between outcome of challenge and change in HRQoL, $F(1,66) = 3.077$, $p=0.084$, with a higher improvement in HRQoL scores in the challenge negative than the challenge positive group (0.762 vs 0.445 respectively).

There were differences between the FC-Negative vs. FC-Positive in presence of asthma. When this was entered into the model, improvement in HRQoL over time remained significant ($p<0.001$) and the interaction became non-significant ($p=0.214$).

Reassurance in results

The mean levels of reassurance following a negative outcome were 3.882 (SD=1.274), with 47.1% (n=16) responding 'extremely', 17.6% (n=6) 'very', 14.7% (n=5) 'moderately', 17.6% (n=6) slightly and 2.9% 'not at all' reassured. The correlation between health anxiety and reassurance for people testing negative was -0.076, $p=0.670$.

Food re-introduction

Participants with a negative challenge outcome responded that 76.5% had re-introduced the food tested back into their diet in normal amounts or small amounts. 2.9% had not re-introduced but were not specifically avoiding while 20.6% were still avoiding. The reasons given by those still avoiding were: fear of reaction (n=2), not confident to try alone (n=4) and reaction on eating food after challenge (n=1).

Study 2

Fifty-three out of 56 eligible individuals, agreed to take part (response rate 94.6%), completing questionnaires before the food challenge test (while on the waiting list) and immediately after test completion. 45 tested negative, and only 8 tested positive. Forty participants (75.5% response rate) completed a questionnaire three months after the challenge. Thirteen participants did not complete the final questionnaire despite being sent a reminder. The mean age of the 53 participants was 33.5 years (SD=12.5) with a range of 18 to 62 years. 71.7% were female, 84.9% (n=45) had educational qualifications and the majority identified their ethnicity as White (69.8%, n=37). Many of the participants suffered with other allergic conditions in particular, asthma 62.3% (n=33), allergic rhinitis 60.4% (n=32) and atopic dermatitis 49.1% (n=26).

The sample included participants with a range of food allergies and symptoms. The mean number of foods that participants reported as having previously experienced symptoms to was 3.09 (SD=2.41, range 1 to 11 foods). 47.2% had experienced symptoms to peanut, 43.4% to tree nuts, fruits 37.7%, shellfish 34%, fish 24.5% as well as a variety of other foods. The symptoms experienced included oropharyngeal 64.2%, skin

71.7%, upper airway 30.2%, respiratory (lower airway) 43.4%, gastrointestinal 50.9% and anaphylaxis 37.7%. The mean age when individuals first experienced allergic symptoms to any food was 20.5 years ($SD=16.4$, range 6 months to 56 years).

The most common foods that were tested with food challenge were tree nuts (34%, n=18), shellfish (24.5%, n=13), peanut (20.8%, n=11), and fish (17%, n= 9). The average time between first experiencing symptoms to a food and undergoing a challenge test to the suspect food was 8.58 years ($SD=12.18$) (range 3 months to 32 years; median 3 years).

Health-related quality of life

Change in HRQoL over time was computed for responders to the follow-up questionnaire, and using an intention-to-treat analysis, where baseline scores of non-responders were used as follow-up scores, thereby assuming no change in HRQoL (Table IV).

In the 40 participants who completed the questionnaires at all time points, there was a significant change from before and after the challenge test in mean total score $F(1,39) = 16.86$; $p <0.001$. Intention to treat analysis was also significant ($F(1,52) = 15.346$; $p <0.001$).

Significant differences were observed across all four subscales of the HRQoL questionnaire, although applying a Bonferroni correction (adopting a revised p value of $p < 0.01$) meant the change in RAE was no longer significant (Table V).

The results showed significant improvement in HRQoL following a food challenge in those testing negative. The small sample size among people testing positive meant the study was underpowered to test for differences in HRQoL according to test outcome.

Emotional distress and mood

There were no significant changes in emotional distress, health anxiety, state anxiety or positive mood over time (Table VI). There were significant differences over time in both the PANAS-negative score and state anxiety, due to lower anxiety and negative mood after the test than at baseline, but no differences between baseline and three months post-challenge (Table VI).

Adrenaline auto-injector possession

Prior to the challenge, 60.4% (n=32) of participants in the whole sample (n=53) reported that they possessed adrenaline auto-injector devices. Following the challenge only 50.9% (n=27) still required these. In the group who tested negative (n=45), the change in proportion of people carrying adrenaline autoinjectors approached significance (60%, n=27 vs 49%, n=22, $p=0.063$). There was no difference in the challenge positive group but the sample size was very small.

Reassurance in results

The mean levels of reassurance following a negative outcome were 4.000 ($SD=1.247$), with 46.4% (n=13) responding 'extremely', 25.0 % (n=7) 'very', 17.9% (n=5) 'moderately', 7.1% (n=2) slightly and 3.6 % (n=1) 'not at all' reassured. The correlation between health anxiety and reassurance for people testing negative was -0.47 , $p=0.812$.

Food re-introduction

Three months after the challenge, 95% of participants had introduced the food tested into their diet (50% normal amounts, 45% small amounts). The reasons given by the 5% still avoiding the food were: fear of reaction, not confident to try alone, reaction on eating food after challenge and not convinced of the negative test.

DISCUSSION

We examined HRQoL, emotional distress, health anxiety and mood among adults undergoing a food challenge, using both cross-sectional and prospective study designs. Study 1 showed that adults who had tested negative (FC-Negative) reported better HRQoL than people living with a clinician diagnosed food allergy who had not undergone a food challenge (Group 1). There were no differences in HRQoL between the FC-Positive group and Group 1. These results remained significant controlling for age, and presence of asthma or GI symptoms, which varied between the groups. The groups did not differ in relation to emotional distress, health anxiety or positive and negative mood. However, the overall sample mean for GHQ-12 was above the scores of 11-12 which is considered to indicate a risk of being diagnosed with a mental illness (20) thus showing that some food allergic adults have high levels of psychological distress.

Consistent with previous research (14) there were significant improvements in HRQoL over time. The retrospective study (Study 1) showed significant changes in total HRQoL scores, with improvements in two out of four of the subscales (Allergen Avoidance & Dietary Restrictions and Food allergy related Health), while the prospective study (Study 2) showed significant improvements in three, with positive changes also observed in Emotional Impact. This suggests people may have greater difficulty recalling the emotional impact of an allergy than other aspects. Following a negative challenge, fewer individuals reported a need to carry adrenaline auto-injector devices than those with a positive test. However, it is not clear why the FC-Negative group did not report lower levels of risk of Accidental Exposure when they have had allergies to particular food groups ruled out.

Contrary to predictions we found no differences in HRQoL among people testing positive compared with those testing negative. In Study 1, the interaction between time and food challenge outcome approached significance, but once group differences in the prevalence of asthma were controlled for, the interaction became non-significant. Having asthma was a significant independent predictor of HRQoL which is consistent with previous findings (8). Food allergies often co-exist with asthma (25), and can also trigger or worsen asthma symptoms making this relationship more complex (26). Study 2 had too few positive challenge outcomes to test for group difference in HRQoL. Previous research has shown people testing positive also report increases in quality of life, although to a lesser extent than people testing negative (14). The benefits of a positive test include greater certainty about which foods to avoid, allowing the affected individual to develop adaptive strategies to better manage their condition that may lead to improvements in HRQoL.

A novel aspect of this study was that health anxiety was also measured that has not been studied previously in food allergic individuals. Health anxiety refers to apprehension and fear that changes in bodily sensations may be indicative of a serious illness (16). Individuals with high health anxiety often fail to be reassured by medical tests (e.g. 17). However, among the negative challenge participants, there was no significant association between reassurance and health anxiety, but this part of the study was underpowered. Following a negative challenge, individuals are advised that they can introduce the food

that they were avoiding back into their diets. In Study 2, 95% of participants re-introduced the food. However, in Study 1 only 76.5% had done so. This is an area that requires further studying in order to understand the reasons why individuals may not be convinced or trust the result to eat the food again.

Of concern is the average time participants reported between first experiencing symptoms to a food and undergoing a challenge test to the suspect food: 12.47 years in Study 1 and 8.58 years Study 2. This may also reflect the lack of education of the public regarding food allergies in adults as well as the limited adult allergy services in the UK and the provision of food challenge tests. There is now also evidence that delaying food challenge tests is associated with direct and indirect economic costs (21-28).

Strengths and limitations

A strength of this study is that it explored an area and a population that has received little attention, exploring HRQoL in adults with clinician-diagnosed food allergy and who had undergone a clinically indicated open food challenge in the UK using a disease specific questionnaire. Furthermore, emotional psychological distress, mood and health anxiety were assessed which has also not been explored in this group.

The large sample of food allergic adults allowed for inclusion of participants with different ages and types of food allergies. However, a larger prospective study is needed to adequately assess whether FC-Positive and FC-Negative groups differ in relation to HRQoL, and to assess the relationship between health anxiety and failure to be reassured following a negative test.

In the prospective study, participants were followed at three months after the challenge test. Future studies can potentially assess HRQoL at longer periods of time after challenge to assess whether this benefit from undergoing a challenge test is maintained as was the case in the retrospective study. Strategies for achieving a good response rate will need to be considered as in this study we found the response rate for the follow up questionnaire was reduced.

In addition, a multi-centre approach to a single centre study, may have strengthened the external validity of our findings and reduced any potential bias due to other aspects of care received by participants that may have positively impacted on their experience.

CONCLUSIONS

The findings from this research indicate that the issues of living with food allergy faced by adults have a negative impact on their HRQoL. Undergoing an open food challenge test was found to significantly improve HRQoL. By making these tests more widely available in clinical practice and clarifying whether an individual is allergic or not, any uncertainty can be dispelled, unnecessary food restrictions can be avoided and HRQoL can be improved.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest.

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