

Effects of elimination diets and clinical findings on mothers' anxiety in infants with food allergy with non-life-threatening reactions

Abstract

Background: In food allergies (FA), the current treatment is eliminating the responsible food from the diet until tolerance develops. We aimed to determine the effects of the mother's elimination diets and clinical findings on the mothers' anxiety in infants with food allergy (FA) with non-life-threatening reactions.

Methods: Our study included 100 infants with FA and 35 healthy infants as control. A data form was prepared to collect information about the infants' and their mothers' socio-demographic characteristics, clinical findings, features of the mother's elimination diet, and FA-related internet search. State-Trait Anxiety Inventory (STAI) was applied to all mothers.

Results: The STAI (state anxiety and trait anxiety) scores of the mothers of the infants with FA were higher than the control group ($p<0.001$, $p=0.001$, respectively). Of the infants with FA, 51% had food protein-induced allergic proctocolitis (FPIAP), 29% had atopic dermatitis (AD), 20% had urticaria-angioedema (U/AE). It was found that state anxiety scores were higher in mothers whose child had FPIAP, who had multiple food eliminations, who followed the allergy groups on social media, and who made the elimination diet herself ($p=0.002$, $n=0.048$, $p<0.001$, $p=0.001$, respectively).

Conclusion: The state anxiety and trait anxiety of the mothers of the infants with FA were higher than the control group, and the state anxiety scores were higher especially in the mothers of infants with FPIAP and multiple food elimination.

Keywords: Food Allergy; Infants; Mothers; Anxiety; Diet

An Impact Statement: The anxiety of the mothers of the infants with food allergy were higher than the control group, and the state anxiety scores higher than the mothers of infants with food protein-induced allergic proctocolitis and multiple food elimination.

Introduction

Food allergies (FAs) have become increasingly more common throughout the world in recent years. Recent studies have shown that the prevalence of FA has increased by up to 10%, mainly in children (1-3). Cow's milk allergy (CMA) and egg allergy are the most common food allergies in infants (4,5). There is no curative treatment that has been put into routine use yet despite the attempts for oral immunotherapy in peanut, milk, and egg allergies (6).

The current approach for management of infants with FAs is to eliminate the offending food that causes allergic reactions until they develop a tolerance, (i) to educate the family about emergency situations and their management in case of accidental intake, (ii) to follow up the growth and development of the infant, and (iii) to follow-up the development of tolerance.

It has been shown that in severe cases of FAs, the risk of life-threatening reactions after accidental intake increases the anxiety of families and children and, therefore, may lead to severe restrictions in their social lives and a decrease in quality of life (7-10). Similarly, studies have shown that mothers of children with food allergy with non-life-threatening reactions have high anxiety, impaired quality of life, and even unnecessarily restricted elimination diets (11,12). However, in children with non-life-threatening reactions, the mothers' anxiety level and the affecting factors are not clearly known.

The state-trait anxiety inventory (STAI) is a well-standardized, 40 item questionnaire designed as a self-report instrument to evaluate both state and trait anxiety. The STAI is a tool widely used for the screening of anxiety in the population (13).

In this study, we aimed to investigate the elimination diet practices and anxiety levels of mothers of infants with different clinical findings and with FA with non-life-threatening reactions.

Material and methods

Study Design

This cross-sectional survey study was conducted between September 2018 and September 2019 in a tertiary referral Pediatric Allergy and Immunology with Child Health and Psychiatry outpatient clinics.

Ethics and Consent

Our university Institutional Review Board approved this study (Approval #: KA18/251). Verbal and written consent of the parents of the children with FA were obtained before participating in the study. All study procedures were conducted following the Declaration of Helsinki and local laws and regulations.

Participants

Infants aged 0-1 year who were referred to our pediatric allergy outpatient clinic with suspicion of FA and diagnosed with CMA and/or egg allergy were included in the study. Healthy children followed for growth development within the same age group constituted the control group. The patients were assigned into three groups based on the clinical finding as follows: food protein-induced allergic proctocolitis (FPIAP), atopic dermatitis (AD), urticaria-angioedema (U/AE).

Infants with food allergies other than cow's milk and/or egg infants with FA with life-threatening reactions (such as anaphylaxis and food protein-induced enterocolitis), and infants with chronic diseases were excluded from the study. In addition, infants with severe atopic dermatitis and infants with exacerbation of atopic dermatitis in the last month were also excluded from the study. Mothers with chronic diseases that may affect their psychological status and mothers with psychiatric diseases with a doctor diagnosis were excluded from the study.

Evaluation of FA

All patients were subjected to a detailed evaluation of the history of FA. The diagnosis of FA was based on the criteria suggested by the European Academy of Allergy and Clinical Immunology (EAACI) in the food allergy and anaphylaxis guidelines (1). The diagnosis of FPIAP was based on the same guidelines (history, improvement of symptoms by eliminating the offending food, recurrence of symptoms following oral food challenge-OFC). OFC was performed to mothers and/or children after 2-4 weeks of eliminating the suspected foods. The AD diagnosis was based on the Hanifin-Rajka criteria [14]. All patients with AD and U/AE underwent skin prick-test (SPT) with food allergens (cow's milk, egg, wheat flour, soy flour, tree nuts, sesame, peanut, fish) by using an allergen test solution (ALK, Denmark) and prick-to-prick test (cow's milk and egg). OFC was performed in all children after 2-4 weeks of eliminating the suspected foods.¹ The children were followed up every three months until tolerance developed.

Data Collection

Socio-demographic Data Form:

After evaluation of FA, the mothers of infants have filled out a socio-demographic data form. This form was prepared to collect data about the socio-demographic characteristics of the mothers and the infants, such as age, sex, maternal education and employment, the number of siblings, type of delivery, whether the mother received support for the infant's care. Also, in this form, the time of onset of clinical findings, the person who made the elimination diet (mother, infant, mother and infant together), the number of avoided food, the person who recommends starting the elimination diet (self-decision, doctor's recommendation, friend's recommendation, internet research), the time spent on the FA-related internet search and whether the mother followed an allergy group on social media were questioned.

The children were categorized according to the number of foods they eliminated. If they eliminated three or more foods, they were categorized in the multiple food elimination group.

State-Trait Anxiety Inventory (STAI):

The State-Trait Anxiety Inventory (STAI) is a self-reported questionnaire composed of 40 items developed to evaluate two different types of anxiety: state anxiety (emotional condition transitory), whose reference frame is the “now, at this moment”, and the anxiety trait (anxiety tendency relatively stable), whose reference frame is “in general, in most of the times.” The STAI has a Likert-type response format with four options (*1=almost never/nothing; 2=some/some times; 3=quite/often; 4=a lot/almost always*). Each graded from a minimum score of 20 to a maximum of 80, which indicates greater anxiety (13). A cutoff score of 40 is commonly used to define probable clinical levels of anxiety (15). A Turkish version of Spielberger's STAI was validated and previously used to measure mothers' anxiety levels (16). The internal reliability of the Turkish version was 0.94-0.96 for state anxiety and 0.83-0.87 for trait anxiety.

Statistical Analysis

G*Power 3.1.9.2 (Düsseldorf University, Germany) program was used to calculate the sample size of the study. It was calculated that the total sample size should be at least 81, given the margin of error (α -error) was 0.05, the effect size was 0.4, and the power of the test ($1-\beta$ error) was 80% (goodness-of-fit tests for contingency tables) (17).

Statistical analyses were performed using IBM SPSS 21.0 (Statistical Package for Social Sciences, SPSS, Inc., Chicago, IL). The results were expressed as the number of cases (percentage) for categorical data or mean \pm standard deviation for continuous data. Non-normally distributed data were presented using medians, minimum-maximum, and interquartile range (IQR). Non-normally distributed data were compared by Kruskal-Wallis tests. Non-parametric tests (the Mann-Whitney U test or the Kruskal-Wallis test) were used to compare data. Spearman's rho test was used for the correlation analysis. For the multivariate analyses were further entered into the logistic regression analysis to determine independent predictors of patient outcome. Hosmer-Lemeshow goodness of fit statistics were used to assess model fit. *P* values <0.05 were considered statistically significant.

Results

The study included a total of 100 children with FAs and 35 healthy children. The median age of children with FAs was 4.0 (3.0) [1-12] months, and 58% were females. The median age of the control group was 5.0 (3.0) [1-8] months, and 42.9% were females. No significant difference was found between children with and without FAs in terms of age; gender; maternal age, education status, employment, the number of siblings, type of delivery, whether the mother received support for the infant's care. The mothers of children with FAs had significantly higher state anxiety ($p<0.001$) and trait anxiety ($p=0.001$) scores compared to those in the control group. The demographic data of the children and their mothers' and anxiety scores were given in Table I.

Of those with FAs, 51% had FPIAP, 29% had AD, and 20% had U/AE. All of the cases were on an elimination diet for at least one food before evaluation of FA. The rate of initiating an elimination diet with mothers' self-decision was 33.4% in the FPIAP group, 20.7% in the AD group, and 15% in the U/AE group. The most common dietary regimen was multiple food elimination. The highest rate of multiple food elimination was in the FPIAP group (74.5%), with a significant difference ($p=0.008$). The most significant reduction in the number of eliminated foods after the evaluation of FA was in the FPIAP group (76.5%) ($p<0.001$). The comparison of groups regarding their demographic data, features of the elimination diet were shown in Table II.

The relationship between mothers' anxiety levels and the factors that may affect anxiety levels were shown in Table III. The state anxiety scores were significantly higher in mothers who had an infant with

FPIAP (compared to those with U/AE, $p<0.001$), in mothers who were on the elimination diet alone (compared to those on the elimination diet together with the infant, $p=0.001$) and who had multiple food eliminations ($p=0.048$) (Figure I).

State and trait anxiety scores were found to be higher in mothers who followed allergy groups on social media ($p<0.001$, $p=0.002$, respectively). State anxiety scores were found to be higher in mothers who spent more than 1 hour on the FA-related internet search but not statistically significant ($p=0.068$). A positive correlation was found between the state and trait anxiety scores ($r=0.65$ and $p<0.001$). When the factors affecting state and trait anxiety scores were analyzed with logistic regression analysis, it was determined that following allergy groups on social media was effective in both state and trait anxiety scores (Table IV) ($p=0.001$, $p=0.003$).

Discussion

In our study, it was determined that the anxiety levels of mothers with children with FA were higher than healthy children, and most of them had a restricted diet more than necessary before the allergy work-up. Among mothers, it was determined that elimination of multiple foods was high, especially in patients with FPIAP, and about three-quarters of them had multiple food elimination either by the family's own decision or by the doctor's recommendation. After the allergy work-up, multiple food allergy was only 3.9% of children with FPIAP. In addition, it was found that the state anxiety levels were higher in mothers of children with FPIAP, mothers who eliminated multiple food, and mothers who followed allergy groups on social media compared to other groups.

In our study, all families of children had started an elimination diet before the evaluation of FA, and a third of these families decided to start the elimination diet by themselves. Studies have shown that 26-76% of the families of children with FAs had started the elimination diet themselves before the evaluation of FA, and even a restricted diet could be applied in children (8,11,18,19). Beken et al. (11) found that 55.2% of the patients evaluated with food allergy suspicion applied food elimination before the evaluation of FA, and even 45.9% of these patients applied multiple food elimination. In this study, it was shown that only 40% of patients had food allergies after OFC. In our study, after the allergy work-up, three-quarters of children with FPIAP, half of children with AD, and one-fourth of children with U/AO had a decrease in the number of eliminated foods. Currently, the only established treatment

method for FAs is to avoid suspicious foods, but an unnecessary stringent elimination diet may lead to nutritional deficiencies in the mothers and children (20).

Studies have found that children with life-threatening FA and their families have higher anxiety scores due to the risk of anaphylaxis after accidental food intake (21-23). It has been shown that mothers' anxiety levels are also high in non-life threatening food allergies such as FPIAP and mild AD. It has been shown that the unproven diagnosis of food allergy and symptoms are effective on the mother's anxiety level, especially in late-type FA (11,21). Cortes et al. (24) have also found that the mother's anxiety was related to symptoms, especially in children with gastric and cutaneous symptoms. Beken et al. (11) found that mothers of children with food allergy aged 0-2 years had higher levels of state and trait anxiety than the control group, and state anxiety levels decreased when food allergy was excluded after OFC in mothers who started the elimination diet themselves. In our study was found that the mothers who had infants with FAs had significantly higher state anxiety scores than the control group. In addition, state anxiety scores were higher in mothers who eliminated multiple food. Deschildre et al. (25) found that a restricted diet in children with a peanut allergy was associated with an increase in the family's anxiety level. It is not clear in the studies whether mothers with anxiety tend to have a more restricted diet or whether a restricted diet increases anxiety. In order to explain this situation, there is a need for more studies in which mothers' anxiety is monitored for a long time and evaluated repeatedly. Interestingly, in our study also was found that the mothers who had infants with FAs had significantly higher trait anxiety scores than the control group. This was an unexpected result for us. Similar to our study, Avcil et al. study found that mothers of children with asthma had higher both state and trait anxiety levels than the control group (26). Recent studies have suggested a close association between prenatal maternal distress and allergic diseases in the offspring. Prenatal maternal distress can lead to steroid imbalance and oxidative stress, which can be a risk factor for the development of allergic diseases in offspring (27). Kim et al. study, genome-wide DNA methylation microarray and pyrosequencing were used to prove epigenetic change for the association between maternal anxiety during pregnancy and AD development in the offspring. This result has been shown to be associated with DNA methylation of MMEL27 (28). Although there are studies that support maternal anxiety as a risk for the development of allergic diseases in their children, this is not clear.

Today, it is effortless to access information through internet searches, but information pollution and the inability to differentiate appropriate information sources may confuse families (29). Some studies have shown that supporting parents' access to educational materials about their children's disease reduce their anxiety and improve their quality of life (30). It has been a common trend that the families of children with chronic diseases follow blogs related to the subject on social media/internet or get involved in the disease-specific support groups. Although these platforms provide social support to families, they may sometimes affect the families negatively and produce the opposite outcome due to the access to information that will further increase their anxiety, excessive generalization, and taking wrong examples (31,32). Beken et al. (11) found that FA-related internet research was more common in mothers who decided to start a food elimination themselves. In our study, detailed data on the content of the internet research could not be obtained and the data were recorded only according to the report of the mother. However, in our study, it was found that anxiety levels were higher in mothers who spend more time on the FA-related internet search and follow an allergy group on social media. We think that this result can be explained as mothers with high basal anxiety levels want to do more research, or mothers confuse because of the accuracy of the information they learn as a result of internet research or whether it is related to the disease of their child.

As a limitation of our study, the anxiety of the mothers were not re-evaluated. Since our study is a cross-sectional study, the anxiety could not be re-evaluated, but we think that re-evaluation of the anxiety may explain the effects of elimination diet on the psychological status of the mothers more clearly. Another limitation of our study was that patients without milk and or egg allergies were not evaluated. However, we evaluated these foods because they are the most frequently encountered allergies in practice, and the most commonly consumed foods in this age group. The heterogeneity of the clinical findings of the patients also seems to be a limitation of our study, but the patients with severe symptoms (anaphylaxis, severe eczema, etc.) were excluded from the study, considering that it may affect the anxiety of the mother. This study was conducted in a private university hospital, and the mothers' education levels were higher than the general population. Therefore, we think that it would be appropriate to compare this study with a multi-center study with a larger number of patients to represent the general population.

Demonstrating that the clinical findings, characteristic of elimination diet, and the internet usage habits affect the mothers' anxiety level who have children with FAs was the strength of our study.

Conclusion

Understanding the concerns of the families of children with FA, educating them about what to do in an emergency, informing them about the natural course of the disease will help them control their anxiety and make it easier for families to cope with the disease. A multidisciplinary treatment approach, including dietary practices and psychological and social support, should be used for the families with children with FAs who were recommended an elimination diet.

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Conflicting Interest

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Fig I: Comparison of mothers' state and trait anxiety scores according to clinical findings (Fig Ia, Fig Id; $p=0.052$), who did the elimination diet (Fig Ib, Fig Ie; $p=0.304$), and characteristic of elimination diet (Fig Ic, Fig If; $p=0.853$).

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