ASTHMA ALLERGY IMMUNOLOGY
ASTIM ALLERJİ İMMÜNOLOJİ

doi: 10.21911/aai.693
Asthma Allergy Immunol 2022;20:148-154

RESEARCH ARTICLE

Received: 29.11.2021 • Accepted: 21.01.2022
Online Published: 31.03.2022

Effect of a Pseudoallergen-Free Diet in Chronic Spontaneous Urticaria: A Pilot Study

Esra SARAC[1], Pelin KUTEYLA CAN[2], Emek KOCATURK[1]

[1] Department of Dermatology, Koc University School of Medicine, Istanbul, Turkey
[2] Department of Dermatology, Bahcesehir University School of Medicine, Istanbul, Turkey

Corresponding Author: Emek Kocaturk ekocaturk@ku.edu.tr

ABSTRACT

Objective: The role of dietary factors in the etiopathogenesis of chronic spontaneous urticaria (CSU) has been a matter of discussion and it is widely accepted that most urticaria cases triggered by food are caused by pseudoallergic reactions. In this prospective study, our aim was to investigate the effect of a pseudoallergen-free diet (PAFD) on disease activity, the need for antihistamine use, and the quality of life in patients with CSU.

Materials and Methods: The study included adult patients who were on follow up for CSU for a duration of at least 6 months and had symptoms every day or every other day. The patients were given a food diary, which also included assessment of daily disease activity. The daily Urticaria Activity Score (UAS), the Chronic Urticaria Quality of Life Questionnaire score at baseline and at the 4th week, and frequency of antihistamine use were obtained. According to the change in UAS (ΔUAS), the patients' response to PAFD was classified as strong (ΔUAS≥8), partial (8>ΔUAS≥4), or no response (ΔUAS<4).

Results: Twenty-three patients, 19 females (82.6%) and 4 males (17.4%), completed the study, the mean age was 43±4.6 years. According to ΔUAS, 6 patients (26.1%) had strong response, 6 (26.1%) had partial response, and 11 (47.8%) were unresponsive to PAFD. The mean ΔUAS value of the patients who responded to PAFD was 8.1 (min:4, max:15). At the end of the study, 9 (39.1%) patients had a significant improvement in their quality of life. There were 6 (26%) patients who both responded to PAFD and had improved quality of life scores. The frequency of antihistamine use decreased in 10 (43.5%) patients.

Conclusion: PAFD may help decrease disease activity in CSU. We observed that the frequency of antihistamine use could be reduced and the patient's quality of life could be improved by adding PFAD to antihistamine therapy.

Keywords: Chronic spontaneous urticaria, diet, pseudoallergen-free diet, quality of life, treatment, urticaria

INTRODUCTION

Chronic spontaneous urticaria (CSU) is defined as urticaria and/or angioedema lasting longer than six weeks in the absence of identifiable physical or other inducible stimuli (1). Dietary factors have been suggested to have a role as a cause of CSU; however, IgE-mediated type I food allergy is considered rare (2). Although some patients blame food as a triggering factor for their attacks, most of these are considered to be caused by pseudoallergic reactions. It has been suggested that pseudoallergens trigger histamine release from cutaneous mast cells through a non-immunological mechanism, and intolerance to pseudoallergens might exacerbate CSU. Preservatives, antioxidants, sweeteners, colorants, salicylic acid, natural coloring and flavoring compounds are responsible for the reactions triggered by foods (3,4).

It has been reported that more than 30% of patients with CSU associate their attacks with food (5,6). Although patients cannot describe a single trigger specifically, a pseudoallergen-free diet (PAFD) trial for 3-4 weeks has been reported to provide some benefit, thus pointing to a possible role of pseudoallergens as triggering factors in CSU. Our hypothesis is that a regularly followed and scheduled PAFD may reduce the severity of the disease in particular CSU patients. The aim of this single-center prospective study was to investigate the effect of PAFD on

ORCID Esra Sarac / 0000-0002-9870-9733, Pelin Kuteyla Can / 0000-0002-9124-5817, Emek Kocatürk / 0000-0003-2801-0959

disease activity, the need for antihistamine use, and the quality of life in patients with CSU.

MATERIALS and METHOD

The study included adult CSU patients with a disease duration of at least 6 months, who experienced urticaria symptoms every day or every other day, and who were poorly controlled with standard doses of second generation H1-antihistamines. Patients who had chronic inducible urticaria, and were pregnant, breastfeeding, under 18 years old, or receiving omalizumab or immunosuppressive treatment were excluded. The study was approved by the local Ethics Committee of Göztepe Training and Research Hospital (approval number: 2009/67-E) and written informed consent was obtained from all participants. Research and publication ethics were complied with. The patients were given a diary that included diet instructions and pseudoallergen-free recipes for every single day of the PAFD. They were asked to note each day in this diary the foods they consumed, the factors that triggered their urticaria attacks, and the use of additional drugs. The list of foods that the patients could consume or should refrain from during the study was added to the diary in a tabular form (Table I). In order to determine baseline disease activity, the patients refrained from any special diet on days 1-7, while PAFD was applied on days 8-31. The diary also included daily UAS [wheals and itching were scored from 0 to 3 (UAS daily)], frequency of daily antihistamine use, and the Chronic Urticaria Quality of Life (CU^2-QoL) questionnaire score on days 7 (baseline) and 31.

The change in UAS (ΔUAS) was calculated by subtracting total UAS over the last 4 days (final UAS4) from the total UAS on days 4-7 (basal UAS4). Accordingly, the patients' response to PAFD was classified as strong (ΔUAS ≥ 8), partial (8 > ΔUAS ≥ 4), and no response (ΔUAS < 4). A change of ≥ 8 points in CU^2-QoL scores between day 7 and 31 was considered as significant change (7). The patients were asked not to use antihistamines as much as possible during the study period and also during one week before the PAFD period; and note in the diary if they used these. Antihistamines were allowed only when extreme itching could not be tolerated and there was generalized urticaria or angioedema. The changes in antihistamine use were calculated based on the difference between the total number of antihistamines taken on days 27-31 and the total number of antihistamines taken on days 3-7.

Statistical Analysis

Statistical analyses were performed using the SPSS software version 26.0 (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA). All numerical variables were reported as the mean ± standard deviation, median, frequency and percentages. P values lower than 0.05 were considered significant. For samples that were not normally distributed, the Mann-Whitney U test and Kruskal-Wallis test were used for comparing the scores of the groups.

RESULTS

Twenty-three patients completed the study. Of these patients, 19 (82.6%) were female and 4 (17.4%) were male, with a mean age of 43 ± 4.6 years (range:18-67). Baseline characteristics of the patients are shown in Table II. According to ΔUAS, 6 patients (26.1%) had a strong response, 6 (26.1%) had a partial response, and 11 (47.8%) were unresponsive (Figure 1). The mean ΔUAS value of the patients who responded to PAFD was 8.1±3.6 (range;4-15, median:7.5). At the end of the study, 9 (39.1%) patients had a significant improvement in their quality of life (39.1%). There were 6 (26%) patients who responded to PAFD both with a decrease in UAS scores and also with improved quality of life scores. The frequency of antihistamine use decreased in 10 (43.5%) patients; the mean value of AH decrease was 3±2.6 [median; 2 (range; 1-9)] in these patients. Although the difference between the groups was not statistically significant, antihistamine use was slightly higher in strong-responders (p=0.181). The mean number of change in antihistamine use was 1.31.2 in strong responders, 0.60.4 in partial responders, and -0.51.2 in non-responders. Distribution of the patients at week 4 according to evaluation parameters and AH need is shown in Figure 2.

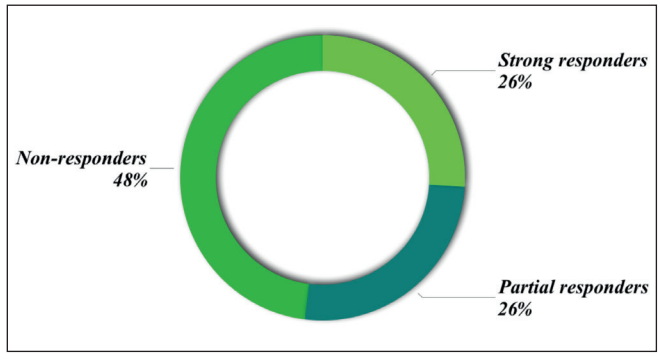

Figure 1. Distribution of PAFD response according to ΔUAS.

Table I: Food list

Food group	Allowed	Not allowed
Staple food, pastries, bakery products	Bread: Grain, millet, corn, bran, rye, buckwheat bread Bread without additives - crispy Flour, flour cake (without eggs) 100% wheat pasta Rice	Instant muesli Bakery bread, slices of bread with additives Cookies and cake with additives Egg pasta
Potato	All natural varieties	Mashed potato powder Ready-made potato products: gratin, croquettes, chips, etc.
Vegetables	All vegetables except those included in the 'not allowed' category	Artichoke, eggplant, peas, mushrooms, spinach, pickled cabbage, tomatoes, olives, red peppers, mixed pickles, beans
Fruit, nuts	None	All
Milk, dairy products	Fresh milk Fresh quark cheese, mozzarella, fresh cheese, cottage cheese, fresh cheddar Natural yogurt, buttermilk, kefir Homemade rice pudding	Herbed cheese, aged cheddar, vegetable/fruit quark cheese, mascarpone, labneh Fruit yogurt Light dairy products Ready-made rice puddings and custard
Meat	Fresh or frozen meat (chicken or red meat) Homemade steak Homemade meatballs	Prepared meat products: salami, sausage Seasoned meat products, such as shashlik Smoked or corned meat, such as ham
Eggs	None	All
Fish, seafood	None	All
Oils and butter	Butter, cold pressed vegetable oils Olive oil for frying	All except those included in the 'allowed' category
Beverages	Soda (non-carbonated) Black or green tea (unflavored)	Fruit juice, lemonade, refreshing drinks Light drinks Coffee, herbal teas Alcohol
Desert	Homemade cakes and pastries (without eggs) Sugar Honey	All other deserts Chewing gum, candies, chocolate Cocoa Sweetened or light desserts
Others	Salt Scallion Onion	Ready sauce (pizza, meatballs) Package soup Soy sauce Ketchup, mustard, mayonnaise, vinegar Garlic Spices, sesame

DISCUSSION

The role of nutrients, which are the main sources of life, in the etiology of chronic urticaria (CU) has been questioned for a long time, as in many other diseases. Although foods can trigger allergic reactions, actual allergy rates are much lower than patient estimates. As a result of the development of the food industry and the widespread use of food additives, the frequency of pseudoallergic reactions triggered by food is increasing. Studies have reported that the rate of sensitivity to food and nutritional additives is 1-68% (8). It has been suggested that additives such as stabilizers, preservatives, colorants, flavorants and sweeteners, as well as naturally occurring aromas and substances such as histamine and salicylic acid in foods are responsible for pseudoallergic reactions (4).

Table II: Baseline characteristics of the patients

	Mean (sd)	Min - Max	n (%)
Age	43 ± 4.6	18 - 67	
Gender			
Female			19 (82.6)
Male			4 (17.4)
Basal UAS4 (sum of the scores on days 4-7)	11.8 ± 6.9	0 - 24	
Basal AH need (number of tablets taken on days 3-7)	3.1 ± 2.1	0 - 20	
Basal CU²-QoL (day 7)	1.8 ± 12.4	29 - 88	

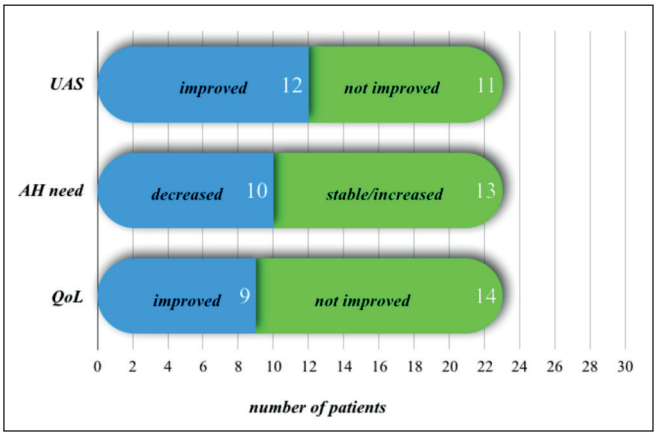

Figure 2. Distribution of the patients at week 4 according to the urticaria activity score (UAS), quality of life scores (QoL), and AH need.

The pathophysiology of pseudoallergen-induced urticaria has not yet been fully elucidated. It is known that small molecules of pseudoallergens cannot bind directly to IgE and do not act like haptens (9). No prior exposure is required for the pseudoallergic reactions to develop. In addition, it is thought that other triggering factors such as the impaired permeability of the gastroduodenal mucosa and the presence of anti-FcepsilonRI-alpha autoantibodies may have a synergistic effect (10-13).

Histamine, which emerges in the gastrointestinal tract after the digestion of food, is broken down mainly by the enzyme diamine oxidase (DAO). It has been shown that an increased blood histamine level can trigger urticaria in individuals with DAO activity deficiency, and enzyme supplementation or a histamine-deficient diet can reduce urticaria attacks (14-17). If patients with CSU also describe gastrointestinal system complaints such as bloating, pain, and diarrhea after food intake, the monitoring of DAO enzyme activity or recommendation of a histamine-poor diet may also be useful to control the disease.

It is known that salicylic acid derivatives cause the disruption of the balance between prostaglandin and leukotriene pathways by inhibiting cyclooxygenase 1 (18). It can be considered that salicylates in foods may cause attacks in patients with CSU through a similar mechanism. In a recently published prospective study, it was shown that a low salicylate diet significantly reduced the symptoms of asthma, rhinosinusitis, and urticaria in patients with hypersensitivity to aspirin or non-steroidal anti-inflammatory drugs (19). In another study investigating the activation of the leukotriene pathway after pseudoallergen intake, it was reported that the urinary leukotriene levels of patients with chronic urticaria responding to PAFD were significantly lower than those who did not respond to this diet, and there was a significant correlation between reduced urticaria activity and reduced urinary leukotriene levels (20).

In CSU, which significantly reduces the quality of life, a significant proportion of patients suspect that there is a relationship between urticaria attacks and food intake and expect a dietary recommendation that lists which foods to avoid for the control of their disease. The clinical findings of urticaria triggered by pseudoallergens are similar to those of type I allergic reactions, and the absence of a specific laboratory or skin test makes the diagnosis difficult. Elimination diets and oral provocation tests should be applied for a definitive diagnosis. Unlike type I allergies, symptoms appear more than four hours after pseudoallergen ingestion and disappear after 10-14 days of following the recommended diet (3,21). The European Academy of Allergy and Clinical Immunology, Global Allergy and Asthma European Network, European

Table III: Summary of the studies with response to a pseudoallergen-free diet

Authors (reference number)	Number of patients	Duration of the diet	Diet response rate	Provocation
Magerl et al. (4)	140	Three weeks	34%	Not performed
Rajan et al. (8)	100	Not applicable	Elimination diet was not performed	Two patients had a positive reaction in the provocation test with 11 food additives.
Akoglu et al. (20)	34	Four weeks	41%	Not performed
Zuberbier et al. (22)	64	Two weeks	73%	Additive capsules containing pseudoallergens caused symptoms in 19% of diet responders.
Pigatto et al. (23)	202	Not applicable	62%	Thirty-seven percent of diet responders had positive results in the placebo-controlled tests of food additives.
Di Lorenzo et al. (24)	838	Four weeks	31.5%	Challenge test with 6 additives was found to be positive in 31.4% of 264 patients whose urticaria improved after food additive free diet.
Bunselmayer et al. (25)	153	Five weeks	68%	Eighty-six percent of full responders and all partial responders showed symptoms with incremental build-up food challenge.
Current study	23	31 days	52%	Not performed

Dermatology Forum, and World Allergy Organization urticaria guideline recommend PAFD for three weeks as an alternative treatment option in patients with CSU that do not respond to conventional treatments (1).

Studies on PAFD have shown a response rate of 34-73% in patients with CSU. Table III presents the summary of these studies with the number of patients, duration of diet, response rate, as well as the rate of response to the provocation test, if applied (4,8,20,22-25). Evaluation criteria are different in these studies; most are not placebo-controlled, and some have not been confirmed by provocation tests. In our study, a significant improvement was observed in the UAS of 52.2% of the patients, and these patients were considered to respond to PAFD.

It is known that CU affects performance in school and work life and reduces the quality of life similar to or more than moderate-severe psoriasis, atopic dermatitis, asthma, and coronary artery disease (26-29). In the current study, we used the Turkish version of the CU^2-QoL questionnaire, which was developed to evaluate the physical, psychosocial and daily effects of chronic urticaria for the last two weeks and previously shown to be reliable and valid (30,31). Patients who have a positive response to the dietary changes are also expected to have increased quality of life in line with reduced urticaria activity. At the end of our study, a significant improvement was observed in the quality of life of in almost 40% of the patients, and there were 6 (26%) patients that both responded to PAFD by means of improvement in disease activity as well as improved quality of life scores. However, 1 (4.3%) patient with a strong response and 1 (4.3%) with a partial response to PAFD reported a decrease in quality of life according to the questionnaires. This suggests that dietary restrictions or prohibited food intake may also adversely affect the quality of life of some patients.

Magerl et al. have used the changes in urticaria severity and DLQI to classify chronic urticaria. They defined cases in which the quality of life deteriorated despite the decrease in disease activity as 'addictive subjects' and suggested that these patients would prefer to eat their daily food freely despite urticaria exacerbations. The authors reported that 7% of the patients belonged to this group (4), which is similar to our findings. In a study by Bunselmeyer et al., it was reported that the quality of life significantly improved in all patients who responded to PAFD (25).

Antihistamines are the first-line treatment for disease management in CSU. Disease activity can be calculated based on daily symptoms, clinical signs, and the need for antihistamine use (standard doses or up to four-fold dose). In the current study, antihistamine use decreased in 43.5% of the patients who adopted the PAFD. King et al. reported that the need for antihistamine use decreased in patients with chronic urticaria who were prescribed a low histamine diet for 6 weeks (32).

The main limitations of this study include the limited number of patients, lack of a provocation test with pseudoallergen-rich foods after PAFD, lack of a control group, and absence of any restriction on the use of other drugs such as NSAIDs and aspirin. Also, antihistamine use was not fully restricted during the study. This may cause an overestimation of the dietary response by reducing the severity of the disease. Due to the limited number of patients and lack of clinical or laboratory parameters of the patients, it was not possible to determine markers that define response to PAFD treatment.

CONCLUSION

In conclusion, although the role of diet in the pathogenesis and treatment of urticaria is not yet fully understood, the results of our study suggest that PAFD may be beneficial in a selected group of patients with CSU who do not have an adequate response to standard treatments. We recommend to use this diet not as a fundamental treatment but as supplementary to ongoing pharmacological treatment in CSU patients. With PAFD, an amelioration in the severity of the disease and a decrease in the use of antihistamines as well as an increase in the quality of life can be achieved in a certain group of patients.

Conflict of Interest

ES and PKC have no conflicts of interest. EK has received honoraria (advisory board, speaker) from Novartis, Sanofi, Menarini, LaRoche Posey and Bayer.

Authorship Contributions

Concept: **Emek Kocaturk,** Design: **Emek Kocaturk,** Data collection or processing: **Emek Kocaturk, Esra Sarac, Pelin Kuteyla Can,** Analysis or Interpretation: **Emek Kocaturk, Esra Sarac, Pelin Kuteyla Can,** Literature search: **Emek Kocaturk, Esra Sarac,** Writing: **Emek Kocaturk, Esra Sarac, Pelin Kuteyla Can,** Approval: **Emek Kocaturk, Esra Sarac.**

REFERENCES

1. Zuberbier T, Aberer W, Asero R, Abdul Latiff AH, Baker D, Ballmer-Weber B, et al. The EAACI/GA2LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. The 2017 revision and update. Allergy 2021 doi: 10.1111/all.15090. Online ahead of print
2. Augey F, Gunera-Saad N, Bensaid B, Nosbaum A, Berard F, Nicolas JF. Chronic spontaneous urticaria is not an allergic disease. Eur J Dermatol. 2011;21(3):349–53
3. Zuberbier T, Pfrommer C, Specht K, Vieths S, Bastl-Borrmann R, Worm M, et al. Aromatic components of food as novel eliciting factors of pseudoallergic reactions in chronic urticaria. J Allergy Clin Immunol 2002; 109: 343-8.
4. Magerl M, Pisarevskaja D, Scheufele R, Zuberbier T, Maurer M. Effects of a pseudoallergen-free diet on chronic spontaneous urticaria: a prospective trial. Allergy 2010; 65: 78-83.
5. D-A Monoret-Vautrin. Allergic and pseudoallergic reactions to foods in chronic urticaria. Ann Dermatol Venereol 2003; 130: 1S35-42.
6. Juhlin L. Recurrent urticaria: clinical investigation of 330 patients. Br J Dermatol 1981; 104: 369–81.
7. Kulthanan K, Chularojanamontri L, Tuchinda P, Rujitharanawong C, Baiardini I, Braido F. Minimal clinical important difference (MCID) of the Thai Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL). Asian Pac J Allergy Immunol 2016; 34(2): 137-45.
8. Rajan JP, Simon RA, Bosso JV. Prevalence of sensitivity to food and drug additives in patients with chronic idiopathic urticaria. J Allergy Clin Immunol Pract 2014; 2: 168-71.
9. Bansal CJ, Bansal AS. Stress, pseudoallergens, autoimmunity, infection and inflammation in chronic spontaneous urticaria. Allergy Asthma Clin Immunol 2019; 15: 56.
10. Buhner S, Reese I, Kuehl F, Lochs H, Zuberbier T. Pseudoallergic reactions in chronic urticaria are associated with altered gastroduodenal permeability. Allergy. 2004;59(10):1118–23.
11. Hide M, Francis DM, Grattan GEH, Hakimi J, Kochan JP, Greaves MW. Autoantibodies against the high-affinity IgE receptor as a cause of histamine release in chronic urticaria. N Engl J Med 1993;328: 1599-604.
12. Fiebiger E, Hammerschid F, Stingl G, Maurer D. Anti-FcepsilonRIalpha autantibodies in autoimmune-mediated disorders. J Clin Invest 1998; 101: 243-51.
13. Zuberbier T, Fiebiger E, Maurer D, Stingl G, Henz BM. Anti-FcepsilonRIalpha serum autoantibodies in different subtypes of urticaria. Allergy 2000; 55: 951-54.
14. Doeun D, Davaatseren M, Chung MS. Biogenic amines in foods. Food Sci Biotechnol. 2017; 26: 1463-74.
15. Schnedl WJ, Schenk M, Lackner S, Enko D, Mangge H, Forster F. Diamine oxidase supplementation improves symptoms in patients with histamine intolerance. Food Sci Biotechnol 2019; 28(6):1779-84.
16. Wagner N, Dirk D, Peveling-Oberhag A, Reese I, Rady-Pizarro U, Mitzel H, et al. A popular myth –low-histamine diet improves chronic spontaneous urticaria – fact or fiction? J Eur Acad Dermatol Venereol 2016; 31: 650-55.
17. Son JH, Chung BY, Kim HO, Park CW. A histamine-free diet is helpful for treatment of adult patients with chronic spontaneous urticaria. Ann Dermatol 2018;30(2):164-72.
18. Wöhrl S. NSAID hypersensitivity – recommendations for diagnostic work up and patient management. Allergo J Int 2018; 27: 114-21.

19. Keszycka PK, Lange E, Gajewska D. Effectiveness of personalized low salicylate diet in the management of salicylates hypersensitive patients: interventional study. Nutrients 2021; 13: 991.
20. Akoglu G, Atakan N, Cakır B, Kalayci O, Hayran M. Effects of low pseudoallergen diet on urticarial activity and leukotriene levels in chronic urticaria. Arch Dermatol Res 2012;304(4):257-62.
21. Zuberbier T. The role of allergens and pseudoallergens in urticaria. Dermatol Symp Proc 2001;6(2):132-34.
22. Zuberbier T, Chantraine-Hess S, Hartmann K, Czarnetzki BM. Pseudoallergen-free diet in the treatment of chronic urticaria a prospective study. Acta Derm Venereol 1995; 75: 484-87.
23. Pigatto PD, Valsecchi RH. Chronic urticaria: a mystery. Allergy 2000; 55: 306-8.
24. Di Lorenzo G, Pacor ML, Mansueto P, Martinelli N, Esposito-Pellitteri M, Lo Bianco C, et al. Food-additive- induced urticaria: a survey of 838 patients with recurrent chronic idiopathic urticaria. Int Arch Allergy Immunol 2005; 138: 235-42.
25. Bunselmeyer B, Laubach HJ, Schiller M, Brehler R. Incremental build-up food challenge - a new diagnostic approach to evaluate pseudoallergic reactions in chronic urticaria: a pilot study, stepwise food challenge in chronic urticaria. Clin Exp Allergy 2009; 39: 116-26.
26. O'Donnell B, Lawlor F, Simpson J, Greaves MW. The impact of chronic urticaria on the quality of life. Br J Dermatol 1997; 136: 197-201.
27. Baiardini I, Giardini A, Pasquali M, Dignetti P, Guerra L, Specchia C, et al. Quality of life and patients' satisfaction in chronic urticaria and respiratory allergy. Allergy 2003; 58: 621-23.
28. Grob JJ, Revuz J, Ortonne JP, Auquier P, Lorette G. Comparative study of the impact of chronic urticaria, psoriasis and atopic dermatitis on the quality of life. Br J Dermatol 2005; 152: 289-95.
29. Itakura A, Tani Y, Kaneko N, Hide M. Impact of chronic urticaria on quality of life and work in Japan: results of a real-world study. J Dermatol 2018; 45: 963-70.
30. Baiardini I, Pasquali M, Braido F, Fumagalli F, Guerra L, Compalati E, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). Allergy 2005; 60: 1073-78.
31. Kocaturk E, Weller K, Martus P, Aktas S, Kavala M, Sarigul S, et al. Turkish version of the chronic urticaria quality of life questionnaire: cultural adaptation, assessment of reliability and validity. Acta Derm Venereol 2012; 92: 419-25.
32. King W, McCargar L, Joneja JM, Barr SI. Benefits of a histamine-reducing diet for some patients with chronic urticaria and angioedema. Can J Diet Pract Res 2000; 61:24-6.