

Evaluation Of Patch Test Positivity In Patients With Chronic Urticaria And Comparison With Voluntary Controls

Kronik Ürtikerli Olgularda Patch Test Pozitifliğinin Değerlendirilmesi ve Sağlıklı Kontrollerle Karşılaştırılması

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Background: Chronic urticaria is one of the enigmas of dermatology. Although studies have shown that %30 - 50 of cases are autoimmune in origin exact role of contact sensitization is still unclear. Objectives: Prick tests are recommended for etiologic work up of chronic urticaria. We aimed to evaluate patch and prick test reactivities in patients with chronic urticaria and compare patch test reactivities with healthy controls.

Material and Methods: We enrolled 27 patients and 20 healthy controls to the study. Patients are selected so that they didn't have a history of allergic rhinitis, conjunctivitis, eczema or contact urticaria and had negative intradermal autologous tests. All laboratory examinations were normal. Both patch and prick tests are performed after the acute flare is over and their medication have been stopped for at least 4-6 weeks while only patch test is performed to the controls.

Results: Fourteen of 27 patients had at least one positive patch test result. Prick test positivity was present in 14 patients as well. Seven of patch positive patients were prick negative and vice versa. Six patients didn't have either patch or prick test positivities. Out of 20 control subjects 4 had positive patch test results.

Conclusion: Patch test positivity was as frequent as prick test positivity. Comparing with healthy controls contact sensitization may be more prevalent in patients with chronic urticaria however whether this is the reason or the result of urticaria is to be further evaluated.

Key Words: **urticaria, contact sensitization, patch test, prick test, contact allergy**

Amaç: Kronik Ürtiker dermatolojide etyolojisi tam aydınlatılmamış konulardan biridir. Son yıllarda yapılan yayınlarda olguların %30 ile 50 sinde otoimmun mekanizmaların sorumlu olabileceği bildirilmiş olup kontakt sensitizasyonun etyolojideki rolü hala iyi anlaşılamamıştır. Kronik ürtiker etyolojik araştırmalarında prik testleri önerilmektedir. Bu çalışmada kronik ürtikerli hastaların deri yama ve prik test sonuçlarının değerlendirilmesi ve yama testi sonuçlarının sağlıklı kontrollerle karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Bu amaçla tüm laboratuvar bulguları normal, otolog serum testi negatif, başka herhangi bir allerjik reaksiyon öyküsü olmayan 27 hasta ve 20 sağlıklı kontrol çalışmaya alınmıştır. Hasta grubunun lezyonları tamamen gerileyip tedavileri kesildikten 4-6 hafta sonra deri prik ve yama testleri uygulanmış, öte yandan sağlıklı kontrollere yalnızca deri yama testi yapılmıştır.

Bulgular: Yirmiyedi hastanın 14 ünde deri yama testi en az bir allerjene karşı pozitif iken, prik testi pozitifliği de 14 hastada bulunmuştur. Prik testi negatif olup yama testi pozitif 7 hasta saptanmış olup, prik testi pozitif iken yama testi negatif gene 7 hasta tesbit edilmiştir. Toplam 6 hastada her iki test de negatif olarak değerlendirilmiştir. Kontrol grubunda ise yama testi pozitifliği 20 kişinin 4ünde saptanmıştır.

Sonuç: Kronik ürtiker etyolojisi araştırılmasında önerilen deri prik test pozitifliği deri yama test pozitifliğinden daha sık bulunmamıştır. Sağlıklı kontrollerle karşılaştırıldığında kronik ürtikerlerde deri yama testi pozitifliği daha sık bulunmuştur. Bu durumun ürtikerin etyolojisi mi yoksa bir sonucu mu olduğu sorusu ise ileri çalışmalarla sorgulanabilir.

Anahtar Kelimeler: **ürtiker, kontakt sensitizasyon, yama testi, prik test, kontakt allerji**

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Chronic urticaria is still one of the enigmas in dermatology. It was shown to be related with many different medical conditions but still exact etiology is controversial especially in a subgroup of patients having no detectable systemic cause. Chronic urticaria was once considered to be a manifestation of an anxiety disorder but in time it is concluded that there has not been good data to support this supposition (1).

It was also thought to be related with infections. Recent data to support or refute an infectious cause of chronic urticaria, is still being debated, but an infectious cause seems to be unlikely according to some authors (1).

An autoimmune mechanism appears to be likely, at least in a subpopulation of patients, but 60 percent of cases remain idiopathic. Autologous skin test was found to be a useful screening test for autoimmune chronic urticaria (1-4).

An increased prevalence of clinically important thyroid disease or subclinical thyroid autoimmunity has been noted in patients with chronic urticaria (5,6). The significance of this is uncertain. At present anecdotal evidence both supports and refutes the idea of prescribing lthyroxine for euthyroid chronic urticaria patients who have thyroid autoimmunity (5).

It is shown that a small proportion of patients like less than 5% may prove to be reactive to certain foods and food additives so diagnostic work up is recommended to include a prick test specially for food allergy (1,7). On the other hand adherence to a diet of rice, lamb and water for five days has shown to have no effect on chronic urticaria or angioedema (1).

An even smaller number of patients were thought to be associated with parasite infestations who usually have blood eosinophilia (7,8).

Chronic idiopathic urticaria is the diagnosis given when diagnoses of urticarial vasculitis, physical urticarias and all possible etiologic factors have been excluded. We aimed to check skin patch and prick test reactivities in patients with chronic urticaria without any identifiable systemic etiologic factor with detailed laboratory tests and negative autologous skin tests and compare their patch test positivities with normal control subjects without any allergic reactions and no history of atopy.

Patients and Methods

We selected patients in an outpatient setting from april 2006 till july 2007. Only adult patients aged between 18 to 60 without any systemic disease and not receiving any systemic treatments for any reason are included to the study.

Patients having physical factors or drugs as a possible causative factor are excluded from the study. As diagnostic procedures we checked complete blood count, erythrocyte sedimentation rate, blood chemistries, urinalysis, thyroid hormones and autoantibodies, stool examination for parasites, anti nuclear antibodies, chest x ray, immunoglobulin and complement levels.

Further tests are performed in suspicious cases like urine culture, sinus tomography, dental and gynecologic examination. Only patients who do not have any positive or suspicious results with these tests are enrolled to the study group.

Selected patients also had negative intradermal autologous skin tests and did not have a history of ec-

Table 1: List of European standard patch test allergens

1	Potassium dichromato
2	4-phenylonodiamine baso
3	Thiuram mix
4	Neomycine sulfate
5	Cobalt chloride hexzahydrate
6	Benzocaine
7	Nickel Sulfate hexzahydrate
8	Clioquinol
9	Colophony
10	Paraben Mix
11	N isopropyl-N-phenyl-4-phenylendiamine
12	Wool alcohols
13	Mercapto Mix
14	Epoxy resin
15	Balsam Peru
16	Burylphenolformaldehyde resin
17	2-mercaptobenzethiazole
18	Formaldehyde
19	Fragrance mix
20	Sesquiterprene lactone mix
21	Quaternium 15
22	Primin
23	Cl+Me-isothiazolinone
24	Budesonide
25	Tixocortol-21-pivalate
26	Methylidibromoglutaronitril (MDBGN)

zema, allergic rhinitis or conjunctivitis. Control group is selected among voluntary health personnel who were in the same age group, who did not have allergic diseases like urticaria, eczema, rhinitis or conjunctivitis, who do not have any systemic diseases and who have not been receiving any medications. We had a total of 20 control cases.

Table 2: List of prick test allergens

1	Positive control (histamine)
2	Negative control
3	Betulaceae
4	Salicaceae
5	Trees mixture
6	Compositae
7	Mixture of 12 grasses
8	D.Farinae
9	D.Pteronyssinus
10	Cladosporium
11	Aspergillus mix
12	Cat hair
13	Dog hair
14	Mixture of hairs
15	Poa pratensis
16	Pinus sylvestris
17	Mixture of 4 cereals
18	Secale cereale
19	Latex
20	Cocroach
21	Mosquito
22	Cocoa
23	Olive
24	Onion
25	Paprica
26	Pepper
27	Tea
28	Wheat flour
29	Mixture of 7 cereals
30	Apple
31	Banana
32	Orange
33	Peach

34	Strawberry
35	Peanut
36	Hazelnut
37	Walnut
38	Tomato
39	Egg (whole)
40	Chicken meat

We performed both patch tests with 26 allergens and prick tests with 40 allergens to all patients while their acute flare was over for a minimum of 4 and a maximum of 6 weeks and while they were not receiving systemic antihistaminics or steroid for at least 10 days. Table 1 has a list of patch test allergens and table 2 is the list of prick test allergens used. On the other hand, we performed only patch tests to the control group.

Results

We had a total of 312 patients with urticaria, 43 has met our selection criteria (13%). Of these 43 patients 27 accepted to have patch and prick tests and so enrolled to the study. In the patient group, mean age was 37.19 ± 6.00 whereas in the control group mean age was 33.25 ± 5.39 .

In the patient group, fourteen patients had a positive reaction to at least one prick test allergen whereas fourteen patients had a positive reaction to at least one patch test allergen.

Seven patients had a positive patch and negative prick test, seven had positive reactions to both patch and prick tests, seven had positive prick and negative patch test results and six had negative results to both patch and prick tests (Table 3).

Fourteen patients who had positive reaction to skin prick tests, according to a recent classification, are not considered to be idiopathic urticaria cases while the rest 13 patients with negative prick tests can be considered as chronic idiopathic urticaria (7). Six of the fourteen patients with positive skin prick tests had a food allergen positivity while the remaining 8 patients were positive non-food derived allergens (table 3). Seven of these 13 patients had a positive patch test reaction. Overall these seven patients had positive reactions to 9 allergens. Three patients had positive reaction towards nickel sulfate hexzahyde, two towards neomycine sulfate, two towards paraben mix, one patient towards potassium dichromato, 4-phenylonodiamine baso, cobalt chloride hexzahydrate, clioquinol, fragrance mix and sosquiterpenoiactone mix.

In the control group, on the other hand we had only 4 positive results out of 20 with patch tests. One of these was nickel, second one to neomycine sulfate, third to paraben mix and last to formaldehyde. When compared with healthy controls, patch test positivity was statistically more prevalent in urticaria group (chi-square test, $p < 0.05$).

Comments

Urticaria was once considered as an Ig E mediated hypersensitivity reaction whereas recent studies showed the existence of different subgroups of the urticaria cases, some of which having an autoimmune mechanism (1-4,9). In chronic urticaria skin prick tests are recommended for the etiologic work up while patch tests are not (10). Although we have limited number of patients, we still had interesting results, for example in our patients

Table 3: List of positive patch and prick test results in patients with chronic urticaria

Patient number	Positive patch(no)	Positive prick(no)
1	7,13	11,12,18
2	3,22,24	7
3	4,26	13,16,17,34,35
4	2,10	7,12,17,21
5	19,22	21,25,32,36,37
6	2,3,5	12,13,21
7	25	6,9,10,16,18,19,21,22
8	----	32,33,34
9	----	3,4,5,6,9,11,13,14,15, 16,20, 21, 22,25,236,32,35,36,38,39
10	---	4,7,8,9,13
11	---	8,31,35
12	---	12,13
13	---	8,9
14	---	7
15	20	-----
16	19	-----
17	1,5,7,10	-----
18	8	-----
19	2,4,10	-----
20	4,7	-----
21	7	-----

group patch test positivity was as common as prick test positivity. Almost half of the positive prick test reactions were towards food, the rest being towards non food allergens (table3). When compared with healthy controls, patch test positivity was statistically more in urticaria group (chi-square test, $p < 0.05$). We performed patch tests 4 to 6 weeks after the acute flare is over which may be quite early when skin is still readily re-

active. Repeating the same tests with same patients 6 months later, in the condition that the patients didnot have a new urticarial attack may result in different findings.

There has been limited reports of chronic urticaria found to be caused by common contact sensitizers(11-14).Interestingly many such patients of chronic urticaria has not exhibited signs of contact allergy before urticari-

al attack. These studies have also shown that testing for contact sensitization can be helpful in the management of chronic urticaria (15).

In another recently published study, out of 121 patients with chronic urticaria, 50 (%41) had positive patch test results (16). Although patients were not selected among idiopathic cases, 47 of 50 patch positive patients were idiopathic

meaning that in only 3 patients there has been another possible etiologic factor identified. On the other hand out of 71 patch negative patients 50 had an etiologic factor identified like chronic infection, thyroiditis, immune or metabolic diseases. This finding was in favor of our patient selection criteria and also confirmed that contact sensitization may be one

of the many possible mechanisms involved in the etiology of chronic urticaria.

Urticaria, at least a sub group of it, can have a delayed type reaction component which may be explanatory to many patients. Patients with chronic urticaria without a detectable underlying etiologic factor can have positive skin patch

test results. Limitation of our study is the lack of data after the elimination of the allergen and evaluation of clinical relevance with larger groups. According to our present findings, delayed type reaction may be involved in the etiopathologic mechanisms of chronic idiopathic urticaria.

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