

Examination of the frequency of patients with pre-diagnosed allergic contact dermatitis attending dermatology outpatient clinics and evaluation of patch test results

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Abstract

Aim: In this study, it is aimed to investigate the frequency of attending dermatology outpatient clinics and patch test results in the light of demographic characteristics of patients who underwent patch tests with a preliminary diagnosis of allergic contact dermatitis (ACD) in 2018-2019.

Material and Methods: The files of patients who had a patch test with a preliminary diagnosis of allergic contact dermatitis were scanned retrospectively. Demographic characteristics such as age, gender, profession, number of attending to the dermatology outpatient clinic with the same complaint and the reactions determined as a result of the patch tests were examined.

Results: A total of 122 patients with 67 (54.9%) male and 55 (45.1%) females were included in this study. The median duration of lesions was 24 (minimum 1, maximum 360) months. Fifty-eight (47.5%) patients had been attending the Dermatology outpatient clinic at least three times with the same complaint. Patients who attended to the dermatology outpatient clinics at least 3 times and had at least one positive patch test were including cobalt positivity as 29.3%, potassium dichromate as 27.5%, nickel as 24.1%, colophony as 13.8% and thiuram mix as 10.3%. There were 81 (66.4%) patients with at least one positive patch test results, 52 (42.6%) with at least two positives, and 33 (27%) with three positives. The three items that were at least one positive were nickel sulfate (26.2%), cobalt (25.4%), potassium dichromate (20.5%), respectively. Three items with three positivity were nickel (13.9%), potassium dichromate (4.1%), and mercaptobenzothiazole (2.5%), respectively. No positivity was found for benzocaine, 2-Methoxy-6-n-pentyl-4-benzoquinone, and clioquinol.

Conclusion: In this study, the frequency of patients with ACD attending to the dermatology outpatient clinics at least 3 times was found approximately 50%. These results emphasize the importance of patch test awareness about the preventive medicine approach in our country. Also, the items causing ACD according to the degree of positivity were reported for the first time in this study. It was found that nickel and potassium dichromate, which are used relatively common in industries, are the most common strong allergens.

Keywords: Allergic contact dermatitis; allergens; patch test

INTRODUCTION

Contact dermatitis is present in 5-10% of patients attending to dermatology outpatient clinics (1). Allergic contact dermatitis (ACD) accounts for 20% of all contact dermatitis and is a type IV (delayed-type) allergic reaction that occurs with repeated skin contact with the same sensitizer in a previously sensitized person (2,3). It has been reported that approximately 4000 chemicals that are very small (<500 daltons) molecules can cause ACD at the present time. These molecules are recognized by Langerhans cells in the epidermis and gain antigenic

properties (4). Allergens that may cause allergic contact dermatitis may change over time as well as geographical and communal differences (3).

The skin patch test is performed to determine the responsible allergens that can cause ACD. In the setting of detecting responsible allergen by a skin patch test, the culprit contact allergens can be prevented, hereby, treatment continuity and protection can be provided (4). The patch testing still cannot be performed on many patients with allergic contact dermatitis. This situation causes patients attending the dermatology outpatient clinic multiple times.

Received: 11.07.2020 **Accepted:** 21.08.2020 **Available online:** 21.09.2020

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In this study, it is aimed to investigate the frequency of re-attending of dermatology outpatient clinics due to the same complaints for ACD. It is also aimed to evaluate patch test results in light of the demographic characteristics of patients who have a preliminary diagnosis of ACD.

MATERIAL and METHODS

Study Design

This study was carried out with 122 patients who attended to Kayseri Develi State Hospital Department of Dermatology and Venereology as pre-diagnosis of allergic contact dermatitis between August 2018 and June 2019. Patch test was performed to all patients. Patient files were retrospectively scanned and age, gender, occupation, the frequency of re-attending of dermatology outpatient clinics due to the same complaints for ACD, and patch test reaction information determined were recorded. Patch test results of patients were examined in terms of demographic features.

Patch test

The patch test was carried out with Chemotechnique Diagnostics®-European Baseline Series S-1000 (European Standard Series) with 2018 and 2019 series, containing 29 allergens. In addition to the 26 common allergens, Benzocaine 5.0%, 2-Methoxy-6-n-pentyl-4-benzoquinone, and Clioquinol are available in the 2018 series, while cain mix, propolis, and hydroxymethyl acrylate are available in the 2019 series. Patch test allergens were glued to the upper backs of patients using IQ Ultra™ chambers (Chemotechnique Diagnostics, Sweden). The first evaluation was made 30 minutes after the opening of the patches at the 48th hour, and the second evaluation was made at the 72nd hour. Although the results of the first evaluation were found to be positive, the reactions that became negative at 72 hours were recorded as irritant reactions. Patch test results were evaluated according to the criteria set by the Contact Dermatitis Research Group [International Contact Dermatitis Research Group (ICDRG)] (Table 1). Patients who applied local steroids to the back area in the last ten days, took systemic steroids or immunosuppressive drugs, pregnant and active eczema were excluded from the study.

Table 1. Patch test evaluation according to International Contact Dermatitis Research Group

0	No reaction, No contact allergy
+/-	Mild erythema, Suspicious reaction
+	Erythema, infiltration and edema, Possible contact allergy
++	Erythema, infiltration and vesiculation, Allergic contact dermatitis
+++	Vesiculobullous and / or ulcerative reaction, Allergic contact dermatitis (definitive)
IR	Irritation, No contact allergy

The study was approved by Erciyes University, Clinical Research Ethics Committee, Kayseri, Turkey (approval date and number 2019/772).

Statistical analysis

The data were analyzed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA) program at the $p < 0.05$ significance level. Descriptive statistics were given by giving frequency and percentages. While numerical changes were shown as mean \pm standard deviation in the normal distribution, the median value was used in cases without normal distribution. Pearson and Chi-square tests were performed for the relationship between categorical variables.

RESULTS

Demographic characteristics of the study population

In this study, there were 122 patients 67 (54.9%) male and 55 (45.1%) female. Thirty (24.6%) of the patients were students, 30 (24.6%) were housewives, 26 (21.3%) were self-employed, 12 (9.8%) were construction workers, 10 (8.2%) were civil servants, 10 (8.2%) were unemployed and 4 (3.3%) were miners. Seventy-eight (63.9%) of patients were married and 44 (36.1%) were single. While the mean age of the patients was 33.24 ± 16.18 years, mean body mass index values was 25.53 ± 5.40 kg/m².

Table 2. Allergen positivity status according to the frequency of attending to dermatology outpatient clinics

Allergens	<3 attending		≥3 attending		p value
	Positive	Negative	Positive	Negative	
Cobalt (II) chloridehexahydrate	14 (21.9%)	50 (78.1%)	17 (29.3%)	41 (70.7%)	0.346
Potassium dichromate	9 (14.7%)	55 (85.3%)	16 (27.6%)	42 (72.4%)	0.052
Nickel sulfatehexahydrate	18 (28.1%)	46 (71.9%)	14 (24.1%)	44 (75.9%)	0.617
Colophonium 20.0%	4 (6.3%)	60 (93.7%)	8 (13.8%)	50 (86.2%)	0.137
Thiuram mix	3 (4.9%)	61 (95.1%)	6 (10.3%)	52 (89.7%)	0.306

The median duration of lesions was 24 (minimum 1, maximum 360) months. Eczema complaints were 30.3% in hand, while 28.7% in the body, 18% in the foot, 11% in hand and foot, 8.2% in full-body, 4.1% in the periorbital area, and 1.6% in the scalp.

Patch test results by frequency of attending dermatology outpatient clinics

There were 58 (47.5%) patients who attended the dermatology outpatient clinic at least three times with the same complaint. Cobalt (29.3%), potassium dichromate

Table 3. The frequency of positivity of allergens in the patch test

Allergens	The positivity by number of patients (%)			Total number of positivity
	1 +	2 +	3 +	
1.Potassium dichromate	10 (8.2%)	10 (8.2%)	5 (4.1%)	25 (20.5%)
2.P-phenylenediamine (PPD)	3 (2.0%)	1 (0.8%)	2 (1.6%)	6 (4.4%)
3.Thiuram mix	5 (4.1%)	2 (1.6%)	2 (1.6%)	9 (7.3%)
4.Cobalt (II) chloridehexahydrate	18 (14.8%)	11 (9.0%)	2 (1.6%)	31 (25.4%)
5.Neomycin sulfate	3 (2.5%)	0 (0.0%)	0 (0.0%)	3 (2.5%)
6.Benzocaine 5.0%*	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
7.Nickel sulfatehexahydrate	5 (4.1%)	10 (8.2%)	17 (13.9%)	32 (26.2%)
8.Fragrance mix I	2 (1.6%)	0 (0.0%)	1 (0.8%)	3 (2.4%)
9.Colophonium 20.0%	9 (7.4%)	1 (0.8%)	2 (1.6%)	12 (9.8%)
10.Paraben mix 16.0%	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
11.2-Methoxy-6-n-pentyl-4-benzoquinone*	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
12.Budesonide	2 (1.6%)	1 (0.8%)	0 (0.0%)	3 (2.4%)
13.Clioquinol*	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
14.Hydroxyisohexyl 3-cyclohexene carboxaldehyde	3 (2.5%)	1 (0.8%)	0 (0.0%)	4 (3.3%)
15.N-isopropyl-n-phenyl-4-phenylenediamine	2 (1.6%)	0 (0.0%)	0 (0.0%)	2 (1.6%)
16.Lanolin alcohol 30.0%	6 (4.9%)	1 (0.8%)	1 (0.8%)	8 (6.5%)
17.Mercapto mix 2.0%	1 (0.8%)	0 (0.0%)	2 (1.6%)	3 (2.4%)
18.Epoxy resin, Bisphenol A 1.0%	1 (0.8%)	0 (0.0%)	2 (1.6%)	3 (2.4%)
19.Peruvian balm 25.0%	3 (2.5%)	3 (2.5%)	0 (0.0%)	6 (4.4%)
20.4-tert-butylphenol formaldehyde resin	1 (0.8%)	2 (1.6%)	0 (0.0%)	3 (2.4%)
21.2-Mercaptobenzothiazole (MBT)	0 (0.0%)	0 (0.0%)	3 (2.5%)	3 (2.4%)
22.Fragrance mix II	0 (0.0%)	2 (1.6%)	0 (0.0%)	2 (1.6%)
23.Sesquiterpene lactone mix	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
24.Quaternium-15	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
25.Methylisothiazolinone	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.6%)
26.Tixocortol-21-pivalate	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
27.Methyl dibromo glutaronitrile	5 (4.1%)	2 (1.6%)	0 (0.0%)	7 (5.7%)
28.Formaldehyde liquid	1 (0.8%)	1 (0.8%)	0 (0.0%)	2 (1.6%)
29.Methylisothiazolinone + methylchlorisothiazolinone	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
30. Cain mix**	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
31. Propolis**	1 (0.8%)	1 (0.8%)	1 (0.8%)	3 (2.4%)
32. Hydroxy methyl acrylate**	2 (1.6%)	2 (1.6%)	0 (0.0%)	4 (3.2%)

* It was administered to 84 (68.9%) patients with 2018 series

**It was administered to 38 (31.1%) patients with 2019 series

(27.5%), nickel (24.1%), colophony (13.8%), and thiuram (10.3%) were positive in patients who attended to dermatology at least three times. The allergen positivity status according to the frequency of attending to dermatology outpatient clinics is shown in Table 2.

Patch test results by demographic characteristics

There were 81 (66.4%) patients with at least one positive according to ICDRG criteria, while 52 (42.6%) with at least two positives, and 33 (27%) with three positives. Five allergens that were at least one positive were nickel

sulfate (26.2%), cobalt (25.4%), potassium dichromate (20.5%), colophony (9.8%) and thiuram (7.3%), respectively. Three allergens with three positivity were nickel (13.9%), potassium dichromate (4.1%), and mercaptobenzothiazole (2.5%), respectively. No positivity was found for benzocaine, 2-Methoxy-6-n-pentyl-4-benzoquinone, and clioquinol (Table 3). The first five common allergens in patch testing were analyzed in terms of demographic characteristics (occupation, gender, marital status, and age) in Table 4-7.

Table 4. The frequency of positivity of allergens by occupation

Occupation	Number of allergens positivity				
	Cobalt (II) chloridehexahydrate	Potassium dichromate	Nickel sulfatehexahydrate	Colophonium 20.0%	Thiuram mix
Student	8 (25.8%)	3 (12.0%)	5 (15.6%)	3 (25.0%)	1 (11.1%)
Construction worker	6 (19.4%)	5 (20.0%)	3 (9.4%)	1 (8.3%)	3 (33.3%)
Miner	0 (0.0%)	2 (8.0%)	1 (3.1%)	0 (0.0%)	0 (0.0%)
Self-employment	7 (22.6%)	7 (28.0%)	9 (28.1%)	3 (25.0%)	2 (22.2%)
Civil servant	2 (6.5%)	1 (4.0%)	2 (6.2%)	1 (8.3%)	0 (0.0%)
Housewife	7 (22.6%)	6 (24.0%)	10 (31.2%)	3 (25.0%)	2 (22.2%)
Unemployed	1 (3.2%)	1 (4.0%)	2 (6.2%)	1 (8.3%)	1 (11.1%)

Table 5. The frequency of positivity of allergens by gender

Allergens	Number of males		Number of females		p-value
	Positive	Negative	Positive	Negative	
Cobalt (II) chloridehexahydrate	16 (23.9%)	51 (76.1%)	15 (27.3%)	40 (72.7%)	0.688
Potassium dichromate	18 (26.9%)	49 (73.1%)	7 (12.7%)	48 (87.3%)	0.054
Nickel sulfatehexahydrate	14 (20.9%)	53 (79.1%)	18 (32.7%)	37 (67.3%)	0.139
Colophonium 20.0%	6 (9.0%)	61 (91.0%)	6 (10.9%)	49 (89.1%)	0.718
Thiuram mix	7 (10.4%)	60 (89.6%)	2 (3.6%)	53 (96.4%)	0.152

Table 6. The frequency of positivity of allergens by marital status

Allergens	Number of Married		Number of Singles		p-value
	Positive	Negative	Positive	Negative	
Cobalt (II) chloridehexahydrate	20 (25.6%)	58 (74.4%)	11 (25.0%)	33 (75.0%)	1.000
Potassium dichromate	23 (29.5%)	55 (70.5%)	2 (4.6%)	42 (95.4%)	0.001
Nickel sulfatehexahydrate	23 (29.5%)	55 (70.5%)	9 (20.5%)	35 (79.5%)	0.276
Colophonium 20.0%	7 (9.0%)	71 (91.0%)	5 (11.4%)	39 (88.6%)	0.670
Thiuram mix	9 (11.5%)	69 (88.5%)	0 (0.0%)	44 (100%)	0.015

Table 7. The frequency of positivity of allergens by age

Allergens	Number of patients < 40 years of age		Number of patients with ≥ 40 years of age		p-value
	Positive	Negative	Positive	Negative	
Cobalt (II) chloridehexahydrate	18 (23.4%)	59 (76.6%)	13 (28.9%)	32 (71.1%)	0.500
Potassium dichromate	9 (11.7%)	68 (88.3%)	16 (35.6%)	29 (64.4%)	0.002
Nickel sulfatehexahydrate	21 (27.3%)	56 (72.7%)	11 (24.4%)	34 (75.6%)	0.732
Colophonium 20.0%	7 (9.1%)	70 (90.9%)	5 (11.1%)	40 (88.9%)	0.758
Thiuram mix	5 (6.5%)	72 (93.5%)	4 (8.9%)	41 (91.1%)	0.724

DISCUSSION

Allergic contact dermatitis occurs as a delayed-type reaction (Type IV) caused by sensitization after exposure to the allergen (1). It is characterized by erythematous, desquamative plaques in the acute stage while there are vesicles and bullae in contact areas in severe cases.

Recurrent contact status to allergens in susceptible individuals is responsible for chronicity (2). As lesions become chronic, lichenification, hyperkeratosis, and fissures begin to develop (3). In ACD, which can be seen at any age, clothing and toy materials play an important role in children while cosmetics and topical drugs play

an important role in adult cases (2). Allergic contact dermatitis is rarely seen in the elderly and newborn period. This may be associated with low allergen exposure in these age groups. Another possible explanation is the distribution of the Langerhans cell which is the main cell in ACD may differ in different age groups (4, 5). In our study, the mean age of patients was 33.2 years. There is no gender prominence in allergic contact dermatitis (5). In this study, a slight male gender predominance was present, although males and females were approximately equally distributed. It is well known that thin skin areas in the body such as eyelids and scrotum are more sensitive to allergens whereas thick areas such as the scalp and soles are less sensitive to allergens. Furthermore, hands are more common areas of involvement since they are more prone to exposure to allergens (6). In this study, the most common region for ACD was the hands while the least region was scalp.

In a previous study, it has been reported that 27% of dermatologists do not perform patch testing since they believe the history of patients is sufficient to detect culprit allergens. The high cost and time issues for patch testing were reported as other reasons (7). According to this study, approximately half of the patients attended the dermatology outpatient clinics at least three times with the same complaints. It has been shown that to make a diagnosis of ACD and detecting allergens earlier by patch test increases the response to treatment, reduces the cost of treatment, and increases the quality of life. Therefore, it appears important to detect contact allergens by patch tests in the earlier attending to the dermatology outpatient clinic as preventive medicine. Dermatologists should increase awareness of this issue. In this study, for the first time, the relationship between the frequency of attending patients with ACD to dermatology outpatient clinics and patch test results was investigated. According to this study, the three most common allergens in patients who attend dermatology outpatient clinics with the same complaint at least three times were cobalt, potassium dichromate, and nickel. These three allergens can cross-react with each other and can be used in many industries areas. This may suggest that the occupational effect may be a more important factor in patients attending to the dermatology outpatient clinics repeatedly with the same complaint. In addition, this condition shows a perspective in terms of allergen profiles in patients presenting with recurrent ACD complaints that cannot be patch tested.

Previous studies reported that the positive reaction frequency in the patch test was about 30 -75% (8-16). In our study, at least one allergen positivity was present in 66.4% of patients. When other studies in allergic contact dermatitis patch test studies were evaluated, Koca et al. reported that the most common sensitizer in the Black Sea region is nickel sulfate (14.8%) followed by cobalt chloride (9.2%), potassium dichromate (6.6%), peru balm (3.6%), and fragrance mixture (3.3%) (16). On the other hand, Çalka et al. reported that the most common sensitizer was

nickel sulfate (24.3%), followed by potassium dichromate (16.5%), thiuram mixture (13.0%), cobalt chloride (12.3%), and paraben mixture (6.1%) in the eastern Anatolia region and Ada et al. reported that the most common sensitizer was nickel sulfate (17.3%), followed by cobalt chloride (7.2%), potassium dichromate (3%), fragrance mixture (2.9%) and paraphenylenediamine base (2.6%) in the Ankara region (8,11). Moreover, Erfan et al. reported that the most common sensitizer was nickel sulfate (29.6%), followed by cobalt chloride (13.6%), potassium dichromate (13%), sesquiterpene lactone mixture (10.7%), and thiuram (5.9%) in the Marmara region (15). To the best of our knowledge, this is the first study based on a patch test for ACD in Kayseri which is among the central province of Turkey. It is noteworthy that in our study, the most frequent sensitization was nickel sulfate (26.2%) as in the literature while cobalt (25.4%), potassium dichromate (20.5%), colophony (9.8%) and thiuram (7.3%) were the other most susceptible substances. It was seen that positive allergens were similar to other studies, however, there was a remarkable sensitivity of the colophony which differs from other studies. It is thought that colophony is a substance used in the furniture industry in Kayseri province and it can be speculated that these high rates are based on the multiple furniture industries in the city. These results suggest that ACD may be relevant to industries of regions.

To the best of our knowledge, there are no studies showing the rate of three degrees of positivity of allergens when studies evaluating patch test results in the literature were scanned. In our study, three positive allergens were nickel (13.9%), potassium dichromate (4.1%), and mercaptobenzothiazole (2.5%), respectively. Although the mercaptobenzothiazole is not among the five most sensitive agents, it was remarkable that the three positivity rate of it was high.

Erfan et al. did not report any N-isopropyl-n-phenyl-4 phenylenediamine, epoxy-resin, peru balm, formaldehyde, quaternium-15, primin, tixokortol-21-pivalate, fragrance mixture-2 in positivity with 169 European series (15). In addition, Koca et al did not report any reaction in formaldehyde in their study with 304 cases (16). On the other hand, Ada et al. reported all cases in their study to have at least one allergen positivity (8). In our study, no positivity was found for benzocaine 5.0%, 2-methoxy-6-n-pentyl-4-benzoquinone, and clioquinol, of note, these substances were removed from the patch test series in 2018. In a study performed by Ada et al. it has been reported that these three agents were positive but even the highest positivity was with benzocaine only as 1.4%. In our study, it was observed that cain mix (0.8%), propolis (2.4%), and hydroxy methylacrylate (3.2%) which were added to the patch test series instead of benzocaine 5.0%, 2-methoxy-6-n-pentyl-4-benzoquinone, and clioquinol, were slightly positive among allergens in 2019 series. It can be concluded that our results support the allergens change in the 2018 and 2019 series.

Potassium dichromate is a contact allergen, mainly found in cement and leathers. Potassium dichromate is also used in some detergents, dyes, and cosmetic products. The frequency of potassium dichromate sensitization in our study was 20.5% that is consistent with the previous studies (8-18). It is reported in the literature that potassium dichromate causes more frequent reactions in men (17,18). In our study, it was found that sensitization with potassium dichromate was slightly higher in males and close to the level of statistical significance among five allergens that was at least one positive in patch test. In the literature, potassium dichromate sensitivity has been shown to increase with age (19,20). Turkmen et al. reported that the positivity of potassium dichromate was statistically significantly higher in patients at age ≥ 40 years compared to age under 40 years (13). In accordance with previous studies, we found the sensitivity of potassium dichromate was significantly higher in married in addition to patients with ≥ 40 years of age.

CONCLUSION

The influence of contact allergens may change over time as well as among different geographical communities. In this study, two-year patch test data of Kayseri are presented. We believe that our study may be useful for the determination of the allergen characteristics of our region since a similar study previously has not been performed in Kayseri. In addition, we determined for the first time the relationship between the patch test results and frequency of attending to the dermatology outpatient clinics with a similar complaint. Therefore, the awareness of the patch test about the protection priority approach in our country was questioned and possible antigen conditions were examined in circumstances where the patch test could not be performed. Finally, three degrees of positivity for allergens that were not shown in any previous study were reported in our study.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The study was approved by Erciyes University, Clinical Research Ethics Committee, Kayseri, Turkey (approval date and number 2019/772).

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