

ORIGINAL PAPER

Results of patch testing to the European Baseline Series in adult patients in Turkey: a five-year experience at a tertiary reference center

Zeynep Yegin Katran, İsmet Bulut

Department of Allergy and Immunology, Süreyyapasa Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

ABSTRACT

Introduction: Allergic contact dermatitis (ACD) is increasing in frequency and has a negative impact on the quality of life. Patch testing is recommended, especially in treatment-resistant cases, atypical cases, workers with hand eczema, and before starting systemic treatment.

Aim: To report the results of patients with ACD who underwent the European Baseline Series at our tertiary referral hospital.

Material and methods: All patients diagnosed with ACD who underwent patch testing between 2018 and 2023 were included in the study.

Results: Between January 2018 and May 2023, 383 patients aged over 18, underwent patch testing with the European Baseline Series (EBS). Of these, 216 (56.3%) patients underwent EBS, while 167 (43.7%) patients underwent the European Patch Series, consisting of 32 allergens applied in our clinic between April 2021 and June 2023. Nickel sulphate was the most common allergen with a positivity rate of 22% (85), followed by gold sodium thiosulfate at 7% (27), cobalt chloride at 6.8% (26), thiomersal and para-phenylenediamine at 4.7% (18), and potassium dichromate at 4.4% (17). In all years, patch test positivity was statistically higher in women than in men. Nickel sulphate and potassium dichromate were statistically significantly more positive in women and men, respectively. Wool wax alcohols, carba mix, cl-me-isothiazolinone, thiomersal positivity decreased over time, while colophony positivity increased significantly over time.

Conclusions: In this study, although the allergens found positive in the European patch test at our reference hospital were similar to previous studies, it was noteworthy that they changed over time.

KEY WORDS

allergic contact dermatitis, patch testing, European Baseline Series, dermatitis.

ADDRESS FOR CORRESPONDENCE

Zeynep Yegin Katran, Department of Allergy and Immunology, Süreyyapasa Training and Research Hospital, University of Health Sciences, Istanbul, Turkey, phone: 05052555625, e-mail: zynpyegin@hotmail.com

INTRODUCTION

Allergic contact dermatitis is a delayed hypersensitivity reaction to a specific allergen, and patch testing is a crucial diagnostic tool for its identification. Patch testing is particularly recommended in cases of treatment-resistant dermatitis, atypical presentations, among employees with hand eczema, and before the initiation of systemic treatments [1].

Contact allergies typically progress through two phases. The first phase, known as the induction phase, involves T cell-mediated sensitization to a specific allergen, often without evident clinical symptoms. Subsequent exposure to the same allergen or a cross-reactive allergen triggers the activation of sensitized T cells, leading to a clinical response in what is termed the elicitation phase. The primary objective of the patch test is to demonstrate this sensitization *in vivo*. The patch testing procedure commonly utilizes the European Baseline Series recommended by the European Environmental Contact Dermatitis Research Group (EECDRG). It is worth noting that this working group periodically introduces new allergens while discontinuing others. These allergens can be tested using pre-made patches or mixed with white petrolatum for practical application on the upper back [2]. Optimal results are typically achieved with 48 h of occlusion [3].

The interpretation of patch test results relies on the assessment of morphological changes such as erythema, infiltrate, papules, and vesicles, as well as tactile examination. The widely accepted reading criteria used for this purpose are provided by the International Contact Dermatitis Research Group (ICDRG) [4]. To correctly identify allergens, the International Nonproprietary Name (INN) system is employed, although chemical names are occasionally used in patch tests. An essential aspect of the patch testing process is the post-test discussion with the patient to help prevent future exposure to allergens.

The incidence of allergic contact dermatitis is on the rise and significantly impacts the quality of life [5].

AIM

In this study, we aim to share the results of our patients who underwent the European patch test for the diagnosis of allergic contact dermatitis at our tertiary referral hospital.

MATERIAL AND METHODS

STUDY DESIGN AND PARTICIPANTS

This retrospective, descriptive study included all patients aged 18 years and older diagnosed with allergic contact

dermatitis who underwent the European Patch Test at our tertiary Allergy and Immunology Clinic. Our clinic, which annually sees the highest number of allergy patients in Turkey, provided the study group of 383 patients aged between 18 and 91 years. Patients with treatment-resistant allergic contact dermatitis underwent patch testing based on their medical history and dermatologic examination. Inclusion criteria required that patients had not used topical steroids within the last 10 days or oral steroids or antihistamines within the past month. The analysis considered age, gender, disease duration (in months), atopy status, patch test results, and any relationships between positive patch test results in patients.

PATCH TESTING PROCESS

Patch testing followed a two-phase process: a standard European patch test was administered between January 2018 and March 2021, utilizing materials from Chemotechnique Diagnostics in Malmo, Sweden. The European Patch Series, encompassing 32 allergens, was applied in our clinic between March 2021 and June 2023. The recommended scheme by the International Contact Dermatitis Research Group (ICDRG) was followed for examination times: the first assessment occurred at 48 h, and the second was conducted at 72 h. If positivity observed at 48 h decreased or disappeared by the 72-hour mark, it was considered indicative of allergic contact dermatitis. The scoring of patch tests adhered to the ICDRG guidelines, categorized as follows: (–) for no reaction, (–/+) for mild erythema/indeterminate reaction, (+) for erythema, infiltration, (+++) for erythema, infiltration, papules, vesicles, and (+++++) for erythema, infiltration, and bullae.

STATISTICAL ANALYSIS AND ETHICS COMMITTEE APPROVAL

Data analysis employed SPSS 22.0 for statistical computations. Differences in means were evaluated through the Mann-Whitney *U* test, with relative risks, odds ratios, and 95% confidence intervals calculated. Categorical parameters underwent analysis using χ^2 and logistic regression. The study had received approval from the Ethics Committee (dated 03.06.2023, protocol code: 116.2017.R-278).

RESULTS

Between January 2018 and May 2023, a total of 383 patients aged over 18 years underwent patch testing with the European Baseline Series (EBS). Among these, 216 (56.3%) patients received the standard European Patch Test between January 2018 and March 2021, while 167 (43.7%) patients underwent the European Patch Series

conducted in our clinic from April 2021 to June 2023. The age range of the patients was 18 to 91 years, with 224 (58.4%) being females. The mean age for women was 40.78 ± 12.85 years, and for men, it was 40.71 ± 12.76 years. The disease duration averaged 21.84 ± 34.89 months for men. Atopy was present in 40.1% of women and 30.1% of men. In total, 126 (56.25%) women and 70 (44%) men had at least one positive allergen. Demographic characteristics are shown in Table 1.

Out of the 383 patients, 196 (51.1%) tested positive for at least one allergen. Among the 216 patients who were tested between January 2018 and March 2021, 118 (54.6%) had at least one positive reaction. For the 167 patients who were tested between April 2021 and June 2023, 78 (46.7%) displayed at least one positive response to an allergen. A comprehensive list of all allergens used in the standard European Patch Test can be found in Table 2. The top 5 allergens with the highest positive reactions were nickel sulfate (24.4%), gold sodium thiosulfate (13.5%), thiomersal (9%), cobalt chloride (6.5%), and wool wax alcohols (5.5%). In our clinic-prepared patch test, detailed allergens and their corresponding test results are displayed in Table 3. The primary allergens with the most positive reactions were nickel sulfate (19.4%), cobalt chloride (7.2%), colophony (6.7%), potassium dichromate (6.4%), and textile dye mix (5.5%). Notably, nickel sulphate ranked the highest in positivity throughout all years, accounting for 85 (22%) cases, followed by gold sodium thiosulfate with 27 (7%), cobalt chloride with 26 (6.8%), thiomersal and para-phenylenediamine with 18 each (4.7%), and potassium dichromate with 17 (4.4%) cases.

According to gender, patch test positivity was higher in women than in men in all years and this was statistically significant ($p = 0.022$). Among all allergens, nickel sulphate positivity was higher in women and potassium dichromate positivity was higher in men than in women and both of these were statistically significant ($p < 0.001$, $p = 0.004$). There was a statistically significant correlation between patient age and disease duration, eosinophil count and eosinophil percentage ($p = 0.009$, $p = 0.009$, $p = 0.013$) (Table 4).

The patches were applied in two different ways during the whole study. When common allergens were analyzed, the allergens that showed statistically significant

changes were as follows: wool wax alcohols, carba mix, cl-me-isothiazolinone, thiomersal positivity decreased over time, while colophony positivity increased over time. The change over time with these allergens was statistically significant and as shown in Table 5.

DISCUSSION

Although our study is a retrospective study, it is one of the studies with the highest number of patients reported from a single center. In this study, 383 patients who underwent European Patch Testing were analyzed. Of the patients who underwent patch testing, 58.4% were females. In all years, nickel sulphate had the highest positive rate with 22% (85), followed by gold sodium thiosulfate with 7% (27), cobalt chloride with 6.8% (26), thiomersal and para-phenylenediamine with 4.7% (18), and potassium dichromate with 4.4% (17). In all years, patch test positivity was statistically higher in women than in men. Nickel sulphate and potassium dichromate were statistically significantly more positive in women and men, respectively. Wool wax alcohols, carba mix, cl-me-isothiazolinone, thiomersal positivity decreased over time, while colophony positivity increased statistically significantly over time.

58.4% of our patients who underwent patch test were females; this result was similar to other studies conducted in our country [6, 7]. At least one allergen was positive in 196 (51.1%) of all patients. The percentage of patch test positivity was similar to previously reported studies from our country [7–10]. According to gender, at least one allergen positivity was statistically significantly higher in females than in males ($p = 0.022$). When we look at the data from the European Surveillance System on Contact Allergies (ESSCA; www.essca-dc.org), it is noteworthy that female gender is a risk factor for patch positivity [11].

The highest positivity was found for nickel sulphate in all patients and this positivity was consistent with the literature [7, 9, 11]. In our study, similar to the literature, nickel sulphate sensitivity was higher in women and there was a decrease in nickel sulphate sensitivity over the years. Nickel sulphate sensitization was statistically significantly higher in the female gender ($p < 0.001$). The best way to prevent nickel sulphate sensitivity is to limit exposure by law. Although different countries have taken

TABLE 1. Demographic characteristics of the study population

Characteristic	Females ($n = 224$)	Males ($n = 159$)
Age [years] mean (SD)	40.78 ± 12.85	40.71 ± 12.76
Duration of ACD [months] mean (SD)	22.35 ± 36.27	21.84 ± 34.89
Atopy (%)	40.1% ($n = 90$)	30.1% ($n = 48$)
Patch test positivity (%)	126 (56.25%)	70 (44%)

measures to prevent nickel sulphate exposure, the most extensive measures have been taken directly by the European Union [12]. First, the use of nickel sulphate was completely banned in Europe. The decisions were relaxed over time [13, 14]. However, it was noted that the per-

centage of nickel sulphate sensitivity decreased in our study, although it was not statistically significant. We think that this situation is related to legal regulations.

The content of the patch test applied in our center has changed over the years in line with the possibilities. It is

TABLE 2. 01.2018–03.2021 distribution of TRUE test (European baseline series) results by gender

Allergen	Females (N = 129)		Males (N = 87)		Total (N = 216)	
	n	%	n	%	n	%
Nickel sulphate	42	19.4	10	5	52	24.4
Gold sodium thiosulfate	19	9.5	8	4	27	13.5
Thiomersal	14	7	4	2	18	9
Cobalt chloride	6	3	7	3.5	13	6.5
Wool wax alcohols	8	4	3	1.5	11	5.5
Epoxy resin	5	2.5	6	3	11	5.5
Carba mix	5	2.5	3	1.5	8	5
Para-phenylenediamine	5	2.5	3	1.5	8	4
Cl-Me-Isothiazolinone	2	1	4	2	6	3
Thiuram mix	3	1.5	3	1.5	6	3
Potassium dichromate	2	1	4	2	6	3
Cain mix	2	1	3	1.5	5	2.5
Balsam of Peru	4	2	1	0.5	5	2.5
Colophony	4	2	–	–	4	2
Black Rubber Mix	3	1.5	1	0.5	4	2
P-Tert-Butylphenol Formaldehyde Resin	4	2	–	–	4	2
Methyldibromoglutaronitrile	2	1	1	0.5	3	1.5
Ethylenediamine dihydrochloride	1	0.5	1	0.5	2	1
Formaldehyde	1	0.5	1	0.5	2	1
Fragrance mix	2	1	–	–	2	1
Disperse Blue 106	1	0.5	1	0.5	2	1
Quinoline mix	2	1	–	–	2	1
Hydrocortisone-17-butyrate	1	0.5	1	0.5	2	1
Quaternium-15	1	0.5	–	–	1	0.5
Paraben mix	–	–	1	0.5	1	0.5
Neomycin sulphate	–	–	1	0.5	1	0.5
Mercapto mix	–	–	1	0.5	1	0.5
Tixocortol-21-pivalate	–	–	1	0.5	1	0.5
Imidazolidinyl urea	–	–	1	0.5	1	0.5
Budesonide	–	–	1	0.5	1	0.5
Mercaptobenzothiazole	–	–	1	0.5	1	0.5
Bacitracin	1	0.5	–	–	1	0.5
Parthenolide	–	–	–	–	–	–
Diazolidinyl urea	–	–	–	–	–	–
Bronopol	–	–	–	–	–	–

noteworthy that new allergens added to the list over the years have also been positive. When contact allergens are monitored using the European Surveillance System on Contact Allergies (ESSCA) system, the need to change the content of the patch test draws attention [15]. The European Patch Test was last renewed in 2019, and the need to add new allergens in 2023 was emphasized [16].

The second most frequently positive allergen was gold sodium thiosulfate, similar to the Thailand study [17]. Wool wax alcohols, colophony, carba mix, cl-me-isothiazolinone, thiomersal and gold sodium thiosulfate showed statistically significant changes over time. Only colophony allergy was on the rise. Considering that colophony is included in hand cleaning materials, person-

TABLE 3. 04.2021–06-2023 distribution of the results of the European Patch Test prepared in our clinic

Allergen	Females (N = 95)		Males (N = 72)		Total (N = 167)	
	n	%	n	%	n	%
Nickel sulphate	27	16.1	6	3.3	33	19.4
Cobalt chloride	7	3.9	6	3.3	13	7.2
Colophony	7	3.9	5	2.8	12	6.7
Potassium dichromate	2	1.1	9	5.3	11	6.4
Textile dye mix	6	3.3	4	2.2	10	5.5
4-Phenylenediamine base	6	3.3	3	1.7	9	5
Thiuram mix	4	2.2	5	2.8	9	5
Balsam of Peru	2	1.1	5	2.8	7	3.9
Budesonide	2	1.1	3	1.7	5	2.8
Fragrance mix	1	0.6	4	2.2	5	2.8
Sesquiterpene lactone mix	1	0.6	3	1.7	4	2.3
Methyldibromoglutaronitrile	1	0.6	3	1.7	4	2.3
Fragrance Mix 2	2	1.1	2	1.1	4	2.2
Mercaptobenzothiazole	2	1.1	2	1.1	4	2.2
Epoxy resin	3	1.7	0		3	1.7
N-isopropyl-N-phenyl-4-phenylenediamine	1	0.6	1	0.6	2	1.2
Wool wax alcohols	1	0.6	1	0.6	2	1.2
Benzocaine	1	0.6	1	0.6	2	1.2
Methylisothiazolinone + methylchlorisothiazolinone	2	1.1	–	–	2	1.1
Tixocortol-21-pivalate	–	–	2	1.1	2	1.1
Paraben mix	–	–	2	1.1	2	1.1
Mercapto mix	1	0.6	0		1	0.6
Neomycin sulphate	1	0.6	–	–	1	0.6
P-tert-butylphenol formaldehyde resin	1	0.6	–		1	0.6
Ethylenediamine dihydrochloride	–	–	1	0.6	1	0.6
Formaldehyde	1	0.6	–	–	1	–
Diazolidinyl urea	1	0.6	–		1	
1-(3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride (Quaternium-15)	–	–	–		–	–
Clioquinol	–	–	–	–	–	–
Carba mix	–	–	–	–	–	–
Lyril	–	–	–	–	–	–
Cl-Me-isothiazolinone	–	–	–	–	–	–

TABLE 4. Allergens showing statistical significance according to gender

Variable		Sex		P-value
		Female	Male	
Patch test positivity	Positive for at least one allergen	126 (64.3%)	70 (35.7%)	0.022
	Negative	98 (52.4%)	89 (47.6%)	
Nickel sulphate	Positive	69 (81.2%)	16 (18.8%)	< 0.001
	Negative	155 (52%)	143 (48%)	
Potassium dichromate	Positive	4 (23.5%)	13 (76.5%)	0.004
	Negative	220 (60.1%)	146 (3.9%)	

TABLE 5. Allergens in both tests for which test results changed significantly over time

Variable		When the patch was applied		P-value
		January 2018–March 2021	April 2021–June 2023	
Wool wax alcohols	Positive	11 (84.6%)	2 (15.4%)	0.037
	Negative	205 (55.4%)	165 (44.6%)	
Colophony	Positive	4 (25%)	12 (75%)	0.018
	Negative	212 (57.8)	155 (42.2%)	
Carba mix	Positive	8 (100%)	0	0.011
	Negative	208 (54.5%)	167 (44.5%)	
Cl-Me-isothiazolinone	Positive	6 (100%)	0	0.038
	Negative	210 (55.7%)	167 (44.3%)	
Thiomersal	Positive	18 (100%)	0	< 0.001
	Negative	198 (54.2%)	167 (45.8%)	
Gold	Positive	27 (100%)	0	< 0.001
	Negative	189 (53.1%)	167 (46.9%)	

al cleaning products and detergents, it is not difficult to understand its increase during the COVID-19 epidemic.

Budesonide, hydrocortisone-17-butyrate, tixocortol-21-pivalate are allergens used to evaluate sensitization to steroids in patch tests. Although not statistically significant, it was noted that the sensitization percentages increased over time. Nevertheless, it has been pointed out that it is not correct to evaluate contact allergy to steroids only with the European Patch Test and additional tests should be performed [18]. Since our study was retrospective, it is difficult to evaluate the clinical significance of the allergens found.

Potassium dichromate positivity was statistically significantly higher in men than in women ($p = 0.004$). This sensitivity is similar to the literature [17].

Considering the most common allergen sensitivity, although patch testing has been done in different countries; sensitivity to gold, nickel sulfate, potassium dichromate, fragrance mix and cobalt chloride is similar to the literature [17].

It is noteworthy that the frequency of fragrance mix 1, fragrance mix 2 and balsam of Peru increases over time. Positivity was observed with a frequency of 12.4% in all patients. The frequency of fragrance allergen positivity is also similar to the literature [19].

Mercaptobenzothiazole positivity was observed in 5 patients. When the patients were advised to stay away from the leather sofa, all of the lesions resolved. This condition was caused by mercaptobenzothiazole used in the production of leather sofas. This condition is also referred to as sofa dermatitis in the literature [20].

The most important limitation of our study was that it was retrospective and the clinical equivalent of the patch test result could not be determined. The European Surveillance System on Contact Allergies (ESSCA) has now created a database system [21]. In this way, the clinical significance of allergens detected positive in the patch test can be better determined.

Allergic contact dermatitis is a disease that affects all age groups and has negative effects on the quality of life.

Making the diagnosis and avoiding the allergen in question is very important in treatment management.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

- Chen JK, Jacob SE, Nedorost ST, et al. A pragmatic approach to patch testing atopic dermatitis patients: clinical recommendations based on expert consensus opinion. *Dermatitis* 2016; 27: 186-92.
- Johansen JD, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing – recommendations on best practice. *Contact Dermatitis* 2015; 73: 195-221.
- Isaksson M, Bruze M, Goossens A, Lepoittevin JP. Patch testing with budesonide in serial dilutions: the significance of dose, occlusion time and reading time. *Contact Dermatitis* 1999; 40: 24-31.
- Fregert S. *Manual of Contact Dermatitis*. Copenhagen, Munksgaard, 1974.
- Kadyk DL, McCarter K, Achen F, Belsito DV. Quality of life in patients with allergic contact dermatitis. *J Am Acad Dermatol* 2003; 49: 1037-48.
- Bilgic A, Bozca BC, Subasi GY, et al. Standard patch test results and clinical relevance: a cross-sectional study of 10-year retrospective experience. *Indian J Dermatol* 2022; 67: 258-64.
- Boyvat A, Kalay Yildizhan I. Patch test results of the European baseline series among 1309 patients in Turkey between 2013 and 2019. *Contact Dermatitis* 2021; 84: 15-23.
- Koca R, Kocaturk E, Savk E, et al. Patch test results to European baseline series in Turkey: a prospective and multicenter study. *Dermatitis* 2021; 32: 397-405.
- Acer E, Erdogan HK, Batan T, Saracoglu ZN. European Standard Series Patch Test results in contact dermatitis patients in a tertiary care hospital. *Sisli Etfal Hastan Tip Bul* 2020; 54: 206-10.
- Dittmar D, Uter W, Bauer A, et al.; ESSCA Network. European Surveillance System on Contact Allergies (ESSCA): polysensitization, 2009-2014. *Contact Dermatitis* 2018; 78: 373-85.
- Machovcova A, Dastychova E, Kostalova D, et al. Common contact sensitizers in the Czech Republic. Patch test results in 12,058 patients with suspected contact dermatitis. *Contact Dermatitis* 2005; 53: 162-6.
- Ahlström MG, Thyssen JP, Menné T, Johansen JD. Prevalence of nickel allergy in Europe following the EU Nickel Directive – a review. *Contact Dermatitis* 2017; 77: 193-200.
- Commission Directive 2004/96/EC of 27 September 2004 amending Council Directive 76/769/EEC as regards restrictions on the marketing and use of nickel piercing post assemblies for the purpose of adapting its Annex I to technical progress. *Off J Eur Union*. 28 Sept 2004 L301/51.
- Lidén C. Nickel in jewellery and associated products. *Contact Dermatitis* 1992; 26: 73-5.
- Uter W, Schnuch A, Wilkinson M, et al. Registries in clinical epidemiology: the European surveillance system on contact allergies (ESSCA). *Methods Inform Med* 2016; 55: 193-9.
- Wilkinson SM, Gonçalo M, Aerts O, et al. The European baseline series and recommended additions: 2023. *Contact Dermatitis* 2023; 88: 87-92.
- Boonchai W, Iamtharachai P. Risk factors for common contact allergens and patch test results using a modified European baseline series in patients tested during between 2000 and 2009 at Siriraj Hospital. *Asian Pac J Allergy Immunol* 2014; 32: 60-5.
- Svendsen SV, Bindslev-Jensen C, Mortz CG. Contact allergy to corticosteroids: is the European baseline series sufficient? *Contact Dermatitis* 2023; 89: 277-83.
- Tai V, Sharifah Rosniza SNC, Tang MM. Contact sensitization to fragrance allergen: a 5-year review in the Department of Dermatology, Hospital Kuala Lumpur. *Med J Malaysia* 2023; 78: 583-8.
- Herman A, Marot L, Baeck M. Sofa dermatitis: value of patch test with 2-(thiocyanomethylthio)benzothiazole. *Contact Dermatitis* 2023; 89: 20-5.
- Oosterhaven JAF, Uter W, Aberer W, et al.; ESSCA Working Group. European Surveillance System on Contact Allergies (ESSCA): contact allergies in relation to body sites in patients with allergic contact dermatitis. *Contact Dermatitis* 2019; 80: 263-72.