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Distribution of allergens detected on patch tests of patients with allergic contact dermatitis and investigation of their atopic background

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Abstract

Aim: Allergic contact dermatitis (ACD) is a delayed hypersensitivity reaction to specific allergens that come in contact with the skin. Detection of the culprit allergen plays a central role in the effective treatment and management of this chronic disease. The present study aims to report distribution of allergens that cause ACD by analyzing patch test results, and investigate atopic background of these patients.

Materials and Methods: Results from patch tests performed on patients with ACD in the Department of Adult Allergy and Clinical Immunology at a tertiary hospital in Anatolian side of Istanbul were retrospectively assessed. Data regarding age, gender, occupation, lesion localization, history of suspected exposure, total Immunoglobulin E levels, concomitant allergic rhinitis and skin prick test results were inspected.

Results: Of the 131 patients, female/male ratio was 91 (69.5%)/40 (30.5%). Patch test results were negative in 56 (42.7%) patients, and positive for at least one allergen in 75 (57.3%) patients. Five most common allergens with a positive result were nickel sulphate (25.2%), gold sodium thiosulfate (13%), cobalt (9.9%), thiomersal (9.9%), and colophony (5.3%), respectively. A comparison between patch test results and genderdid not demonstrate any statistical significance. Young patients had a significantly higher positive reaction to thiomersal ($p = 0.008$). No correlation was found between atopic background and ACD.

Conclusion: Patch test results significantly contribute in the differential diagnosis and management of patients with dermatitis. Metals and thiomersal were the most common allergens detected by patch tests in our study. This is in correlation with previous research. We believe that types of allergens may go through an alteration as the environment and lifestyle changes over time, and that our findings contribute to determine which allergens to be used in patch tests in the future.

Introduction

Allergic contact dermatitis (ACD) is a delayed hypersensitivity reaction to specific allergens that come in contact with the skin. The skin lesion is an eczema-like dermatitis characterized by pruritus, and erythematous macules, papules, vesicles and bullae in acute cases, and lichenification in chronic cases [1-3]. The reported prevalence is 15-28% in general population [4]. Patch testing is used to confirm the diagnosis of ACD, and identify the allergens that cause the skin reaction. It is recommended to perform a patch test to every patient with chronic dermatitis due to unpredictable nature of the disease [5]. It has been postulated that individuals with atopic dermatitis are prone to have ACD due to immune dysregulation including common cytokine pathways, and frequent use of ointments and topical medication [6].

The present study aims to share results from standard serial epicutaneous patch tests performed on patients with ACD, assess frequency and distribution of culprit allergens, and investigate atopic background with skin prick tests.

Materials and Methods

The study was conducted in the Department of Adult Allergy and Clinical Immunology at a tertiary hospital in Anatolian side of Istanbul. Results of patch and skin prick

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tests performed between September 2019 and September 2020 on patients referred with an initial diagnosis of contact dermatitis based on dermatological examination were retrospectively analyzed. One hundred thirty-one patients were enrolled.

Patients

Data regarding past medical history, physical examination, age, gender, occupation, lesion localization, history of suspected exposure, total Immunoglobulin E (IgE) levels, concomitant allergic rhinitis, skin prick test results, and patch test results were inspected. A total IgE level of ≥100 UI/mL (normal range, 0-100 UI/mL) was accepted as high.

Skin prick testing

Skin prick tests were performed using standard commercially available allergen extracts (grasses mix, cereals mix, tree mix, Dermatophagoides (D). pteronyssinus, D. farinae, acarus siro, cockroach, cat epithelia, dog epithelia, aspergillus fumigatus, alternaria, clodosporium, lepidoglypus destructor, tyrophagus putrescentlae, artemisia vulgaris, parietaria officinalis, plantago lanceolata, ambrosia artemisiifolia, corylus avellana, alder, olea europoea, ash, oak, populus alba , betula alba)(Alk-Abello, Lincoln Diagnostics, Dallas, TX, USA). Skin prick tests were performed on both forearms in accordance with international guidelines. Histamine (10 mg/mL) was used as positive control, and sterile saline 0.09% as negative control. A wheal diameter of ≥3 mm greater than the negative control after 15 minutes of application was considered as a positive prick test [7].

Patch testing

A written informed consent was obtained from each patient. Patients were instructed to avoid use of topical corticosteroids for 7 days, systemic steroids for 3 weeks prior to test application. The Thin-Layer Rapid Use Epicutaneous (T.R.U.E.®SmartPractice, Denmark)Test which includes 36 allergens in 3 tapes (panels 1, 2 and 3) was used. (Table 1). The patches were applied to a clean, dry, hairless and lesion-free area of the upper back. Patients were advised to keep the test area dry and avoid sweating. Patches were removed 48 hours later and test sites were marked. First reading was done following a 30-minute rest. Second, and third in necessary cases, readings were done 72 and 96 hours after application. Tests were interpreted as negative (-) if there was no reaction; weak positive (+) if there was erythema and infiltration; strong positive (++) if there was erythema, infiltration, papules and vesicles; extreme positive (+++) if there was erythema,infiltration, coalescing vesicles and bullae [8].

Statistical analysis

Normal distributions of numerical variables were tested with the Shapiro-Wilk test. While comparing the groups in terms of the variables with normal distribution, the independent samples t test was used, and the Mann Whitney U test was used for the variables that were not normally distributed. Continuous variables are presented as median and range (minimum-maximum). Categorical variables are presented as counts and proportions. Pearson's chi-square test or Fisher's exact test was used to compare groups. IBM SPSS Statistics for Windows version 20 (IBM Corp., Armonk, N.Y., USA) was used for all statistical analyses. A two-sided p value of <0.05 was considered to be statistically significant.

Results

Of the 131 patients, female/male ratio was 91 (69.5%)/40 (30.5%), and median age was 36 (range, 29-48). There were 45 (34.4%) housewives, 18 (13.7%) factory workers, 11 (8.4%) students, 9 (6.9%) healthcare workers, and 18 (13.7%) patients from other occupations (cook, engineer, teacher, retired).

Lesions were located in hands in 38.2% of patients, scalp and face in 47.3%, hands and feet in 8%, arms in 35.9%, legs in 20.6%, feet in 0.8%, and torso in 30.5%. Forty-six (35.1%) patients had allergic rhinitis symptoms, 34 (26%) patients had a positive skin prick test, and 24 (18.3%) patients had elevated total IgE levels. The general characteristics of the patients are presented in Table 2.

[Table2]

Five most common allergens with a positive result were nickel sulphate (25.2%), gold sodium thiosulfate (13%), cobalt (9.9%), thiomersal (9.9%), and colophony (5.3%), respectively. Patch test results were negative in 56 (42.7%) patients, and positive for at least one allergen in 75 (57.3%) patients. Thirty-eight (29%) patients had a positive test for one allergen, whereas 37 (28.2%) had a positive test for more than one allergens. The distribution and percentages of positive allergens are shown in Figure 1, and the distribution and percentages of patients with more than one allergen positive are shown in Figure 2.

Of 33 patients with nickel allergy, 15 had allergic rhinitis symptoms with a positive skin prick test in 5, and a negative skin prick test in 10. A detailed history of all 10 patients with a negative skin prick test revealed increase in rhinitis symptoms after nickel-rich food (e.g. spinach, chocolate) intake.

Twenty-four (18.3%) patients had a history of suspected exposure, and 11 (45.8%) of them had compatible positive allergy test results. Of the patients with a positive allergy test result compatible with a history of suspected exposure, 6 were healthcare workers (5 allergic thiomersal and 1 allergic to formaldehyde), 2 were factory workers (1 allergic to colophony and 1 allergic to Cl+ Me- isothiazolinone), and 3 were housewives (1 allergic to paraphenylenediamine, 1 allergic to cobalt and 1 allergic to formaldehyde).

A comparison between patch test results and gender, existence of atopy, total IgE levels and occupations did not demonstrate any statistical significance. Statistically significant difference was only detected between allergy to thiomersal and age. Median age of patients with a negative reaction to thiomersal was 37.5 (range, 31-49), and median age of patients with a positive reaction to thiomersal was 28 (range, 25-36) (p = 0.008).

Table 1. . TRUE Test® allergens.

Allergen	µg/cm2	Allergen	µg/cm2
Colophony	1200	Mercapto Mix	75
Wool alcohols	1000	Gold Sodium Thiosulfate	75
Paraben mix	1000	Mercaptobenzothiazole	75
Balsam of Peru	800	Potassium dichromate	54
Caine mix	630	Ethylenediamine dihydrochloride	50
Neomycin sulphate	600	Epoxy resin	50
Imidazolidinyl urea	600	Disperse blue 106	50
Bacitracin	600	p-tert-Butylphenol formaldehyde resin	45
Diazolidinyl urea	550	Thiuram Mix	27
Fragrance mix	430	Cobalt dichloride	20
Carba mix	250	Hydrocortisone-17-butyrate	20
2-Bromo-2-nitropropane-1 3-diol (Bronopol)	250	Thimerosal	7
Nickel sulphate	200	Methyldibromo glutaronitrile	5
Quinoline Mix	190	Cl+ Me- Isothiazolinone	4
Formaldehyde	180	Tixocortol-21-pivalate	3
Quaternium-15	100	Parthenolide	3
p-Phenylenediamine	80	Budesonide	1
Black rubber mix	75		

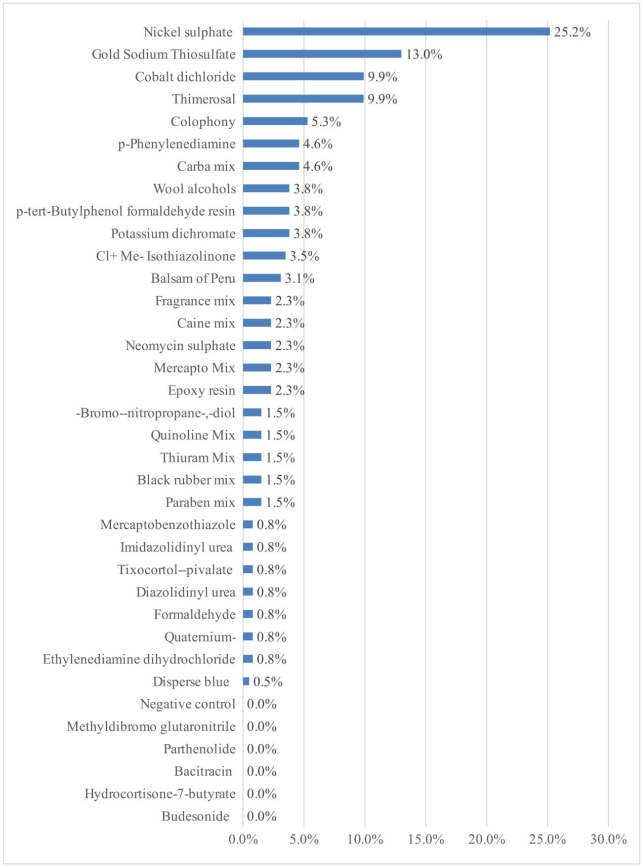

Figure 1. Distribution of allergens in positive patch tests

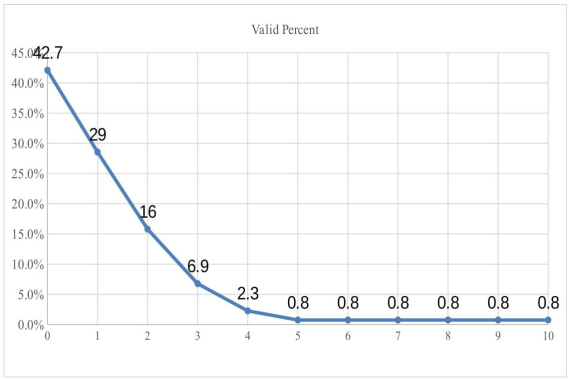

Figure 2. Distribution of patients with more than one positive allergen reactions

Discussion

Detection of the culprit allergen plays a central role in the management of ACD. Previous research shows a 45-65% rate of positive patch test results, and a female predominance among patients with ACD [9-11]. In the present study, 57.3% of the participants had a positive patch test, and most of the participants were women. However, distribution of allergens did not significantly differ between genders.

Metals (nickel sulphate [25.2%], gold sodium thiosulfate [13%] and cobalt [9.9%]) were the most common allergens detected by standard patch tests in our series. Metals were followed by thiomersal, colophony, carbamate mix, para-phenylenediamine, wool alcohol, potassium dichromate and para tertiary butylphenol formaldehyde resin. Sensitivity to nickel sulphate has been reported to be between 12-30.7% [12, 13]. Similarly, we observed a nickel sulphate sensitivity of 25.2%. Human contact with metals such as gold, chrome, copper, cobalt, nickel and silver is very frequent in the present day. Examples include cloth-

ing ornaments, dental materials, kitchen appliances, jewelry, mobile telephones and electronics. İn the 21st century a trend of an increase in nickel sensitivity which is largely attributed to increased use of nickel-containing electronic devices, and body piercings and other ornaments, has been seen [14]. Nickel hypersensitivity can also cause allergic reactions in the respiratory tract[15]. One third of patients with nickel sensitivity in our study demonstrated rhinitis symptoms following nickel-rich food intake. Patients with ACD due to nickel hypersensitivity may demonstrate systemic nickel allergy syndrome [16]. Therefore, along with a dermatological examination, ACD patients should be questioned for rhinitis and/or asthma symptoms, headaches, abdominal pain and fatigue following a nickel-rich meal. Limitation of nickel contact has been shown to improve symptoms [17-19]. Patients with nickel allergy should be informed regarding nickel-containing products, nickel-rich foods, and even implantable materials such as dental or orthopedic implants, surgical staplers or intrauterine devices. Second most common allergen in the present series was gold sodium thiosulfate, followed by cobalt. Coexistence of allergy to nickel, gold and cobalt has been frequently reported, however, controversy remains whether this is caused by cross-reaction, or true allergic reaction [20, 21]. Further research is needed.

Thiomersal was the most common allergen following metals in the present study. Thiomersal is used as a preservative in vaccines, allergen extracts, antiseptic solutions, cosmetics and contact lens solutions. Previous research also reports that thiomersal is among the most common allergens [11, 22]. In the current study we observed thatyoung patients had a significantly higher positive reaction to thiomersal (p = 0,008).In the study of Yu DS et al. similar to our study, thiomersal sensitivity was found to be higher in the younger age group [23].Van 't Veen AJ et al. conducted a study on 2461 patients between 1987-1992 and found the rate of tomersal sensitivity to be 1.3%. It is remarkable that thiomersal susceptibility rates have increased over the years[24]. The high susceptibility rates in the young patient population today can be considered as a precursor that the thimerosal susceptibility rates will increase further in the coming years. We believe that high incidence of thiomersal sensitivity among young patients is a result of improved vaccination programs. Among 9 healthcare workers in the study, 5 had sensitivity to thiomersal and reported worsening of symptoms after contact with antiseptic solutions. In addition to vaccination programs, we believe increased use of antiseptic solutions contribute to increased rate of thiomersal sensitivity.

The most common allergens following thiomersal were colophony (5.3%), carbamate mix (4,6%), paraphenylenediamine (4.6%), wool alcohol (3.8%), potassium dichromate (3.8%) and para tertiary butylphenol formaldehyde resin (3.8%). Colophony is used in pharmaceuticals, carbamates are used in rubber products, para-phenylenediamine is used in hair dyes, wool alcohol (lanolin) is used in cosmetics, potassium dichromate is used as an ingredient in cement and for leather tanning, and formaldehyde resin is used in cosmetics and topical medications. Rates of sensitivity to these allergens were similar to previous reports [2, 5, 8, 11, 25-27].

Twenty-six percent of patients had atopy in the present study, and we did not observe atopic background to be a risk factor for ACD. Previous research also shows that incidence of ACD is similar between atopic and non-atopic individuals [28, 29].

In conclusion,a detailed history, physical examination, and patch test contribute significantly to the diagnosis and treatment management of a patient with dermatitis.Metals and thiomersal were determined as the most common allergens in the data we obtained from patch test results in our study, and these data were found similar to the studies conducted in our country and in the world. With the changing world and technology, it is expected that there will be changes in allergen types. We think that by sharing the patch test results data, it will be a guide to recreate the allergen types to be used in the standard series.

Nelson JL, Mowad CM. Allergic contact dermatitis: patch testing beyond the TRUE test. J Clin Aesthet Dermatol 2010; 3: 36-41.

Ethical approval

Our study was conducted according to the Principles of Helsinki Declaration and the ethical committee approval was taken from Kartal Dr. Lutfi Kırdar City Hospital Ethical Committee (Decision no: 2020/514/179/24).

References

1. Cohen DE, Rao S, Brancaccio RR. Use of the North American Contact Dermatitis Group standard 65-allergen series alone in the evaluation of allergic contact dermatitis: a series of 794 patients. Dermatitis 2008;19: 137-141.
2. Landeck L, Schalock PC, Baden LA, Neumann K, Gonzalez E. Patch-testing with the standard series at the Massachusetts General Hospital, 1998 to 2006. Dermatitis 2009;20: 89-94.
3. Tyssen JP, Linnenberg A, Manne T, Johansen JD. The epidemiology of contact allergy in the general population-prevalence and main findings. Contact Dermatitis. 2007; 57: 287-299.
4. Carlsen Bc, Menne T, Johonsen JD. 20 years of standard patch testing in eczema population with focus on patients with multiple contact allergies. Contact Dermatitis 2007; 57: 76-83.
5. Czarnobilska E, Obtulowicz K, Dyga W, Spiewak R. A half of schoolchildren with 'ISAAC eczema' are ill with allergic contact dermatitis. Journal of the European Academy of Dermatology and Venereology 2011; 25: 1104–1107
6. Nelson HS. Variables in allergy skin testing. In: Dolen W, ed. Skin Testing. Philadelphia, PA: WB Saunders; 2001:281–290.
7. Wahlberg JE. Patch testing. In: Rycroft RJG, Menne T, Frosch PJ, Lepoittevin JP,eds. Textbook of Contact Dermatitis. 3rd ed.Berlin:Springer-verlag, 2001. p.437-68
8. Reduta T, Bacharewicz J, Pawlos A. Patch test result in patients with allergic contact dermatitis in the Podlasie region. Postepderm Alergol 2013; 6: 350-357.
9. Shakoor Z, Al-Mutairi AS, Al-Shenaifi AF, Al-Abdulsalam AM, Al-Shirah BZ, Al-Harbi S. Screening for skin-sensitizing allergens among patients with clinically suspected allergic contact dermatitis. Saudi Med J 2017; 38: 922-927.
10. Türkmen D, Altunışık N. Malatya ilinde 169 alerik kontakt dermatitli hastada yama test sonuçları. Türkiye Klinikleri J Dermatol 2018; 28: 114-122
11. Shah M, Lewis FM, Gawkrodger DJ. Nickel as an occupational allergen. A survey of 368 nickel-sensitive subjects. Arch Dermatol 1998;134: 1231-1236.
12. Shum KW, Meyer JD, Chen Y, et al. Occupational contact dermatitis to nickel: experience of the British dermatologists (EPIDERM) and occupational physicians (OPRA) surveillance schemes. Occup Environ Med 2003; 60: 954-957
13. Warshaw EM, Aschenbeck KA, DeKoven et al. J Am Acad Dermatol.2018;79:664-671.

14. Ricciardi L, Arena A, Arena E, et al. Systemic nickel allergy syndrome: Epidemiological data from four Italian allergy units. International Journal of Immunopathology and Pharmacology. 2014; 27:131–136.
15. Ricciardi L, Arena A, Arena E, et al. Systemic nickel allergy syndrome: Epidemiological data from four Italian allergy units International Journal of Immunopathology and Pharmacology 2014; 27: 131–136.
16. Matsuzaka K, Mabuchi R, Nagasaka H, Yoshinari M, Inoue T. Improvement of eczematous symptoms after removal of amalgam-like metal in alveolar bone. Bull. Tokyo Dent. Coll 2006; 47: 13–17.
17. Laeijendecker R, Dekker SK, Burger PM, Mulder PG, Van Joost T, Neumann MH. Oral lichen planus and allergy to dental amalgam restorations. Arch Dermatol 2004; 140: 1434–1438.
18. Yaqob A, Danersund A, Stejskal VD, Lindvall A, Hudecek R, Lindh U. Metal-specific lymphocyte reactivity is downregulated after dental metal replacement. Neuro Endocrinol Lett 2006; 27: 189–197.
19. Marcusson JA. Contact allergies to nickel sulfate, gold sodium thiosulfate and palladium chloride in patients claiming side-effects from dental alloy components. Contact Dermatitis 1996;34: 320-323.
20. Fowler J Jr, Taylor J, Storrs F, et al. Gold allergy in North America. Am J Contact Dermat 2001;12: 3-5
21. Wohrl S, Hammer W, Focke M,Gotz M, Jarisch R. Patch testing in children, adults ant the elderly: Influence of age and sex on sensitization patterns. Pediatr Dermatol 2003; 20: 119-123.
22. Yu DS, Kim HJ, Park YG, Bae JM, Kim JW, Lee YB.J Dermatolog Treat. 2017 May;28(3):258-262.
23. van 't Veen AJ, van Joost T.Contact Dermatitis. 1994 Nov;31(5):293-8.
24. Warburton KL, Bauer A, Chowdhury MM, Cooper S, Krecisz B, Chomiczewska-Skora D et al. ESSCA results with the baseline series, 2009-2012: rubber allergens. Contact Dermatitis 2015; 73: 305-312.
25. Warshaw EM, Raju S, DeKoven JG, Belsito DV, Zug KA, Zirwas MJ, Maibach HI et al. Positive patch test reactions to carba mix and iodopropynyl butylcarbamate: data from the North American Contact Dermatitis Group, 1998-2008. Dermatitis 2013; 24: 241-245.
26. Malinauskiene L, Blaziene A, Chomiciene A, Isaksson M. Formaldehyde may be found in cosmetic products even when unlabellel. Open Med 2015; 10: 323-328.
27. Duarte I, Lazzarini R,Kobata CM. Contact dermatitis in adolescents. Am j Contact Dermat 2003; 14: 200-202
28. Giordano-Labadie F, Rance F, Pellegrin F, Bazex J, Dutau G, SchwarzeHP. Frequency of contact allergy in children with atopic dermatitis: results of a prospective study of 137 cases. Contact dermatitis 1999; 40: 192-195