

## Evaluation of Skin Patch Test Results with Contact Allergens in Children-19

Azize P Metbulut\*, Ilknur Kulhas Celika, Irem Turgay Yagmura, Betul Karaatmaca, Muge Toyrana, Ersoy Civeleka, Emine Dibek Mısırlıoğlu

Department of Pediatric Allergy and Immunology, Ankara City Hospital, Ankara, Turkey

### ABSTRACT

**Background:** Contact dermatitis one of the most common skin disease. Allergic contact dermatitis (ACD) is a hypersensitivity reaction that occurs in those having previously been sensitive to allergens and having repeated allergen exposure. Sensitivity develops with piercings, tattoos, topical treatments and exposure to cosmetics.

**Objectives:** The aim of the study is to identify common allergens causing contact dermatitis in children.

**Methods:** This is a retrospective review of children who were aged between 5 months -18 years and diagnosed with Contact Dermatitis between April 2012 and May 2019 and who applied to the Pediatric Allergy and Immunology Clinic. All patients were tested with T.R.U.E (Thin-Layer Rapid Epicutaneous) test.

**Results:** A total of 234 children, including 111 boys (47.4%) were evaluated. Ninety eight patients (41.8%) had positive results. There were no significant difference between age groups, gender and having allergic disease in terms of positivity. The most frequently determined allergens were nickel sulphate (n:30[30.6%]), Cl+Me-isothiazolinone (n:15[15.3%]) and thimerosal (n:14[14.2%]).

**Conclusions:** Nickel is the most common contact allergen in patients with contact dermatitis.

**Keywords:** Contact dermatitis; Children; Patch test; Allergic contact dermatitis; Nickel; CL+Me- isothiazolinone; Thimerosal; Allergen; Delayed hypersensitivity reaction; Contact sensitization

### INTRODUCTION

Allergic Contact Dermatitis (ACD) is a type IV (delayed) hypersensitivity reaction that occurs in those who have previously been sensitive to allergens and have repeated allergen exposures [1]. Today, the prevalence of ACD in children tend to increase [2]. Sensitivity develops with early ear piercing, piercings, permanent and temporary tattoos, topical treatments and exposure to cosmetics [3]. Patch testing is a method that confirms the diagnosis of allergic contact dermatitis and allows us to find the antigen that causes contact sensitization. Nickel, cobalt, potassium dichromate, chemicals in hair dyes, substances in cosmetic products, creams, preservatives and perfumes in locally used drugs are the most common substances that cause the development of contact dermatitis. The prevalence of contact sensitization varies with respect to age, sex and geographic localization [4-7]. The patch test positivity rate ranges from 32.6% to 67% due to testing with different age groups, methods and antigens [4]. Indeed, there is a limited data about

children in the literature. Allergic contact dermatitis should be considered in recurrent lesions that do not respond to atopic dermatitis treatment and have localized lesions. In children diagnosed with Atopic Dermatitis (AD), allergic contact dermatitis develops more easily due to their susceptibility to skin sensitivity and skin barrier dysfunction. First line therapy in AD is skin hydration, which means frequent use of moisturizers and emollients that includes multiple components with different ingredients. These ingredients lead AD patients to develop cutaneous sensitization [8]. Diagnosis of ACD or AD is not simple in case eyelids, hands and flexural areas of the neck are involved. Patch testing is the gold standard for the diagnosis of ACD [9]. The aim of this study is to identify common allergens causing contact dermatitis in children.

### METHODS

This is a retrospective review of children who were aged between 5 months-18 years applied to the Pediatric Allergy and

**Correspondence to:** Azize Pinar Metbulut, Ankara City Hospital, Department of Pediatrics, Division of Pediatric Allergy and Immunology, Ankara Turkey, E-mail: pinar298@yahoo.com

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Immunology Clinic and diagnosed with Contact Dermatitis between April 2012 and May 2019. Patients were diagnosed as 'contact allergy'; because there was no evidence where and how the children were exposed to these allergens. The study protocol was approved by the Institutional Ethics Committee of Ankara City Hospital (E1-20-341). Medical history and demographic information such as age, sex, patient history and family history of allergic diseases were acquired from hospital records. Patients with atopic dermatitis, asthma, allergic rhinitis were recorded. Atopic dermatitis was defined in the accordance with the criteria of Hanifin and Rajka [10]. Patients underwent routine laboratory examination including complete blood count and serum total IgE level. Some of them underwent skin prick tests for aeroallergens (house dust mite, cockroach, animal danders, mix grasses and tree pollens) and common food allergens (cow's milk, egg, wheat). All the patients were tested with T.R.U.E (thin-layer rapid epicutaneous) test (manufacturer is Mekos Laboratories AS). The patch tests were applied on the upper back of the patients with T.R.U.E test including 3 panel with 36 allergens. Written informed consent were taken from patients. The patients were advised not to use antihistamine during the three day period of the test and any cream containing corticosteroid. After applying the patch test, the patients were evaluated at 48 and 72 hours. The results were interpreted according to EAACI position paper for practical patch testing in allergic contact dermatitis [11].

### Statistical analysis

Results were expressed as percentile (absolute numbers), as mean and standard deviation, or as median and interquartile range (IQR) as required. SPSS 22 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. To compare variables, the chi-square test and Mann-Whitney U test were used. P-value of <0.05 was considered statistically significant.

### RESULTS

A total of 234 children, including 111 boys (47.4%) were evaluated. The median age of children was 7.5 years old (IQR 3.79-11.83). Ninety eight of the patients (41.8%) were observed to have positive results: 13 patients in <2 years age group, 60 patients in 2-11 years age group, and 25 patients in >12 years age group. There was no significant difference between age groups, gender and having allergic disease in terms of positivity (respectively P-value 0.263, 0.085, 0.968). There was no significant difference between serum eosinophilia level (percent and absolute number) and serum IgE level in terms of positivity (respectively P-value 0.319, 0.48, 0.048). One positive allergen was detected in 52 patients (53%), two in 27 patients (27.5%), three in 13 patients (13.2%), four in 5 patients (5.1%) and five in 2 patients (2%). The most frequently determined allergens were nickel sulphate (n:30[30.6%]), Cl<sup>+</sup> Me- isothiazolinone (n: 15[15.3%]) and thimerosal (n:14[14.2%]). Demonstrates the detection rates of the allergens by TRUE test with respect to age and sex. Eighty eight patients had allergic diseases and 37 (42%) had atopic dermatitis. For atopic dermatitis patients, patch test was positive in 13 patients (35.1%) and the most frequently determined allergen was nickel sulphate (n:5[38.4%]). There was no significant difference between the groups with and without

atopic dermatitis in terms of TRUE test positivity (P-value .365). Skin prick test was performed in 161 patients (68.8%) and mostly found positive with pollens (n:32[19.8%]).

### DISCUSSION

In this study, 234 children were evaluated with TRUE test and 98 patients had positive results. There was no significant difference between age groups in terms of positivity. The most frequently determined allergens were nickel sulphate, Cl<sup>+</sup> Me- isothiazolinone and thimerosal. Thirty seven patients had atopic dermatitis and patch test was positive in 13 patients. There was no significant difference between the groups with and without atopic dermatitis in terms of TRUE test positivity.

We found patch test positivity in 41.8% of the study population. This result is compatible with other previously published studies in children that have patch test positivity ranges between 32.6%-67% [3]. In literature, there is limited data about ACD in Turkish children. In a study in Turkish children, between 1993 and 2005, 118 of the 360 patients (32%) diagnosed with contact dermatitis were found positive in the patch test. When patch testing with contact allergens is performed in patients who apply for contact dermatitis, suspicious allergens/allergens can be detected in half of them. Therefore, it is important to evaluate these patients with patch testing for contact allergen detection.

In our study, the youngest patient was 5 months old. In our case, nickel was detected as an allergen in the TRUE test performed due to the atopic dermatitis that did not respond to the treatment. In a study by Fisher and et al, 1 week old infant was reported with a positive patch test reaction to epoxy resin, manifesting as band like dermatitis above the wrist because of a vinyl band that was made of an epoxy resin [12].

In our study, the most commonly positive allergen determined as nickel sulphate and 30 patients (30.6%) had nickel sulphate positivity. In a study by Onder et al from Turkey, nickel sulphate was the most common positive allergen in children (57%) [6]. In literature, nickel sulphate allergen was the most commonly positive during patch tests [4-7]. In accordance with these data, we have found nickel as the most common allergen. Nickel is one of the most common metals in the environment. Nickel is found in jewellery, earrings, wrist-watches and watchstaps, buttons on clothes, zippers, gaslighters, batteries, coins, keys, clasps, eyeglasses frames, orthodontic, and orthopedic devices. The foods that are reported to be excessive in nickel are legumes, grain flour, oats, nuts, soybeans, fish, shellfish, chocolate and potatoes. Dietary nickel exposure may trigger dermatitis in individuals who are sensitive. Also, herbal drugs, herbal teas, and some multi-vitamins contain high levels of nickel. Exposure to some medical tools such as nickel-containing infusion cannulas, mitral-valve prostheses, intravenous catheters, dental instruments have also been reported to cause reactions in sensitized individuals [13,14]. In our study one of the reason of common nickel positivity in children may be early ear piercing in Turkish culture. Piercing is very common in Turkish children even in the first years of life.

The second mostly positively detected allergen was Cl<sup>+</sup> Me- Isothiazolinone (MCI) 15.3% (n:15). In a study by Kundak et al,

performed in Turkish children between 2013 and 2017, 89 children aged 3-18 years who were diagnosed with contact dermatitis performed with TRUE test and the most common positivity was found in methylchloroisothiazolinone (16.3%) [13]. This substance is a protective used in personal hygiene products, wet wipes, skin cleansers and also in industrial oils and paper coatings [14,15].

The third mostly positive allergen was thimerosal in our study with 14% (n:14.2) positivity. Thimerosal was commonly used as an antiseptic sprays and a protective in many medicines and vaccines [14]. In Zafir's study, thimerosal sensitivity was the third most common susceptibility in Israeli children [16]. In Turkey, hepatitis B vaccine, Td vaccine and rabies vaccine include thimerosal as preservative [17]. A decade age in two studies, patch test positivity for thimerosal between adults and children were compared and thiomersal was found more common among children. Frequency declined at ages greater than 30 years old [18,19]. In the past, thimerosal content was higher in vaccines. Today antiseptic sprays are also widely used for striving hygiene. These datas implied that our patients were sensitized to thimerosal allergen due to commonly used antiseptic sprays.

The other mostly positive allergens were cobalt dichloride, butifenolformaldehyde resin and colophony (n:8 [8.1%]). Cobalt (II) chloride hexahydrate can be found in most paints, bricks, tiles, cement and in metal tools such as keys, jewelries and orthopedic and dental tools. Since both cobalt and nickel are commonly found in the same metal products, an allergy may be developed from both metals. In our study cobalt and nickel association was present only in 4 patients. Butylhydroxytoluene (BHT) is an antioxidant food additive and also found in cosmetics, pharmaceuticals, rubber and petroleum products. In Yu's study, BHT prevalence was between 1% and 1.8% [15]. In our study BHT prevalence was 8.1%. Colophony (or rosin) is found in personal care products, diapers, feminine hygiene products, topical remedies, surface coatings, lubricants, glues and sealants [14]. In Yu's study, colophony positivity was reported between 1.8% and 2.2% [15]. In our study it was found as 8.1% and they were mostly between 2-11 years age.

Frequency of p-phenylenediamine and gold sodium thiosulphate positivity in patch test was both found as 7.1%. Phenylenediamine (PPD) is a chemical material used in the production of many types of paints and pigments, including nearly all hair-coloring products, textile dyes, photocopying and printing inks, oils and petrol [14]. Gold sodium thiosulphate is a common sensitizer with symptoms linked to gold in jewelries [14]. In our study gold sodium thiosulphate was found more in younger children may be caused by early ear piercing in Turkish children where gold is common.

Potassium dichromate positivity was found as 6.1% in our study. Potassium dichromate is found naturally in our environment: in sand, cinder, clay, and soil. It can be found in objects made of steel and chrome-plated [14].

Carba mix, fragrance mix, balsam of peru, black rubber mix and imidazolidinyl urea positivity were 5% in our study. Carba mix are used as fungicides and pesticides, and additionally in the

production of many rubber materials. Fragrance mix are used to add taste or odor to a material for magsking product's unpleasant odor. Balsam of Peru may still be found as a fragrance, flavoring material or antibacterial content. Black rubber mix or its components is used to make black or dark gray rubber materials such as shoes, clothes, eyeglasses. Imidazolidinyl urea is an antimicrobial substance used as a protective in cosmetics, shampoos, deodorants, body lotions, and in some topical medicines [14].

Ethylenediamine dihydrochloride is a substance that is used to manufacture diverse drugs and industrial compounds. The most common source of allergic reaction to ethylenediamine dihydrochloride is contact with topical antifungal, antibacterial, and cortisone skin cream mixtures. Caine mix are local anesthetics. Mercapto mix [A] are used in components of rubber products such as gloves, condoms, hose and tubing materials etc. Wool alcohols (or lanolin) are commonly used in cosmetics and drugs. Neomycin sulphate is an antibiotic commonly used in many prescription as an antibacterial. Parabens are used as protectives in many drugs, cosmetics, personal care, and hygiene materials. Quaternium 15 is commonly used in personal care materials, industrial varnishes, inks and paints. Quinolines are a group of synthetic antibacterial agents. Formaldehyde is used in the production of polymers, textiles and leather. Bronopol is an antimicrobial agent frequently used as a protective in many types of cosmetics, personal care products, and topical medications. Epoxy is a synthetic resin which are used in many industrial materials, some vinyl gloves, eyeglass frames, handbags, necklaces and also in dentist materials. Parthenolide is commonly found in the flowers and fruits. Disperse blue 124/106 are used in synthetic textiles. Methylidibromo glutaronitrile is frequently used in cosmetics and personal care products [14].

Today, it is important to test more allergens, when children are exposed to a lot of cosmetic and technological products. The more information we have about these allergens, the more it will help us to suspect the diagnosis and to perform correct allergen test. In this study, unlike other studies, it was aimed to draw attention to this issue.

In children diagnosed with AD, allergic contact dermatitis develops more easily due to their susceptibility to skin sensitivity and skin barrier dysfunction. In our study, patch test was positive in 13 AD patients (35.1%) and the most frequently determined allergen was nickel sulphate (n:5[38.4%]). In our study, there was no significant difference between the patients with and without atopic dermatitis in TRUE test positivity. In a study performed in Turkey, 134 children aged 2-206 months with AD were tested with patch test and %33.8 of AD patients had at least 1 positive reaction [20]. In another study from Turkey, between 2014 and 2016, 112 children, aged 1-18 years with AD were tested with patch tests and %17 of AD patients were sensitized with either cosmetic or standard series [21].

## CONCLUSION

The most common allergens are nickel sulphate, Cl<sup>+</sup> Me-isothiazolinone and thimerosal. It is important to evaluate the children with complaints with patch test with large panels

containing common allergens and to evaluate the story in detail about contact with these allergens. Further research is needed to clarify the sensitization in children who have contact dermatitis.

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