Fragrance and Cosmetic Contact Allergy in Children

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Opinion statement

A consensual definition of childhood must be established concerning contact allergy. Little is known about contact allergy to fragrances and cosmetic products in children. Thus, contact allergy is under-recognized. Fragrances are one of the main causes of allergic contact dermatitis. Recently, French cosmetovigilance has shown that cosmetic contact allergy is frequently diagnosed as allergic contact dermatitis but also in some cases as urticaria. Children have to be tested when they suffer from contact urticaria or eczema, whatever their age. The etiological treatment is always to avoid the allergen; some immediate allergic reactions require the patient to own emergency treatment. Actually, there is a lack of knowledge. Each case of contact allergy due to cosmetic products has to be reported to the relevant cosmetovigilance system. Moreover, more studies concerning the relevance of positive patch tests to the applicable markers have to be conducted to improve our knowledge about contact allergy to fragrances and cosmetic products in children.

Introduction

Fragrance is a pleasant smell due to perfumed volatile molecules. Many fragrances have to be labeled because they are known to be allergenic. Fragrances are not specific to cosmetics, as they can also be found in topical drugs, toys, food, or detergents.

The European Union (EU) definition of cosmetic products is “any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips, and

external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odors and/or protecting them or keeping them in good condition.” Cosmetic products must also comply with the annexes and rules for labeling in the relevant EU regulation [1]. Cosmetics are different from drugs that can treat illness and from medical devices that are also used for medical

purposes; for cosmetic products, there is no risk–benefit balance. The youngest children’s cosmetic products are mainly soaps, body cleansing products, wet wipes, creams, shampoos, toothpastes, and perfumes. For example, wet wipes can induce sensitization to a cosmetic ingredient such as methylisothiazolinone [2]. The ingredients in cosmetic products are not specific, as they can also be found in detergents, toys, and industrial products. Some products are “cosmetic like”—they seem to be a cosmetic product as the definition suits them, but they do not fulfill the conditions in the annexes of the regulation. For example, black henna tattoos are supposed to only change the appearance of the skin, but actually they can induce sensitization to paraphenylenediamine, as they do not fulfill the conditions in Annex III of the regulation regarding this ingredient [3].

The definition of “children” is unclear in the EU. A child can be seen as any human under the age of

18 years, unless the age of majority is attained earlier under a state’s own domestic legislation. Regarding contact allergy, it would be better to complete this definition with “unless the age of working is attained earlier under a state’s own domestic legislation.” Because many cases of allergic contact dermatitis are due to work, children have the same allergenic risk that adults have when they start working. The variation between the different definitions of “children,” the variability of patch testing conditions, and the differences in the origin and habits of the patch-tested population make comparison of the different studies difficult. However, contact allergy is underdiagnosed in children because such cases are often seen as atopic only. Actually, even the youngest children may be prone to contact allergy and to react to cosmetics or fragrances, either used for their own skin care or transmitted by adults who are in close contact with them (proxy dermatitis).

Pathogenesis

Allergy is a clinical manifestation of a specific immunological reaction to a substance called an allergen. Usually, there is no reaction after the first contact with the allergen, because the immune system needs time to be sensitized. Contact allergy is provoked by contact between the allergen and the skin. There are two types of contact allergy:

1. *Immediate contact allergy*: A few minutes after contact, the allergen activates mast cells binding specifically to immunoglobulin (Ig)-E, which release histamine and other mediators. They trigger skin vasodilatation, contract bronchial smooth muscles by recruitment, increase leakage of fluid from blood vessels, and cause heart muscle depression. If the patient survives, all of the symptoms disappear quickly.
2. *Delayed-type or allergic contact dermatitis*: The contact between the skin and the allergen activates specific cellular recruitment, which induces delayed inflammation in 48 hours or more.

Epidemiology

Regarding allergic contact dermatitis, sensitization rates from 26.6 % to 96 % have been reported in selected groups of children [4]. There are no specific data on allergic contact dermatitis due to fragrances or cosmetic products. Some studies have reported that fragrances were the second most common allergens identified in children referred for patch testing. The most common allergens were metals, but some patch test reactions to metals can be irritating and induce a false positive result. At school, patch tests exploring the current spectrum of contact allergens show that fragrances are the second most frequent allergen

after metals [5]. The question arises whether allergic contact dermatitis due to fragrances has become more frequent in children in recent years. Fragrance mix allergy doubled in frequency between 1985 and 1997 in children 0–18 years of age referred for contact allergy. Furthermore, children must be tested with their own cosmetic products. Regarding immediate contact allergy, there have been only a few reported cases.

Clinical presentations

Immediate contact allergy can be unrecognized, for it is transient. Some cases of urticaria due to allergy to wheat or to oat extracts contained in cosmetics have been reported. The link between food allergy and the use of peanut or almond oil in cosmetics has also been discussed.

Allergic contact dermatitis causes eczema: erythema, pruritus, and blistered skin at the contact points. After the acute phase, the skin is scaly and takes some weeks to be repaired. Allergic contact dermatitis can worsen/increase atopic dermatitis.

Diagnosis

Immediate contact allergy has to be differentiated from non-immunological contact urticaria. Non-immunological contact urticaria is less serious, and its localization is not necessarily reproducible. In fact, the challenge is to keep in mind that allergic etiology is possible and, thus, testing is helpful. Testing is performed with suspected products and then, if necessary, with the product's ingredients. The product is tested first by an open test, then if negative by a closed open test, and then by prick tests. The test is considered positive if the Lewis triad (erythema, edema, and pruritus) is detected and if other people do not react when they are tested with the same product in the same conditions. Some specific IgE can be sampled in the blood but is not always found, and sometimes Western blot analysis is needed [6, 7].

Allergic contact dermatitis should be suspected when children have persistent eczema, even at an early age. Before the age of 3 years, reactions in children have to be considered atopic unless the localization is typical, such as diaper dermatitis, isolated foot dermatitis, asymmetric perilesional exanthema, or umbilical dermatitis. Atopic dermatitis should also be considered if symptoms in children appear from spring to autumn or in cases of lack of efficacy of a treatment. In children over 3 years of age, allergic contact dermatitis should be suspected for the same reasons. Moreover, the possibility of allergic contact dermatitis has to be taken into account in children with no history of atopy or with recently diagnosed dermatitis. There is no particular clinical characteristic of allergic contact dermatitis due to fragrances or cosmetic products in children other than what is known in adults; it is of huge interest to obtain a detailed anamnesis in order to specify the environment of the child and all his contact regarding fragrances and cosmetic products. However, children themselves may surreptitiously use some cosmetic products, such as their mother's cosmetic products. Therefore, the diagnosis may not always immediately be evoked. Patch testing is performed with either a children's special baseline series [8, 9] or with the adult baseline series. All products identified in the personal history

have to be tested. The main fragrance markers in the baselines series are fragrance mix I 8 % in petrolatum, fragrance mix II 14 % in petrolatum, and *Myroxylon pereirae* 25 % in petrolatum. Colophonium 20 % in petrolatum can also be considered a fragrance marker. Hydroxymethyl-pentyl-cyclohexene-carboxaldehyde is another frequent allergen in children. Patch tests with these allergens are not known to be irritating in children. Proxy allergic contact dermatitis due to fragrance in children has been reported. The relevance of each positive patch test has to be researched and can be found in the cosmetic product information or in other sources. For the same patient, the relevance can be found in different sources.

In a review in 1997, Conti et al. [10] found that 44 % of children's reactions to preservatives, such as formaldehyde releasers, parabens, the methylchloroisothiazolinone Euxyl K400, and the antioxidant butylhydroxyanisole, were atopic. Since 1997, Euxyl K400 has therefore been prohibited in European cosmetic products. Regulation of formaldehyde and formaldehyde releasers has been reinforced, and the public has been informed that parabens are harmful preservatives, so they are rarely used in cosmetic products. The main cosmetic markers in the baseline series are used not only in cosmetic products but also in detergents, food, and industrial products. Therefore, the frequency of contact dermatitis due to cosmetic products cannot be evaluated by the rates of positive patch tests to these allergens without establishing their relevance by reading products labels. Leave-on cosmetic products can be tested by patch tests, and rinse-off cosmetic products have to be tested by open tests. The reading is done on day 2 and on day 3 or 4, according to the International Contact Dermatitis Research Group (ICDRG) guidelines. Positivity to a leave-on cosmetic product has to be confirmed by a repeated open application test, because some irritating reactions can occur behind the patch. When allergic contact dermatitis is due to an identified cosmetic product, the child must be tested with the ingredients to determine the allergen unless it has been identified in the other tests. There are no data on the main cosmetic allergens specifically relevant to children. In adults, the main allergens in cosmetic products are fragrances, preservatives, surfactants, and paraphenylenediamine [11]. Allergy to paraphenylenediamine in children is mainly due to black henna tattoos but can also be due to shoes or to the mothers' hair dyes by proxy contact. In some selected populations of children, propolis 20 % in petrolatum is a frequent allergen, which can be found in biocosmetic products and in folk medicine [12]. Some sunscreens have been found to be allergens in children. Regularly, allergic contact dermatitis in children is due to new allergens in cosmetic products, such as octocrylene [13], glucosides or fructooligosaccharides [14], or chondroitin sulfate [15]. Sometimes, an ancient allergen such as wool alcohol is reactivated because it is used again despite its reputation.

Prognosis

Immediate contact allergy can be severe, but no fatal reactions to fragrance or to cosmetic products have been reported in children. Immediate contact allergy to an edible allergen can be confused with food allergy [16].

Allergic contact dermatitis can be generalized if the contact is not avoided. Persistence throughout life of reactivity acquired during childhood has not been studied. Systemic contact dermatitis from ingestion of an allergen has been reported.

Treatment

Pharmacological management of the acute phase

Immediate contact allergy is treated with antihistamines. In cases of severe reaction, use of some emergency drugs may be necessary, such as corticosteroids, adrenaline, or spray with beta-2 mimetic.

Allergic contact dermatitis is treated with topical corticosteroids.

Other considerations

Allergen avoidance is the only preventative treatment for this disease. The child and his parents have to be trained to read the ingredients on cosmetic labeling and to avoid those containing his allergen. He has to adapt his professional orientation accordingly: for example, a child sensitized to paraphenylenediamine cannot become a hairdresser. In cases of severe immediate reaction to an edible allergen, some dietary advice should be delivered. If appropriate, emergency drugs must be available to the patient at all times in case of accidental allergen uptake.

New trends

As cosmetic product formulations change over time, and as new allergens appear, physicians' knowledge has to be constantly updated. Because of these facts, some confraternal sentinel networks have been created. In 1996, the Groupe d'Etude de Recherche en Dermato-Allergologie (GERDA) decided to create the Réseau de Vigilance en Dermato-Allergologie (REVIDAL-GERDA) [17]. Its aim has been to dispense the right information at the right moment and in the right place for optimal use of the information; the way to do that was centralization and analysis of reported cases. In cases of repeated notifications about a product or an ingredient, immediate information for the entire network and a signal for boosted vigilance are generated (all similar cases will be then reported). Regarding allergic contact dermatitis due to cosmetic products in children, REVIDAL-GERDA discovered reactivity to octocrylene and to glucosides in cosmetic products. The cases of allergic and photoallergic contact dermatitis due to octocrylene were numerous, and firms were forced to stop using this sunscreen in creams for children.

In Europe, the safety of cosmetics has been regulated by the Cosmetic Products Regulation (EC regulation number 1223/2009) since July 2013 [1]. This legislation requires manufacturers to ensure the safety of their cosmetic products in normal use and under reasonably foreseeable conditions. This new European regulation gives the cosmetic industry the responsibility to place only safe cosmetic products on the market and to provide a system for postmarket monitoring. For these reasons, all cases have to be reported to the industry. Firms should avoid the main known allergens in children's cosmetics and may liaise with a confraternal network for their updating.

This legislation also requires national market surveillance authorities to monitor compliance with the regulation. Moreover, the European Council adopted a resolution in 2006 recommending that the Member States implement a system for registering undesirable effects of cosmetic products (cosmetovigilance) as a public health protection directive. Cosmetovigilance has been operational in France since 2004 and has begun in Belgium, Denmark, Germany, Sweden, Norway, and Italy. Cosmetovigilance systems vary regarding the method of registration (legal requirement or voluntary), participants (health professionals or consumers), and agencies responsible for cosmetovigilance registration [18]. In France, this agency is the Agence Nationale de Sécurité des Médicaments (ANSM). All cases of contact allergy to cosmetic products in children must be declared to the cosmetovigilance system in the country where the undesirable effects occur. In 2010, the French cosmetovigilance system showed that undesirable side effects were often contact allergy, including immediate reactions (5 cases) and delayed reactions (57 cases), but that some side effects were not allergic; 15 cases concerning children were registered [19]. As many cases of sensitization to paraphenylenediamine by black henna tattoos had been registered with the French agency by 2007, a media campaign was conducted, which included activities such as interviews (with radio stations and newspapers), articles in women's magazines, and posters sent to all physicians. At the same time, the sale of black henna tattoos was prohibited in France, and the frequency of reported cases decreased dramatically; new cases of sensitization to black henna tattoos have been due to some products being sold in the market for tattooing at home or black henna tattoos made outside France. Cases of contact allergy to fragrances, to preservatives, or to other ingredients have to be declared to the agency in charge of the relevant product.

Conclusion

Little is known about contact allergy to fragrances and cosmetic products in children. All cases must be registered with the relevant cosmetovigilance system for optimal knowledge of the problem. Immediate reactions to cosmetics can occur and must be tested and declared. Patch testing with fragrance allergens is safe and can be done at the same concentration in children as is used in adults. The relevance of positive patch tests must be precisely determined to allow registration of the case. Testing with the child's own cosmetic products may allow new allergens to be identified. Future studies could provide data on the frequency of contact allergy to fragrance mix II and to the components of fragrance mixes I and II, and on the relevance of positive patch tests. Follow-up studies will be useful regarding persistence of sensitization throughout life and regarding quality of life.

Compliance with Ethics Guidelines

Conflict of Interest

Martine Vigan declares that she has no conflict of interest.

Florence Castelain declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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