

Allergic and toxic reaction caused by fragrances – a case report

Reakcja alergiczna i toksyczna wywołana substancjami zapachowymi – opis przypadku

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Post Dermatol Alergol 2010; XXVII, 6: 511–514

Abstract

Adverse reactions after applying cosmetics constitute an increasing clinical problem. Fragrances are the principal allergens of cosmetic products and together with preservatives are among the top 5 most frequent contact allergens. The contemporary diagnostics of contact allergy to fragrances is based on patch tests with fragrance mix. The purpose of the study was to report a case of high contact sensitivity with accompanying toxic reaction to fragrance mix I and II and Lyrall. Patch tests were performed with the Standard European Set of contact allergens. The first reading after 48 h was positive (+++) with fragrance mix I, whereas within the area with Lyrall and fragrance mix II single blisters containing clearly visible light yellow liquid were observed. After 72 h no variation of the test result was recorded.

Key words: Lyrall, fragrances, allergy to cosmetics.

Streszczenie

Występowanie reakcji niepożądanych po zastosowaniu kosmetyków stanowi narastający problem kliniczny. Substancje zapachowe są głównym alergenem preparatów kosmetycznych i obok konserwantów należą do 5 najczęstszych alergenów kontaktowych. Współczesna diagnostyka alergii na substancje zapachowe opiera się na wykonaniu naskórkowych testów płatkowych (NTP) z *perfume mixture*. Celem niniejszej pracy było przedstawienie przypadku wybitnej nadwrażliwości kontaktowej z towarzyszącym odczynem toksycznym w odniesieniu do mieszanki zapachowej I, II oraz Lyrallu. W odczycie NTP po 48 godz. stwierdzono kontaktową reakcję ocenioną na trzy plusy w odniesieniu do mieszanki zapachowej I, natomiast w miejscu założonego testu z Lyralliem oraz mieszanką zapachową II obecne były pojedyncze pęcherze z wyraźnie widocznym poziomem jasnożółtego płynu. Po 72 godz. odczyt testu nie zmienił się i pęcherze nadal były obecne.

Słowa kluczowe: Lyrall, substancje zapachowe, alergia na kosmetyki.

Introduction

Fragrances are the principal allergens of cosmetic products and together with preservatives are among the top 5 most frequent contact allergens [1, 2]. There are approximately 5000 aromatic compounds currently used in the perfume industry and it is estimated that a single perfume may contain from 50 to 300 molecules, which create characteristic scents [3]. Exposure to perfumed molecules is multiple and practically permanent. Fragrance molecules

are found not only in cosmetic products, but also in a wide variety of manufactured products, including household domestic and food products (where they are used as flavours) and even in topical medicaments (where they maintain antiseptic properties) [3, 4]. It is estimated that an average adult uses nine cosmetics daily, while more than 25% of women use 15 or more [5]. Adverse reactions to cosmetics constitute an increasing clinical problem. Although they are observed often, the real frequency is not

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exactly known. Most individuals who experience mild reactions, such as erythema or stinging sensations, simply change to another product. There is agreement about the percentage of 1 to 2 in terms of sensitization to cosmetics in the general population, accounting for 6-14% of all cases of allergic contact dermatitis [1, 6].



Fig. 1. The first reading (after 48 h): FM I (+++), in the area with Lyrall and FM II single blisters containing light yellow liquid are visible

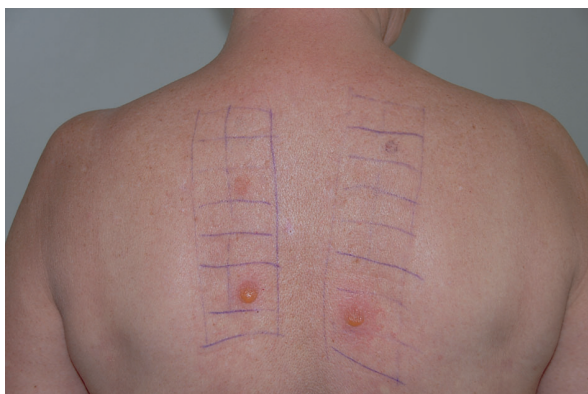


Fig. 2. The second reading (after 72 h): FM I (+++), in the area with Lyrall and FM II single blisters containing light yellow liquid are visible

The contemporary diagnostics of contact allergy to fragrances is based on patch tests with fragrance mix. Fragrance mix I (FM I) is a mixture of eight aromatic substances (one natural compound, oak moss absolute, and other synthetic fragrances) and identifies 70-80% of fragrance allergy cases [6]. According to the recommendations of the European Society of Contact Dermatitis (1 March 2008) the European baseline series was enlarged by adding new substances: fragrance mix II (FM II) and Lyrall (hydroxyisohexyl 3-cyclohexene carboxaldehyde) [7].

Case report

A 66-year-old patient was hospitalized in the Department of Dermatology, University of Medical Sciences in Poznań in order to diagnose and apply treatment of papuloerythematous lesions of the skin in the region of the lower and upper lip. Primary skin lesions (increasing erythema and oedema) and recurrent stinging sensations had been observed already one month earlier. The patient complained of "hypersensitivity" to creams for everyday use and difficulty in proper selection of cosmetics. No coexisting diseases were detected.

During hospitalization in our clinic all performed laboratory tests were within the normal range. The direct examination for *Demodex folliculorum* within the skin of the face was negative. Results of skin prick tests performed with main aeroallergens were negative. Patch tests were performed with the Standard European Set of contact allergens (Chemotechnique, Sweden). The first reading after 48 h was positive (+++) with FM I, whereas in the area with Lyrall and FM II single blisters containing clearly visible light yellow liquid were observed (fig. 1). After 72 h no variation in the test result was recorded (fig. 2). Readings were performed according to ICDRG guidelines.

Discussion

Cosmetics, according to their definition, are generally perceived as safe and well tolerated. In fact, even products labelled as hypoallergenic can cause adverse reactions. Murphy *et al.* described a 25-year-old woman with exacerbation of eczema, which was related to the use of two new skin products promoted as hypoallergenic and preservative free, ideally suited to atopic individuals. A detailed study revealed the presence of two preservatives, methyl dibromoglutaronitrile and formaldehyde [8]. Preservatives are second to fragrances as a cause of allergic contact dermatitis. The other responsible chemicals are phenylenediamine, lanolin, and Balsam of Peru.

The range of undesirable effects related to the use of cosmetics includes contact dermatitis (both allergic and irritant), photosensitivity, phototoxic dermatitis, contact urticaria and pigmentary disturbances. Among adverse reactions to fragrances, the most common clinical manifestation seen by dermatologists is allergic contact der-

matitis [9, 10]. Investigators from Brazil determined the frequency of dermatoses associated with the use of cosmetics. In a group of 176 patients, the main condition triggered by these products was contact dermatitis, observed in 49 cases, and a diagnosis of allergic contact dermatitis was made only in 4 patients. The other dermatoses reported as a side-effect of cosmetic use were seborrhoeic dermatitis aggravated by use of the product, alopecia and dermatitis caused by inappropriate use of cosmetics [11].

Fragrances are usually number 2 after nickel sulfate among patients with positive patch test results [9, 10]. Patch testing with FM I has been widely used as an indicator of fragrance contact allergy since the late 1970s (Larsen 1977) [2, 3, 12]. However, Larsen *et al.* noted that as much as 33% of fragrance sensitivity may be missed if only those eight recommended substances are tested. Based on European multicentre studies, additional markers of fragrance allergy were added to the European baseline patch series: fragrance mix 2 (FM II) and hydroxyisohexyl 3-cyclohexene carboxaldehyde (HMPCC) or Lyrall. Systemic investigation has shown that FM II detects patients sensitive to fragrances missed by FM I [7]. Furthermore, the ability to diagnose fragrance allergy is now increased and can reach 95% [3]. Frosch *et al.* reported positive results with FM II in 2.9% of tested patients with the concentration of 14%, and additionally he found that approximately 1/3 of the patients reacting to FM II were negative to FM I [13].

FM II contains citral, farnesol, coumarin, Lyrall, citronellol and cinnamal at 14.0% in petrolatum. The most common of this set of allergens is Lyrall followed by farnesol [7]. Lyrall is the trade name of a mixture of 4-(4-hydroxy-4-methyl-pentyl)-3-cyclohexene carboxaldehyde (70%) and 3-(4-hydroxy-4-methyl-pentyl)-3-cyclohexene carboxaldehyde (30%), manufactured by International Flavors & Fragrances (IFF, New York, USA) [6]. HMPCC as a synthetic fragrance is commonly used in consumer products and has a characteristic sweet scent [6]. Patch test concentration of Lyrall in FM II is 2.5%, while as an individual ingredient test concentration is 5%. The prevalence of positive reaction to Lyrall in European studies is between 1.5% and 3%, whereas in a USA study it was only 0.4% [1, 14]. This difference is attributed to the presence of Lyrall in higher concentrations in deodorants in the EU compared with the USA. In a Danish study 25 popular perfume products were investigated in terms of the content of fragrance allergens, including HMPCC. The concentration of Lyrall reached a maximum of 0.2%, which is 10-fold higher than the maximum tolerable concentration considered safe by the EU Scientific Committee [15]. According to the International Fragrance Association (IFRA) the recommended maximal concentration in both leave-on and rinse-off products is 1.5% (2003) [14].

The face is a classic area of involvement for contact dermatitis caused by fragrances. However, lesions of the neck as well as armpits and behind the ears should also

arouse suspicion of an allergy to perfumes [3, 10]. Because of the more intense use of scented products by women, men are much less affected. However, in men eczematous eruptions may be provoked by the use of aftershave lotions, appearing within the beard area and adjacent parts of the neck. Although the characteristic age of fragrance allergy is the mid-forties, in adolescents such sensitivity is also diagnosed [2, 4]. A Danish study performed on a group of 1146 12-16 year old children revealed positive reactions to the fragrance mix in 1.6% of girls and 2.1% of boys [16].

In the presented case report we observed allergic (to FM I) and toxic reactions (to FM II and Lyrall) to fragrances. Taking into account available data concerning this issue, no blisters in the area with FM II and Lyrall were detected previously, and no mentions of coexistence of allergic and toxic reactions in the same case report were recorded. We suppose that in the area with FM II the blister formation was provoked by the Lyrall. As mentioned above, in FM II all compounds are in 14% concentration (with Lyrall at 2.5%), while Lyrall, as a separate allergen, is in 5% concentration. With regard to the case presented here, it may be suggested that there is a group of patients who react in a toxic way to standardized concentrations of allergens used in patch tests and that these concentrations may be too high. According to Larsen, the mix was originally formulated in 16% in petrolatum (2% for each hapten). Due to the frequently observed irritant reactions the concentration was decreased in 1984 to 8% (1% for each hapten) [9]. To identify the concentration of Lyrall that is sufficiently low not to cause an allergic reaction in patients with proven sensitization, researchers from Germany conducted repeated open application test (ROAT) in 64 patients. The concentration of Lyrall safe for sensitized people should be in the range of 0.009-0.027% (0.18-0.34%), depending on the product type [17].

To sum up, the current case report was presented due to the frequent occurrence of allergic and toxic contact reaction caused by fragrances observed in recent years. Because of the continuously increasing number of new fragrance molecules (due to developments in the fragrance industry, and changing fashion), there is a need to conduct further investigations on this subject to enlarge the set of tested allergens. It is also worthwhile to study their concentration to select patients with allergic and toxic reactions.

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