Insect Repellents and Contact Sensitization: An Observational Study

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Use of insect repellents is an inexpensive and practical measure for preventing insect bites, through producing a coating that has a smell or flavour that is offensive to insects (1–3). Many compounds, both natural and synthetic, have been used for their repellent activity against arthropods (4–6).

The number of cases of allergic contact dermatitis due to insect repellents reported in the literature is small despite their widespread use and the increasing number of available products (3, 7).

The aim of the present study was to investigate the prevalence of sensitization to insect repellents in the territory of Ferrara, located on reclaimed lagoon areas in the north of Italy, an area characterized by an exceptional presence of mosquitoes.

MATERIALS AND METHODS

A total of 106 consecutive patients, 72 females (67.9%) and 34 males (32.1%), presenting to our dermatological department for various skin complaints, were enrolled for allergological investigation. All the patients gave their written consent. The following data were collected: demographics, occupation and hobbies, specifying whether indoor or outdoor, previous dermatoses, history of atopy, and use of insect repellents, specifying the kind of repellents used.

All patients were patch-tested with the Società Italiana Dermatologia Allergologica Professionale Ambientale (SIDAPA) baseline series (Lofarma S.p.A., Milano, Italy) as well as an additional insect repellent series, containing 10 insect repellents selected among those commercially available according to frequency of use in commonly marketed products: dimethyl phthalate 5% pet, eucalyptus oil 2% pet, lemon oil 2% pet, citronellol 2% pet, pyrethrum 2% pet, dibutyl phthalate 5% pet, diethyl toluamide (DEET) 1% pet, menthol 1% pet, thymol 1% pet, hydroxycitronellal 5% pet. Insect repellent allergens were supplied by F.I.R.M.A. SpA, Florence, Italy. Allergens were applied on Finn Chambers on Scanpor®, SmartPractice, USA. Patch test readings were performed at 48 and 72 h. To avoid misinterpretation, doubtful results were not considered.

The results of the patch tests were recorded in a database and statistically analysed. Binary data were analysed with χ^2 or Fisher's exact test according to conditions. Quantitative data were analysed by means of Student's *t*-test, in the case of normality and homoscedasticity, or, alternatively, by means of Mann-Whitney *U* test. Statistical significance was defined as $p<0.05$.

RESULTS

Eighty-seven patients (82.1%) reported using insect repellents on a regular basis, mainly aerosol and pump sprays. Forty-four patients (41.5%) proved positive to at least one allergen of the SIDAPA baseline series. Concerning the insect repellent series, 8 patients (7.5%) showed 12 positive reactions (**Table I**). Among these 8 sensitized patients, all but one referred a regular use of insect repellents. The risk of having at least one sensitization among the regular users was no different from that of the other subjects (odds ratio (OR) 1.5287, 95% confidence interval (95% CI) 0.1775–13.1675, $p=0.574$, Fisher's exact test). The occurrence of positive reactions was not related to the type of topical repellent used ($p=0.629$, χ^2 test). Regarding the frequency of sensitization, there were no significant differences by sex ($p=0.437$), indoor/outdoor occupation ($p=0.560$), indoor/outdoor hobby ($p=0.445$) and atopic diathesis ($p=0.546$) according to Fisher's exact test. On the other hand, the patients sensitized to repellents were found to be younger than the others ($p=0.010$, Student's *t*-test).

Among the 8 patients with positive reactions to repellents, 7 had at least one positive reaction to common allergens of the SIDAPA baseline series, for a total of 14 concomitant reactions. The risk of being sensitized to common allergens was higher among the subjects sensitized to repellents compared with patients without any sensitization to them (OR 11.5405, 95% CI

Table I. Positive reactions to allergens of the insect repellents series and concomitant sensitizations to allergens of the baseline series

Pat. No.[a]	Insect repellents series	Società Italiana Dermatologia Allergologica Professionale Ambientale (SIDAPA) baseline series
4	Dibutyl phthalate 5%	Nickel sulphate 5%
12	Dibutyl phthalate 5%	Nickel sulphate 5%
16	Eucalyptus oil 2%	Paraphenylenediamine 1%
31	Hydroxycitronellal 5%	Fragrance mix I 8%, fragrance mix II 14%, dibromodicyanobutane 0.3%, Lyral®, MCI/MI 0.01%
49	Hydroxycitronellal 5%, lemon oil 2%, citronellol 2%, pyrethrum 2%, thymol 1%	Fragrance mix I 8%, fragrance mix II 14%, Lyral®
61	Hydroxycitronellal 5%	MCI/MI 0.01%
89	Hydroxycitronellal 5%	Fragrance mix I 8%, fragrance mix II 14%
99	Dimethyl phthalate 5%	

[a]The reported numbers correspond to the consecutive ones attributed to the patients at enrolment; MCI/MI: methylchloroisothiazolinone/methylisothiazolinone.

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1.3649–97.5756, $p = 0.0085$). Out of the 14 positive reactions to allergens of the baseline series, 7 (50%) were fragrances and 5 (35.7%) preservatives commonly present in cosmetics or topical remedies. The risk of sensitization to fragrances contained in the baseline series was significantly higher among the patients sensitized to allergens of the repellent series compared with patients with no sensitization to them (OR 7.75, 95% CI 1.3578–33.5557, $p = 0.035$).

DISCUSSION

The present observational study highlights the wide use of insect repellents in the geographical area of analysis, as more than 80% of the study subjects reported being regular users. Our results indicate that contact sensitization to ingredients commonly contained in insect repellents is not rare (prevalence 7.5%). However, patients sensitized to repellents are frequently sensitized to preservatives and fragrant compounds, namely hydroxycitronellal, thymol, citronellol, lemon oil, and eucalyptus oil, commonly found in cosmetics and natural products other than insect repellents. It is therefore questionable whether, and to what extent, repellents are the actual sources of such sensitization. A wide spectrum of topical cosmetics, body care products and medicaments may account for part of the contact allergies to the allergens contained in the study integrative series. Thus, an integrative insect repellent series seems to be of doubtful diagnostic usefulness. On the other hand, no positive reactions have been found to DEET, the active ingredient most widely used in topical insect repellents. Moreover, in our study population one female subject sensitized to dibutyl phthalate reported that she was not a user of insect repellents. Thus, other sources of contact sensitization apart from repellents must sometimes be searched for.

The high rate of sensitization to natural compounds confirms that, despite their presumed harmlessness, botanical ingredients can cause contact dermatitis (8, 9).

The main limitations of the study were: (*i*) the relatively small number of patients included; (*ii*) picaridin, one of the most used chemical repellents, was not included in the integrative series as it was not available; thus, cases of sensitization to this specific repellent could go unrecognized by the present survey (10); (*iii*) the clinical relevance of positive patch test reactions could not be defined with certainty because of the large number of insect repellents used over the patients' lifetimes.

Despite these limitations, this is the first study to specifically address the frequency of sensitization to insect repellents, and indicates that patients who are sensitized to repellents are frequently also sensitized to other fragrances, thus suggesting their susceptibility to contact sensitization to fragrances in general.

The authors declare no conflicts of interest.

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