

ORIGINAL ARTICLE

THE PREVALENCE OF ALLERGIC CONTACT SENSITIZATION IN A GENERAL POPULATION IN TROMSØ, NORWAY

Lars Kåre Dotterud

Department of Dermatology, University Hospital of Northern Norway, Tromsø, Norway
larskd@start.no

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ABSTRACT

Objectives. This study investigated the prevalence of contact sensitization in a general adult population and the relationship between the history of metal dermatitis and sensitization to metal allergens.

Study design. A cross-sectional population study using patch tests and a questionnaire was conducted among adults in Tromsø, Northern Norway.

Methods. A random sample of 830 participants aged 18–75 years were invited to participate in the patch testing and completed a 1-page self-administered questionnaire.

Of the adults, 531 (64%) were actually TRUE tested (using a standardized, ready-to-apply patch test system) and completed the self-administered questionnaire about ear piercing, metal reactions, skin reactions to different allergens, atopic dermatitis, eczema, cooking equipment and diet.

Results. The study showed that nickel (19.2%; women 31.1% and men 5.0%), fragrance mix (3.4%) and cobalt (1.7%) were the most prevalent allergens causing contact sensitization. For all other allergens, less than 1.1% tested positive. Eighty-four (45.2%) subjects with a positive history of metal dermatitis had negative patch tests.

Conclusions. Contact sensitization was found frequently in this general adult population, especially to nickel and perfumes with a predominance among females. An eczematous reaction caused by cheap earrings seemed to be the best indicator for metal sensitivity.

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Keywords: atopic dermatitis, contact sensitization, contact dermatitis, ear piercing, nickel allergy, perfume allergy

INTRODUCTION

Contact sensitization has become a significant public health problem (1). About 25% of cases with contact dermatitis are caused by sensitization to contact allergens (2). The onset of contact allergy is preceded by skin contact with a specific allergen or a closely related clinical substance (haptens), which elicits a specific immunologic inflammatory response (3).

In many parts of the world, more than 20% of the adult population are suffering from contact allergy (2,4). It is a well-known occupational risk in health care personnel, metal workers, brick layers and hairdressers (2,5). A recent study from Denmark reported an increase in the prevalence of contact sensitization from 15.9% to 18.6% (among 15–41-year-old subjects) between 1990 and 1998 (6). Contact sensitization to nickel, perfume, preservatives and rubber seem to be most common (1,2,6). Still, few population-based studies have been conducted; most studies of contact allergy have been performed in clinical settings.

In this paper, we present patch test and questionnaire results from a general adult population in Tromsø, Northern Norway.

MATERIAL AND METHODS

We conducted a contact allergy study among adults in Tromsø, Northern Norway which was approved by the Ethical Committee of the University of Northern Norway. The study group was selected from the large population-based Tromsø study (7), and 830

randomly selected participants aged 18–75 years were invited to participate in patch testing. Of these, 531 (64%) participated in patch testing and completed a 1-page self-administered questionnaire (8). They were asked about ear piercing, metal reactions (e.g., dermatitis under metal items or jewelry) and number of lobe perforations, and about skin reactions to different allergens (e.g., rubber, perfume and preservatives), atopic dermatitis (AD) and eczema. In addition, details about cooking equipment and diet (e.g., chocolate, cocoa, hazelnuts, soya products, etc.) were collected.

The TRUE test is a ready-to-use, standardized patch test system reported to be a good screening test for allergic contact dermatitis (ACD) in the general population (9). We only applied panel 1, since the study primarily was designed to study nickel allergy. Panel 1 (ALK-Abelló) contains 12 allergens and allergen mixes, among them nickel sulphate (10). The patch tests were applied for 48 hours and read after 72 hours using the following grading scales: Positive test were considered + (diffuse confluent erythema with palpable infiltration), ++ (erythema and infiltration with papules and vesicles) and +++ (strong erythema with papulovesicles or bullae). Irritant reactions were recorded and defined as follicular (pore) pattern or weak macular erythema without infiltration. No skin change was considered a negative test (11).

Lifetime prevalence of AD means the total proportion of adults with past and/or present symptoms of AD. *Self-reported AD* was diagnosed if the answer to the following question was positive: “Have you ever had

AD (childhood eczema)?” That is, a long-lasting itchy rash for more than 4 weeks on one or more of the following regions: face, neck, wrist, ankles, elbow or knee flexures. *Contact dermatitis* was defined as positive answer to: “Have you ever had dermatitis (eczema) which appears on direct contact with certain substances?” That is, irritants (water, soaps, detergents, etc.) and/or allergens (nickel, rubber, perfume, etc.) that often appear on hands but may also appear on other body sites. *Contact sensitization* was defined as a positive reaction to 1 or more of the 12 allergens. *Positive metal sensitivity* was defined as a positive patch test to nickel, cobalt or dichromate, whereas metal dermatitis was defined as an eczematous reaction caused by contact with metal items (12).

We wanted to explore the relationship between a self-reported history of metal dermatitis and metal sensitivity as diagnosed by a TRUE test, and regarded the test result as the “gold standard.” We calculated test characteristics for the various questions on metal dermatitis. *Sensitivity* was the probability of an appositive test (in this case, if the participant answered “yes” to the actual question) if the disease was truly present (testing positive to metal). *Specificity* was the probability of a negative test (the answer “no”) if the disease was absent (testing negative to metal). *Positive predictive value* gave the percentage of allergic subjects among those with a positive answer and *negative predictive value* gave the percentage of non-allergic subjects among those with a negative answer to the actual question (13).

Statistical analyses

For data management and analyses, the statistical software package SAS (SAS institute, NC, USA) and Epi-info were used. The differences between the groups and risk estimates were assessed with the Mantel-Haenszel test.

RESULTS

Selected self-reported characteristics have been given in Table I. We found high life-time prevalence of atopic dermatitis (22.1%), contact dermatitis (46.8%) and skin reactions to metals (35.0%), all being more frequently reported by women than by men. Ear piercing was ten times more common among women than among men.

Table I. Self-reported selected characteristics of the study population (531 adults) in Tromsø, Norway.

	Total n=531 %	Men n=242 %	Women n=289 %
Age in yrs (mean)	43.4	44.4	42.7
Atopic dermatitis	22.1	19.3	24.2
Contact dermatitis	46.8	29.3	59.8
Metal dermatitis	35.0	12.0	54.3
Ear piercing			
Total	50.1	7.9	85.8
18–29 years	56.5	20.6	91.4
30–49 years	56.3	9.2	91.6
≥50 years	34.4	0	69.3

The results from patch testing (Table II) showed that among the 12 allergens, sensitization to nickel was the most prevalent in both men and women (5.0% and 31.1%, respectively; $p<0.01$), followed by the fragrance mix (3.4%) and cobalt (1.7%). Sensitization to all

other substances was infrequently observed (1.1% or less). Interestingly, no sensitization to neomycin, wool alcohols or ethylenediamine dihydrochloride was found.

Irritant reactions were observed frequently for nickel (3.2%), cobalt (1.9%), dichromate (1.9%) and fragrance mix (1.7%).

When we adjusted for age, we found a statistically significant relationship between ear piercing and nickel sensitization in women (OR=4.3; 95% CI 2.3–8.2). In men, the increased risk resulting from ear piercing was not statistically significant (OR=1.8; CI 0.6–5.9).

We wanted to study to what extent having a history of reaction to metals could predict

metal sensitivity (nickel, cobalt or dichromate) as diagnosed by patch testing. Test characteristics have been given in Table III. Metal dermatitis was reported by 35.0% of the participants and metal sensitivity was found in 19.8%, corresponding to high sensitivity (84.1%) and negative predictive values (94.8%), and a low positive predictive value (47.3%). Reporting of reactions to wrist watches, necklaces/bracelets/rings and metal buttons each showed low sensitivity and low predictive values when compared with metal patch test results. The question on reactions to cheap earrings seemed to be the best indicator for metal sensitivity (Table III).

Table II. Frequency of positive patch tests using TRUE test (panel one) in 531 adults in Tromsø by allergen and sex.

Substances	Concentration mg/cm ²	Total (n=531)		Men (n=242)		Women (n=289)		Irritant reaction	
		n	%	n	%	n	%	n	%
Nickel sulphate	0.20	102	19.2	12	5.0	90	31.1	17	3.2
Fragrance mix	0.43	18	3.4	6	2.5	12	4.2	9	1.7
Cobalt dichloride	0.02	9	1.7	3	1.2	6	2.1	10	1.9
Balsam of Peru	0.80	6	1.1	2	0.8	4	1.4	2	0.4
Colophony	0.85	6	1.1	2	0.8	4	1.4	3	0.6
Potassium dichromate	0.023	4	0.8	2	0.8	2	0.7	10	1.9
Epoxy resin	0.050	4	0.8	3	1.2	1	0.3	4	0.8
Quinoline mix	0.19	3	0.6	1	0.4	2	0.7	2	0.4
Caine mix	0.63	2	0.4	1	0.4	1	0.3	0	0
Ethylenediamine dihydrochloride	0.05	0	0	0	0	0	0	3	0.6
Neomycin sulphate	0.23	0	0	0	0	0	0	1	0.2
Wool alcohols	1.00	0	0	0	0	0	0	0	0

Table III. Validation of metal sensitivity in 531 adult in relation to a history of reactivity to metals (PPV=Positive predictive value, NPV=Negative predictive value).

	Sensitivity %	Specificity %	PPV %	NPV %
Cheap earrings	84.4	42.7	58.0	74.5
Necklaces/bracelets/rings	44.4	66.7	55.6	56.1
Wrist watches	70.0	57.3	60.6	67.1
Metal buttons	53.3	80.2	71.6	64.7
History of metal dermatitis	84.1	75.6	47.3	94.8

DISCUSSION

The study showed that nearly 1 in 5 adults had contact sensitization to nickel. Moreover, we found that 1 in 3 women and 1 in 7 men had contact sensitization diagnosed by the TRUE-test. These very high figures are in line with a recent study among adults in Sør-Varanger, Northern Norway (14).

The TRUE-test has become a global standard in assessment of allergic contact dermatitis (1,15). This test has become commercially available and standardized, and consequently, is clinically useful. A recent paper with meta-analytic techniques from the clinical conditions found high agreement with other usual patch tests (15). In our study, 12 allergens (Panel 1) were tested, including the most relevant allergens nickel, cobalt, fragrance mix, balsam of Peru, colophony, epoxy resin and sensitization agents mostly used in medicaments. We decided not to use Panel 2 to lower costs. We did so because the study primarily was designed to investigate nickel allergy and not contact allergy in general. The study participants were a reference group to the study of nickel allergy in a population living in a nickel-polluted area (16,17). Indeed, some highly relevant allergens then were missed. However, the allergens of Panel 1 are estimated to cover over 90% of the most relevant allergens (15,18).

The overall response rate in our study was 64%. This may have led to selection bias. However, the participants in our patch test study were drawn from the large population-based Tromsø study that focused mainly on cardiovascular illnesses. The people were not informed in advance that they might be asked to participate in patch testing. Our figures are also in line with the Sør-Varanger study, which was conducted at the same

time and in the same random manner (14,16). We believe that the investigation is representative of the background population, and thus, selection bias is only a minor problem. Recall bias may have occurred, however, since we used questionnaires and the design of the study left little room for interpretation by the subjects. Some degree of misclassification may also have occurred, which is difficult to avoid in all types of epidemiological studies (13). Thus, episodes of AD and contact dermatitis in early childhood may have been forgotten and even misunderstood by the subjects or by physicians. The clinical manifestations of contact dermatitis share predilections with AD (e.g., appearing on the face, neck, wrists and hands). Confounding this is an additional source of error, which is due to a mixture of effects (i.e., between exposure and disease) and a factor that is associated with exposure and development of contact allergy. The participants may have modified their behaviour (e.g., modifying their contact to irritants and allergens). Thus, the risk of observation bias and confounding factors make studies of environmental influence on the development of contact allergy difficult to interpret.

Nickel sensitivity accounted for nearly two-thirds of the positive tests, which has also been reported in other European studies (4,6) and estimated in a meta-analysis of published TRUE test data (15). Most participants in our study with nickel sensitivity were female. In comparison, the sex difference in Nigeria is small (19), and in Kuwait, a prevalence of nickel sensitivity three times higher in men has been reported (20). This difference seems to be strongly related to ear piercing and the use of nickel alloys, especially among women. Men are more likely to be sensitized by occupational exposure (21).

In 1994, the European Union issued a directive on the release of nickel from metal objects in

cutaneous contact (22), which entered into full force in 2001 in EU countries, including Norway. A recent Danish study of schoolgirls suggested that implementation of the nickel-exposure regulation from the early 1990s protected females from becoming sensitized to nickel (23). This trend has not been seen in adults yet, but a falling rate of sensitization is expected in Europe (18).

The main sources of primary sensitization to fragrance chemicals are cosmetic products, particularly deodorants and fine perfumes. We found that 3.4% of the general adult population was allergic to fragrance mix, a finding also recently reported in an out-patient clinic in Portugal (2) and estimated in a meta-analysis of published TRUE test data (15). In contrast, 2 population-based studies from Germany reported a prevalence of fragrance sensitivity that was three to four times higher (4,24). The target group of the cosmetic industry has been women, but men, and more recently children, are the new and growing consumer groups. It is therefore to be expected that fragrance allergy will be an increasing health problem in these groups (26,27). Few reactions were found to colophony and balsam of Peru. These figures are in line with a previous study from Denmark (1,25), however, lower than reported in out-patient clinic studies (18,28). Moreover, there does not seem to be a concomitant positive patch test to balsam of Peru in fragrance-sensitive patients, which suggests that balsam of Peru is not a reliable marker of fragrance allergy (27).

The incidence of sensitivity to perfumes and colophony depends not only on the intrinsic allergenicity of the compound but also to what extent the population is exposed to the allergen. There are obvious variations in the prevalence of these allergens from country to country, which may reflect differences in exposure and different

levels of allergen concentration used for patch testing (29). Moreover, we found that dichromate, epoxy resin and other sensitizers did not seem to play any important role in Norway, as reported in some studies (1,4) but contrary to a study from Nigeria (19). A Danish study found an overall decrease in dichromate allergy from 3.0% in 1985–1986 to 1.2% in 1997–1998. This reduction may be due to the addition of ferrous sulphate to cement in Denmark since 1981 (18). Furthermore, Zacharia et al. found that leather tanned with dichromate was considered a likely source of sensitization in 24% of the population, cement in 13% and other no relevant source about 57% (30).

Subjects with a history of metal reaction are often told that patch testing is unnecessary. However, many subjects (45.2%) with a positive history of metal dermatitis had negative patch tests. A number of cases of irritant reactions to metals may have been erroneously interpreted as allergic reactions by the subjects. The relative low specificity and low positive predictive value indicate that questionnaire diagnosis of metal dermatitis cannot be used as a screening instrument for the detection of cases with metal allergy in large study populations.

In conclusion, we found frequent contact sensitivity in the general adult population. Nickel, cobalt and perfumes are the dominating allergens eliciting contact sensitivity. Many subjects (45.2%) with a positive history of metal dermatitis had negative patch tests. However, the question on reactions to cheap earrings seemed to be the best indicator for metal sensitivity.

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Lars Kåre Dotterud, MD, Ph.D.
 Nymosvingen 2
 N-2609 Lillehammer
 NORWAY
 Email: larskd@start.no