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Pattern of patch test reactivity among patients with clinical diagnosis of contact dermatitis: a hospital-based study

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BACKGROUND AND OBJECTIVES: Contact allergy is associated with a significant morbidity all over the world. This study was performed to investigate the pattern of sensitization by contact allergens in the local population.
DESIGN AND SETTING: Retrospective study to investigate patch test reactivity among patients with clinical diagnosis of contact dermatitis who were referred to the allergy clinic at the King Khalid University Hospital, Riyadh, between April 2008 and March 2010.
PATIENTS AND METHODS: Of the 196 patients referred to the allergy clinic over the 2-year period, 91 (46.4%) patients reacted to one or more patch test allergens, and these patients were included in this study. The study group included 82 (91.1%) of Saudi nationality and 9 (8.9%) patients of other nationalities. The patch test was performed using the T.R.U.E TEST, containing 24 allergens/allergen mixes.
RESULTS: Of the 91 cases who reacted positively to one or more allergens, 67 (73.6%) were females with a mean age of 37 (8.3 years) and 24 (26.4%) were males with a mean age of 34 (11.6 years). Thirty-three (36.2%) patients reacted to nickel sulfate, 14 (15.3%) to *p*-phenylenediamine, 13 (14.2%) to *p*-tert-butylphenol-formaldehyde resin, 13 (14.2%) to thimerosal, and 9 (9.8%) to colophony. Reactivity against the rest of the allergens was not remarkable. A significantly higher percentage of females reacted to nickel sulfate (84.8% vs 15.2% in males; *P*=.0001), p-tert-butylphenol-formaldehyde resin (92.3% vs 7.7%; *P*=.0001), and thimerosal (76.9% vs 23.1%; *P*=.03).
CONCLUSIONS: Patch test reactivity to nickel sulfate was high. The pattern of contact allergy observed in this study indicates the need for large-scale investigations to identify local allergens responsible for contact allergy and for formulation of policies directed towards avoidance of exposure.

Contact dermatitis (CD) is a common clinical condition affecting the skin. Most commonly it is caused by irritants and only a relatively small proportion is due to allergy. Allergic contact dermatitis (ACD) frequently involves the hands and face.[1] During the acute phase the most common symptom is itching, which may be associated with vesicle and bullae formation. Scaling and lichenification are features of chronic ACD.[2] As opposed to irritant contact dermatitis (ICD), ACD is believed to be an immunological reaction and requires prior allergen sensitization.[3] However, there is evidence indicating that the immune system plays a significant role in the pathogenesis of ICD as well.[4] ICD is thought to be a non-antigen-specific inflammatory process mediated by haptens[5] and associated with release of cytokines and recruitment of dendritic cells.[6,7] Hapten-induced ICD is thought to evolve into ACD by acquisition of antigenic properties by haptens subsequent to their binding and modification of self-proteins.[8] Recently it has been suggested that ICD and ACD are closely associated, and the induction of ICD may be a prerequisite for the development of ACD.[9]

ACD comprises about 6% to 10% of all dermatology clinic visits and is associated with significant morbidity.[10] Allergen sensitization is believed to be dependent on the degree of exposure to the allergen and exhibits

strong individual variation. Genetic predisposition appears to be an important factor, as some individuals are more easily sensitized to common allergens than others.[11] In addition, regional and environmental factors may also influence the exposure patterns and could be responsible for the variations in the patterns of skin reactivity observed in different parts the world.[12,13]

The patch test is a useful tool for the detection and identification of contact allergens, despite the fact that 10% to 15% of normal healthy individuals may react to one or more allergens.[14,15] In patients with ACD, detection of the relevant agent by patch testing is crucial for instituting appropriate prevention and treatment.[16] Avoidance of the relevant allergen/s has recently been shown to be associated with significant improvement in over 85% of patients with ACD.[17] Over 3000 chemicals are known to cause ACD but, fortunately, only a small number of these chemicals are responsible for symptoms in the majority of cases.[18] Thorough knowledge of the common allergens and a comprehensive history of the patient's exposure to possible allergens will be valuable for selecting the test panels for patch testing. This retrospective study examines patch test reactivity to common allergens in patients with clinical suspicion of CD over a period of 2 years.

PATIENTS AND METHODS

A total of 196 patients with the clinical diagnosis of CD were referred to the allergy clinic at KKU Hospital for patch testing between April 2008 and March 2010. Because of the lack of access to the patient records, clinical data could not be collected.

The patch test was performed using T.R.U.E. Test (Thin-layer Rapid Use Epicutaneous Test, Mekos Laboratories AS, Denmark) with a panel of 24 allergens/allergen mixes. The test panel was applied on the upper part of the patient's back on healthy skin free of acne, scars, dermatitis, or any other skin condition that might interfere with the interpretation of the results. Patients were instructed to wear the patch for 48 hours without removing it and to avoid contact with water. Interpretation of the results was performed first after 48 hours and then again 72 to 96 hours after the application. This protocol allowed sufficient time for the allergic reactions to fully develop and for mild irritant reactions to disappear. Patients were instructed to report back to the clinic in case of delayed reactions. The interpretation of the results was performed in accordance with the recommendations of the International Contact Dermatitis Research Group (ICDRG) and the North American Contact Dermatitis Group (NACDG). Statistical analysis of the data was performed using MedCalc software version 11.5.1.0 for comparison of the proportions. $P \leq .05$ was considered statistically significant.

RESULTS

Out of 196 patients suspected to have CD, 91 (46.4%) individuals tested positive to either one or more allergens; these included 24 males with a mean age of 34 (11.6) years and 67 females with a mean age of 37 (8.3) years. These 91 patients included 82 (91.1%) of Saudi nationality and 9 (8.9%) patients of other nationalities. Among the 91 patients, 56 (61.5%) reacted positively to a single allergen. A female preponderance was evident among the patients with CD, with 67 (73.6%) females compared to 24 (26.4%) males showing positive reaction to either one or more allergens in the patch test panel. **Figure 1** shows the pattern of patch test reactivity among the patients with CD. Nickel sulfate was found to be the most frequently reacting allergen, with 33 (36.2%) patients showing reaction to the allergen. A positive reaction was seen with *p*-phenylenediamine in 14 patients (15.3%), with *p*-tert-butylphenol-formaldehyde resin in 13 patients (14.2%), with thimerosal in 13 patients (14.2%), and with colophony in 9 patients (9.8%). Reactivity against the rest of the panel was not remarkable. **Table 1** shows the gender differences among the patients with CD where notable numbers of patients reacted to patch test allergens. The group of 33 patients reacting positively to nickel sulfate had a significantly higher proportion of females (28/33; 84.8%) than males (5/33; 15.2%) ($P=.0001$). Although the difference was not as marked as with nickel sulfate, a significantly higher number of females than males reacted to *p*-tert-butylphenol-formaldehyde resin ($P=.0001$) and thimerosal ($P=.03$).

DISCUSSION

Nickel sulfate was found to be the most frequently (36.2%) reacting patch test allergen in this study. Similar findings were noted in an earlier study performed among adolescents between the ages of 10 to 19 years where 56% of patients reacted to one or more patch test allergens and among them 31% were found to be allergic to nickel.[19] Patch test reactivity between 13% and 17% has also been reported.[20,21] The NACDG has consistently ranked nickel as the most frequently reacting allergen among positive patch test reactions. Because of the presence of nickel in a large variety of products it is very difficult to avoid contact with nickel and this is probably the main reason for the high incidence of nickel allergy.[22] An increase in patch test reactivity to nickel among patients with CD has also been observed: two separate studies, one per-

formed from 1994 to 1996 and the other from 1998 to 2000, reported nickel reactivity in 14.3% and 16.2% of patients, respectively.[23] Collectively, these data indicate that nickel sulfate is not only a common contact sensitizer but that allergy to nickel is gradually increasing, probably due to the increased exposure to nickel.

A significantly higher proportion of females with CD reacted to nickel in the present study. Women have already been reported to be at a higher risk of acquiring allergy to nickel (20.4% vs 5.8% in men).[20] Differences in exposure have been postulated to be the cause for this disparity. Early skin contact with nickel in earrings or pins have been implicated in the increased skin reactivity to nickel among females.[24] Attempts to decrease exposure to nickel in Denmark by legal restriction on earrings with high nickel content have resulted in 64% reduction in nickel allergy among young girls.[25] It has also recently been reported that nickel regulation in Denmark has not only decreased nickel allergy among young females, it has also reduced the occurrence of new cases.[26] Since 2001, the European Parliament and European Council have also imposed restrictions on the use of objects containing nickel that may cause skin sensitization.[27] Nickel allergy appears to be a major public health problem that requires serious consideration and implementation of policies directed towards reducing skin contact with nickel.

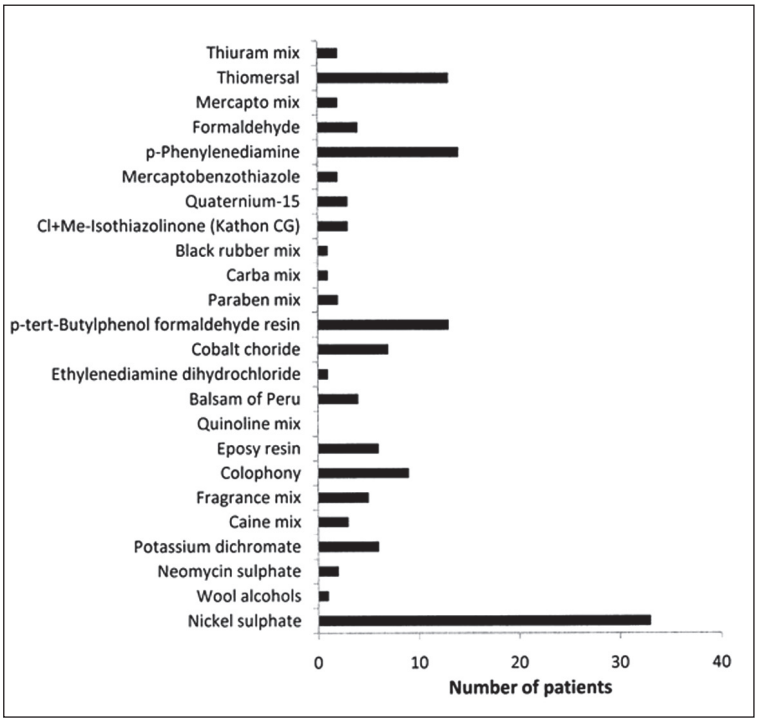

Figure 1. Pattern of allergen patch test reactivity among patients with contact dermatitis (n=91).

Table 1. Gender differences among patients with contact dermatitis in cases where notable patch test allergen reactivity was observed.

Allergen	Number of patients	Number of females (%)	Number of males (%)	*P*
Nickel	33	28 (84.8)	5 (15.2)	.0001
p-Phenylenediamine	14	6 (42.8)	8 (57.2)	Not significant
p-tert-Butylphenol formaldehyde resin	13	12 (92.3)	1 (7.7)	.0001
Thimerosal	13	10 (76.9)	3 (23.1)	0.03
Colophony	09	7 (77.7)	2 (22.3)	Not significant

p-Phenylenediamine (PPD) is commonly used in hair dyes and in Bandrowski base, a trimer that forms quickly upon storage of PPD and is believed to be the main allergen in patients reacting to PPD.[28] A sizeable proportion (15.3%) of patients with CD reacted to PPD in the present study, higher than the proportion (7%) reported in a recent study from Thailand.[29] A significant increase in the skin reactivity to PPD has been observed and this alteration in PPD reactivity has been attributed to the changes in exposure patterns.[30] The use of hair dyes is increasing[31] and, consequently, so is the exposure to PPD, thus accounting for the substantially high prevalence of symptoms such as redness, scaling, itching, or edema following hair dye application.[32] It is therefore imperative to introduce measures to curtail exposure to this sensitizer.

p-tert-Butylphenol-formaldehyde resin is an alkylphenol resin made from p-tert-butylphenol and formaldehyde. It is included in many adhesive formulations. Glues containing *p*-tert-butylphenol-formaldehyde resin are used in leather products such as shoes, watchstraps, handbags, building materials, motorcars, and electrical products.[33] Positive patch test reactions to *p*-tert-butylphenol-formaldehyde resin were detected in 14.2% of the patients with CD in the present study, and reactivity was more frequently seen among females. This appears to be a significantly high percentage when compared to the previous reports that have documented reactivity to *p*-tert-butylphenol-formaldehyde resin of 2.3% in 1984, 1.7% in 1996,[34] and 2.2% in 2000.[35]

Thimerosal patch test reactivity observed in the present study was 14.2%, which was also higher than the recently reported figures of 6.4%[36] in adults and 1.7% in children.[37] Thimerosal has for long been used as a preservative in medical preparations and vaccines.

Its use in vaccines was abandoned in the United States due to public concern.[38]

Although the present study examined a relatively small number of patients with CD, comprised predominantly of Saudi nationality, it does however reveal a pattern of sensitization by contact allergens that this study population was exposed to. High reactivity to nickel has previously been reported from Saudi Arabia in 1995,[39] though the pattern of allergen reactivity was different to what has been found in the present study. Large-scale studies are needed to further investigate the local allergens responsible for CD in Saudi Arabia, which will aid implementation of appropriate measures for avoidance of exposure.

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