

Common Contact Allergens in Patients with Chronic Vesicular Dermatitis of Palms and Soles: A Retrospective Study

Abstract

Background: Chronic and recurrent vesiculation over the palms and soles is termed chronic vesicular dermatitis. Its etiology is multifactorial and contact allergy plays an important role. **Aim:** The aim of the study is to evaluate the clinical relevance of patch test reactivity to common contact allergens in chronic palmoplantar vesicular dermatitis. **Materials and Methods:** An observational study was conducted enrolling 152 patients of chronic palmoplantar vesicular dermatitis. Patch testing was carried out with the Indian Standard Battery and also with the materials used by patients. Statistical analysis was carried out using SPSS software. **Results:** Among 152 patients, 91 were female and 61 male. The peak incidence was in the 14–24 years age group. Their occupations included housewives 48, laborers 26, factory workers 16, farm workers 14, and shopkeepers 12. Patch tests were positive in 79 (52%) patients, including 43 (28.3%) female and 36 (23.7%) male. Patch test reactivity was observed with nickel in 25 (16.4%); potassium dichromate in 21 (13.8%); fragrance mix in 17 (11.2%); *p*-phenylenediamine in 14 (9.2%); black rubber in 10 (6.6%); mercaptobenzothiazole in 8 (5.3%); and parthenium in 8 (5.3%) patients. Clinical relevance of positive patch tests was determined in 47 (59.5%) patients. **Conclusions:** Though patch test reactivity was higher in females as compared with males, the difference was not statistically significant. Clinical relevance of positive patch tests was established with nickel in 9 (19.1%) patients; antigens associated with rubber including black rubber, mercaptobenzothiazole, and thiuram mix in 7 (14.9%); potassium dichromate in 7 (14.9%); *p*-phenylenediamine in 6 (12.8%); and parthenium in 4 (8.5%) patients.

Keywords: Chronic vesicular dermatitis, clinical relevance of patch tests, Indian Standard Battery

Introduction

Chronic vesicular dermatitis (CVD) of the palms and soles is characterized by chronic and recurrent vesiculation on an erythematous base over the palms and soles. The dermatitis is aggravated by daily household activities with exposure to irritants/allergens such as soaps, detergents, cosmetics, and hair dye or by occupational activities with exposure to cement, cutting oils, rubber, and parthenium plant with remission only when the patient abstains from these activities.^[1-3] Apart from having adverse psychosocial impact on the patient, CVD also constitutes a major socioeconomic burden.

CVD of the hands has been considered to be a subtype of hand eczema, and it is known that contact allergy to common antigens such as chromates, nickel, fragrance, *p*-phenylenediamine, parthenium, and rubber plays an

important role.^[3-6] Contact with allergens is largely determined by occupation and socioeconomic status.^[7,8]

Although the terms have not been clearly defined, Storrs has made an important distinction between CVD due to contact allergens with recalcitrant vesiculation and pompholyx with episodic vesiculation on a nonerythematous base.^[9] CVD has a chronic recurrent course without any remission as compared to pompholyx which is characterized by episodes of vesiculation and periods of complete remission.^[10]

Patch test results vary according to the type of test kits/series used and are considered significant only if their relevance has been established clinically. The aim of the study was to evaluate the role of common contact allergens in CVD by patch testing with standard series antigens and also to determine the clinical relevance of positive patch test results.

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Materials and Methods

CVD may be defined by recalcitrant vesiculation on an erythematous base over the palms and soles. A total of 152 consecutive patients with CVD of the palms and soles diagnosed clinically were enrolled in the study after written informed consent from patients or guardians and approval from the Institutional Ethics Committee. Children below 12 years of age, pregnant and lactating women, those with active dermatitis, patients with immunosuppression, or on systemic corticosteroids were excluded from the study. Patients with dermatophytosis or candidiasis (confirmed by 10% KOH mount) were also excluded.

The demographic and clinical details, including occupation, education, monthly income, atopic diathesis, smoking, duration of dermatitis, number of exacerbations in a year, and clinical pattern, were recorded. History of exposure to and recurrence of vesiculation on re-exposure to materials used by patients was also noted.

All enrolled patients underwent patch testing using a set of 20 common antigens out of the Indian Standard Battery recommended by Contact and Occupational Dermatoses Forum of India (CODFI). The aluminum chambers mounted on hypoallergenic tape as well as the antigens were supplied by Systopic Laboratories (P) Ltd., New Delhi, India. In addition, the patients underwent patch testing with their own materials in the “as is” form brought by themselves. The non-hairy part of the upper back was gently cleansed with ethanol, allowed to dry and patches applied for 48 h (D2), and readings were taken 1 h after the removal of patches and also after 96 h (D4). The results were graded according to the International Contact Dermatitis Research Group (ICDRG) criteria.^[11] A false-positive irritant reaction may occur on D2 and hence only morphologically positive patch test reactions (+, ++, or +++) on D4 were considered significant. Sharp-edged margins with fine wrinkling of surface were indicative of an irritant reaction.

Three types of relevance were considered: (i) Possible: based on the history of use of materials known to be associated with the allergen; (ii) Probable: based on positive patch test reactions not only with the allergen but also with materials used by the patient; and (iii) Strong: based on recurrence of vesicular dermatitis on re-exposure to the materials.^[12] Owing to ethical considerations, patients were not re-exposed to their own materials to elicit recurrence of vesicular eczema.

Patch tests with patients' own materials were carried out with hair dyes used by the patients in a concentration of 1% in petrolatum, cosmetic creams and emollients “as is” by the conventional method.^[11] Semi-open patch tests were carried out with materials with irritant properties, including shampoos, liquid cleaning detergents, paints, varnishes, and aqueous cutting fluids by applying a small quantity (~15 µl) with a cotton tipped ear bud on 1 cm² area of skin, allowing it to dry, and covered it with permeable tape. The semi-open

method was also used with pieces of rubber from footwear, latex gloves, and tyres brought by the patients by placing a small piece of rubber on an area of skin and covering it with permeable tape. Readings of semi-open patch tests were taken in the conventional manner on D2 and D4.^[11] Statistical analysis of data was carried out.

Results

Out of 152 patients enrolled, 91 (59.9%) were female and 61 (40.1%) male. Their age ranged from 14 to 81 years (mean 33.21). The highest incidence of CVD was in the 14–24 years age group with 46 (30.3%) patients followed by 44 (28.9%) patients in the 25–34 years, 38 (25%) in the 35–44 years, 15 (9%) in the 45–54 years, 7 (4.6%) in the 55–64 years, and 2 (1.3%) in the 65 years or above age group. On the basis of their educational status, occupation, and monthly income, the majority (97; 63.8%) were from the lower middle-class followed by 27 (17.8%) from the upper lower class, 25 (16.4%) from the lower class, and 3 (1.9%) from the upper-middle socioeconomic class as per Revised Kuppuswamy's scale.^[8] Occupational profile of the patients is illustrated in Table 1.

Forty (26.3%) patients had a personal or family history of atopy; 11 (7.2%) were smokers; 60 (39.5%) felt that hot and humid weather worsened their condition, while 40 (26.3%) considered contact with various substances to be an aggravating factor.

The clinical patterns of CVD included palmar in 99 (65.1%), palmoplantar in 41 (27%), and plantar in 12 (7.9%) patients. The duration of the dermatitis ranged from 1 to 2 years in 85 (55.9%), 2–3 years in 34 (22.4%), and more than 3 years in 33 (21.7%) patients. The number of acute exacerbations in a year ranged from one in 36 (23.7%) patients, two in 65 (42.8%), three in 28 (18.4%), four in 14 (9.2%), and five in 9 (5.9%) patients.

Out of 79 (51.9%) patients with positive patch test reactions to one or more Indian Standard Battery allergens, 43 were female while 36 were male. Only one patient had an irritant reaction. Statistical analysis revealed that higher patch test reactivity in females as compared with males was not significant, as shown in Table 2.

The frequency of patch test reactivity to Indian Standard Battery allergens is illustrated in Table 3. The clinical

Table 1: Occupational profile of the patients (n=152)

| Occupation | Number | Percentage |
|-----------------|--------|------------|
| Housewives | 48 | 31.6 |
| Laborers | 26 | 17.1 |
| Factory workers | 16 | 10.5 |
| Farm workers | 14 | 9.2 |
| Shopkeepers | 12 | 7.9 |
| Others | 36 | 23.7 |
| Total | 152 | 10 |

Table 2: Patch test reactivity to standard series antigens in females as compared with males (n=152)

| Patch test result | Females n (%) | Males n (%) | Total n (%) |
|-------------------|---------------|-------------|-------------|
| Positive | 43 (28.3) | 36 (23.7) | 79 (51.9) |
| Negative | 48 (31.6) | 24 (15.8) | 72 (47.4) |
| Irritant reaction | 0 (0) | 1 (0.7) | 1 (0.7) |
| Total | 91 (59.9) | 61 (40.1) | 152 (100) |
| P-value | 0.146 | | |
| Chi-square | 3.85 | | |

Table 3: Frequency of patch test reactivity to Indian Standard Battery antigens (n=152)

| Allergen | Females | Males | Total (%) |
|---------------------------|---------|-------|-----------|
| Nickel sulphate 5% | 19 | 6 | 25 (16.4) |
| Potassium dichromate 0.1% | 7 | 14 | 21 (13.8) |
| Fragrance mix 8% | 12 | 5 | 17 (11.2) |
| Paraphenylenediamine 1% | 9 | 5 | 14 (9.2) |
| Black rubber 0.6% | 5 | 5 | 10 (6.6) |
| Mercaptobenzothiazole 2% | 4 | 4 | 8 (5.3) |
| Colophony 10% | 4 | 4 | 8 (5.3) |
| Parthenium 15% | 1 | 7 | 8 (5.3) |
| Epoxy resins 1% | 0 | 6 | 6 (3.9) |
| Parabens mix 15% | 3 | 2 | 5 (3.3) |
| Cobalt sulphate 1% | 1 | 4 | 5 (3.3) |
| Formaldehyde 1% | 3 | 1 | 4 (2.6) |
| Thiuram mix 1% | 2 | 1 | 3 (2) |
| Lanolin 30% | 2 | 1 | 3 (2) |
| Balsam of Peru 25% | 3 | 0 | 3 (2) |
| Neomycin 20% | 1 | 1 | 2 (1.3) |
| Benzocaine 5% | 0 | 2 | 2 (1.3) |
| Chlorocresol 1% | 2 | 0 | 2 (1.3) |
| Nitrofurazone 1% | 0 | 0 | 0 (0) |
| | 78 | 68 | 146 |

relevance of positive patch tests was established in 47 (59.5%) patients. Out of these 47 patients, relevance was determined in 26 patients on the basis of patch testing with the patient's own materials as given in Table 4. Clinical relevance was determined in the remaining 21 patients on the basis of history of exposure to and/or vesiculation on contact with materials associated with nickel, cobalt, parthenium, and potassium dichromate. The consolidated details of clinical relevance of patch test reactivity are demonstrated in Table 5.

Discussion

Vesicular eruptions of the palms and soles are considered to be forms of spongiotic dermatoses that have adapted to the morphology of palmar and plantar skin.^[13] Contact allergens play an important role in the etiology of hand eczemas, including chronic vesicular dermatitis.^[9,14] Other factors include a correlation with smoking and a flare on oral challenge with metal salts.^[4,15]

A systematic review of 183 articles indicates that eczema in association with atopy is more prevalent in higher

socioeconomic status groups.^[7] This is in contrast to findings of our study in which the majority of patients (97; 63.8%) belonged to the lower middle-class as per revised Kuppaswamy's scale with educational status up to High School Certificate level, occupational status of skilled or semi-skilled workers, and monthly family income up to 7000 Indian rupees.^[8]

The contact allergens with the highest frequency of patch test reactivity in chronic palmoplantar vesicular dermatitis in our study are common allergens that have previously been implicated in various studies on hand eczema.^[3-5,14] Sensitization by allergens such as *p*-phenylenediamine and parthenium that evoke a positive patch test reaction after an initial negative result may develop as a complication of patch testing.^[11] A positive patch test may have "past relevance" not related to the present dermatitis.^[16] Hence evaluating the clinical relevance of positive patch tests assumes considerable importance. Patch testing with the patient's own materials to which he has been exposed helps in establishing the clinical relevance of positive patch test reactions.^[16]

Out of 79 patients, 23 (31.6%) with positive patch tests to standard series antigens in our study were housewives. Clinical relevance of positive patch tests was established in 47 patients out of which 14 (29.8%) were housewives with clinical relevance to nickel, *p*-phenylenediamine, fragrance mix, parabens, colophony, formaldehyde, balsam of Peru, black rubber, and cobalt.

Patch test reactivity to potassium dichromate in 21 (13.8%) patients in our study is higher than the report of 8% from Rohtak, India but lower than the figure of 20.8% from Poitiers, France in cases of pompholyx.^[17,18] This may be attributed to the fact that Rohtak, India has primarily an agricultural economy. In the present study, clinical relevance of patch test reactivity to potassium dichromate was established in 8 (14.9%) patients, including manual laborers and factory workers.

Patch test reactivity to nickel in 25 (16.4%) patients in the present study is consistent with various studies on hand eczema^[3-6,14] but at variance with and lower than 20.19% reported from Milano, Italy in patients of pompholyx.^[19] Clinical relevance was established in our study in 9 (19.1%) patients, including four shopkeepers who were exposed to nickel due to handling coins. This is consistent with a report from Sheffield, England in which retail clerks in a departmental store developed contact dermatitis to nickel due to handling coins.^[6] Sensitization to nickel may occur not only due to contact with jewelry and metal objects in clothing but also systemically from water, saucepans, or orthopedic implants.^[4,20]

Patch test reactivity to allergens associated with cosmetic products and hair dyes including fragrance mix, *p*-phenylenediamine, colophony, parabens mix, formaldehyde,

Table 4: Results of patch testing with patients' own materials

| Material | Concentration/application | Patch test method | Positive patch test results | | |
|----------------------------|--|-------------------|-----------------------------|------------|-------|
| | | | In males | In females | Total |
| Piece of rubber | Applied directly from footwear/and covered with tyre/gloves permeable tape | Semi-open | 5 | 2 | 7 |
| Cosmetic cream/emollient | "As is" | Conventional | 2 | 5 | 7 |
| Hair dye | 1% in petrolatum | Conventional | 2 | 4 | 6 |
| Paints/varnishes | Applied "as is" with cotton tipped ear bud | Semi-open | 4 | 0 | 4 |
| Shampoos/liquid detergents | As above | Semi-open | 1 | 0 | 1 |
| Aqueous cutting oils | As above | Semi-open | 1 | 0 | 1 |
| Total | | | 15 | 11 | 26 |

Table 5: Relevance of patch tests by occupation with positive patch tests to their own materials (n=47)

| Antigen | Positive patch tests to Indian Standard Battery antigens (n=79) | | | | | | Female (43) | Male (36) | Relevance n (%) |
|-----------------|---|------------------|-------------------------|---------------------|---------------------|----------------|----------------|--------------|--------------------|
| | Housewives (23) | Laborers (16) | Factory-workers (11) | Farm-workers (7) | Shop-keepers (9) | Others (13) | | | |
| Nickel sulphate | 3 | | 1 | | 4 | 1 | 7 | 2 | 9 (19.1) |
| Pot dichromate | | 5 | 2 | | | | 0 | 7 | 7 (14.9) |
| PPD | 2 | | | | 1 | 3 | 4 | 2 | 6 (12.8) |
| Parthenium | | 1 | | 3 | | | 0 | 4 | 4 (8.5) |
| Epoxy resin | | 2 | | | | 2 | 0 | 4 | 4 (8.5) |
| Fragrance mix | 3 | | | | | | 3 | 0 | 3 (6.4) |
| Black rubber | 1 | 1 | | | | 1 | 1 | 2 | 3 (6.4) |
| MBT | | 1 | | 1 | | 1 | 1 | 2 | 3 (6.4) |
| Colophony | 1 | | 1 | | | | 1 | 1 | 2 (4.3) |
| Formaldehyde | 1 | | 1 | | | | 1 | 1 | 2 (4.3) |
| Thiuram mix | | 1 | | | | | 0 | 1 | 1 (2.1) |
| Balsam of Peru | 1 | | | | | | 1 | 0 | 1 (2.1) |
| Parabens mix | 1 | | | | | | 1 | 0 | 1 (2.1) |
| Cobalt | 1 | | | | | | 1 | 0 | 1 (2.1) |
| Relevance n (%) | 14 (29.8) | 11 (23.4) | 5 (10.6) | 4 (10.6) | 5 (10.6) | 8 (17.0) | 21 (44.7) | 26 (55.3) | 47 (100) |

lanolin, and balsam of Peru was observed in 54 (35.5%) patients in our study. Two-thirds (66.7%) of these patients were female. Patch test reactivity to *p*-phenylenediamine in 9.2% of patients in our study is much higher than the report of 5% in cases of pompholyx from Poitiers, France.^[18] This may be attributed to a regulation adopted by the European Commission setting a maximum limit of *p*-phenylenediamine concentration in hair dyes and a mandatory warning on the label. Clinical relevance of positive patch tests to allergens associated with cosmetic products including hair dyes was established in 15 (31.9%) patients in our study on the basis of positive patch tests to products used by the patients.

Patch test reactivity of 3.9% to epoxy resins in patients of vesicular palmoplantar dermatitis in our study is comparable to that of 4.9% in hand eczemas reported from Dharan, Nepal.^[3] Clinical relevance of patch tests reactivity to epoxy resins was established in 4 (8.5%) patients including painters and manual laborers in the present study on the basis of semi-open patch tests with paints and varnishes that were brought by the patients.

The highest patch test reactivity in our study after nickel was observed not only with potassium dichromate but

also with allergens associated with rubber. Patch tests to allergens associated with rubber including black rubber, mercaptobenzothiazole, and thiuram mix were positive in 21 (13.8%) patients. Clinical relevance of positive patch test reactions was established in 7 (14.9%) patients on the basis of positive semi-open patch tests with materials from footwear, rubber gloves, or retreaded types brought by the patients. Our result is consistent with the relevance of 14% in patients of dyshidrotic eczema reported from Marseilles, France.^[21]

In a study of indoor cases of atopic dermatitis, 8 (16%) out of 50 patients developed dyshidrotic eczema within 4–12 days of admission.^[22] Atopic diatheses of 50 and 42.7% in patients of dyshidrotic eczema has been reported from Milano, Italy, and Marseilles, France, respectively, in studies mentioned earlier.^[19,21] In the present study, only 26.3% had an atopic diathesis.

The limitations of our study include: (i) small sample size of patients in each occupational group and the limited number of standard series allergens used for patch testing. (ii) dimethylglyoxime test to detect the presence of nickel in jewelry, metal objects in clothing, and in saucepans

could not be carried out. (iii) re-exposure to materials used by the patients to elicit recurrence of vesiculation was not carried out due to ethical concerns.

To conclude, it is important to differentiate between chronic palmoplantar vesicular dermatitis with recalcitrant vesiculation that does not remit unless the patient abstains from exposure to household/occupational allergens from pompholyx, which is idiopathic and characterized by episodic vesiculation on a nonerythematous base. The most frequent contact allergens with clinical relevance of positive patch tests are nickel, followed by antigens associated with rubber including black rubber, mercaptobenzothiazole, and thiuram mix; potassium dichromate; *p*-phenylenediamine; parthenium; epoxy resin and fragrance mix. An atopic diathesis of 23.6% in the present study is at variance with and lower than that reported in patients with pompholyx. Allergens associated with cosmetic products and hair dyes have emerged as major contact sensitizers in chronic vesicular palmoplantar dermatitis. Patch test reactivity to *p*-phenylenediamine in our study is much higher than that reported in a French study on pompholyx mentioned earlier. Allergens associated with rubber were found to be the most frequent contact allergens after nickel with clinical relevance of patch test reactivity and may play an important role in chronic vesicular palmoplantar dermatitis.

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Conflicts of interest

There are no conflicts of interest.

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