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Patch Testing in Allergic Contact Dermatitis over the Lower Extremities

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Abstract

Background:

There is an increased incidence of allergic contact dermatitis (ACD) over the lower extremities due to over-the-counter topical preparations, occupational risk, and usage of several chemicals in the manufacture of designer footwear.

Aims and Objectives:

The aim of the study was to identify the common allergens and polysensitization pattern involved in ACD over the lower extremities.

Materials and Methods:

It is a cross-sectional study, wherein a total of 80 patients were recruited over a period of 18 months. Demographic and clinical characteristics were noted. Patch test was done with the Indian standard series. Interpretation of patch test readings was read according to the International Contact Dermatitis Research Group criteria at 48 and 96 h.

Results:

There were 45 males and 35 females (M:F= 1.3:1). Mean age was 41.65 years. Most of the patients belonged to 21–40 years age group. Farmers, homemakers, and students were commonly affected. Most common presentation was itching, hyperpigmentation, and scaly plaques over the feet. Patch test was performed in 75% of the patients. One or more positive results were observed in 57% of the patients. Common allergens noted were potassium dichromate (35%), followed by nickel sulfate (23.5%), mercapto mix, and mercaptobenzothiazole. Potassium dichromate and nickel were the common allergens reported in males and females, respectively. Neomycin was the common medication responsible for dermatitis medicamentosa. Polysensitization was seen with mercapto mix, mercaptobenzothiazole, potassium dichromate, and fragrance mix.

Conclusion:

Potassium dichromate and nickel were the common allergens responsible for ACD over the lower extremities. Polysensitization was seen commonly with mercapto mix, mercaptobenzothiazole, and fragrance mix.

Recommendation:

Screening for usage of topical preparations and late patch test readings (96 h or more) is recommended.

KEY WORDS: *Allergic contact dermatitis, lower extremities, nickel, patch test, potassium dichromate*

Introduction

Allergic contact dermatitis (ACD) is a delayed-type of hypersensitivity reaction in response to the exogenous agents. It occurs only in sensitized individuals, and population estimates vary from 1.7% to 6%. [1] Application of various topical medications and usage of several chemicals to manufacture footwear have resulted in increased incidence of ACD over the lower extremities.[2]

The lower leg is particularly prone to contact allergy. ACD from medicaments and dressings predominates, especially in those with varicose eczema and ulcer.[3] The feet have a peculiar anatomical feature, such as the highest concentration of eccrine sweat glands in the plantar region; this leads to increased maceration and enhances the absorption of chemicals, potentially increasing the risk of ACD.[4]

ACD is a very challenging problem in dermatology with considerable morbidity and economic impact. Patch test has been established as a useful tool for the diagnosis of ACD and exact identification of contact allergens.

The main purpose of this study was to identify the common allergens involved and observe the polysensitization pattern among patients with ACD over the lower extremities with the help of patch testing using the Indian standard series (ISS). By identifying the exact cause, we can advice to avoid the allergens and thus reduce morbidity and cost to patient.

Materials and Methods

It is a cross-sectional study conducted from October 2014 to April 2016 over a period of 18 months. A total of 80 patients with suspected ACD over the lower extremities irrespective of age and sex were included in the study. ACD involving sites other than legs and feet were excluded. Pregnancy and lactating patients and patients who used systemic steroids and other immunosuppressives in the past 2 weeks were also excluded. Demographic and clinical characteristics were recorded. Relevant investigations such as potassium hydroxide mount and skin biopsy were done to rule out tinea pedis and plantar psoriasis. The ISS was used for patch testing and interpreted according to the International Contact Dermatitis Research Group (ICDRG) criteria. Allergens were manufactured and obtained from Chemotechnique Diagnostics, Sweden, marketed by Systopic Laboratory, New Delhi. Test with pieces of footwear material was not done because of practical problem.

Patches were applied to the upper back using aluminum patch test chambers mounted on a micropore tape. They were removed after 2 days, and readings were taken on 48 h and 96 h for all patients. The patients were asked to avoid any topical therapy or antihistaminic during the procedure.

Statistical analysis was done using descriptive data, Cramer's V, and Chi-square test with SPSS software 20.0 (IBM Corporation, Chicago, IL, USA). $P < 0.05$ was considered statistically significant. This study was approved by the Institutional Ethics Committee.

Results

A total of 80 cases of ACD over the lower extremities were included in the study. There were 45 (56.2%) males and 35 (43.8%) females. The mean age of the study group was 41.65 years with maximum being 81 year and least being 14 year. Majority of people who had ACD belonged to 21–40 years age group ($P < 0.001$).

Farmers were the most common group affected with ACD over the lower extremities [23 (28.75%) patients] ($P=0.001$). It was followed by homemakers [16 (20%) patients], students [12 (15%) patients], and masons [7 (8.75%) patients]. Disease duration ranged from 15 days to 30 years among which 57.5% ($n=46$) had the disease for <1 year ($P<0.001$).

The most common symptom was itching followed by burning sensation. Majority of patients presented with hyperpigmented scaly plaques, followed by hyperpigmented patches, lichenification, oozing, and crusting. None of the patients had a history of atopy. The most common site affected was the dorsa of the feet (57.5%) ($P<0.001$) and legs (27.5%).

Various topical preparations were used in patients presented with ACD over the lower extremities. Majority of them used combination preparations in the form of steroids and antibiotics (32.5%), followed by unknown topicals (31.3%).

Patch test was performed in 60 (75%) patients. One or more positive results were observed in 34 (57%) patients [Figures 1 and 2]. Thirty showed positive reactions and four showed doubtful reactions at the end of 48 h. However, those cases who had doubtful reactions at 48 h showed positive reaction at the end of 96 h. Maximum positive results were 1+ ($P<0.001$), graded as per the ICDRG criteria [Table 1].

Potassium dichromate was found to be the most common allergen with 12 positive results (35.3%). It was followed by nickel (23.5%), mercapto mix (17.7%), 2 - mercaptobenzothiazole (14.7%), fragrance mix (14.7%) and colophony (11.8%) [Figure 3]. Potassium dichromate ($P=0.02$) was the common allergen noticed in males compared to females. However, nickel was the common allergen noticed in females ($P=0.002$) [Table 2].

Multiple patch test reactions were seen in 13 patients ($P<0.01$) [Table 3]. Polysensitization was seen commonly with mercapto mix, mercaptobenzothiazole, potassium dichromate, and fragrance mix.

Discussion

ACD over the lower extremities is a common condition noticed in our center. It is due to the constant exposure to several ingredients encountered in day-to-day life. The identification and avoidance of the external agents is of paramount importance in the management of ACD. Patch test is considered to be the diagnostic test for the identification of the allergen; however, it is often underutilized.[5]

We found that ACD over the lower extremities is more common among males than in females. The male predominance noticed in our study could be due to the increased risk of exposure to allergens in their working environment. Similar results were documented by Bajaj *et al.*[1] Where 56.6% were male and by another study[6] from Manipal on footwear dermatitis. Men usually wear more occlusive footwear either in the form of shoes or chappals and are involved in more strenuous activity. It leads to increased sweating and possible risk of contact sensitization to footwear chemicals.[6]

Studies in the past on sex prevalence have shown varying results.[7,8] Females were more commonly affected in a study done by Priya *et al.* on foot eczema. It may be due to the usage of variety of footwear and increased exposure to water, soaps, and detergents in Indian women.[7] A study[8] on the pattern of lower leg and foot eczema in south India showed that 61% were female and 39% were male, which was in contrast to our study.

Young adults were commonly affected in our study (21–40 years). This could probably be due to the increased exposure to environmental allergens as the working and earning members belong to this age group. Previous studies also confirmed our findings.[7,9]

Most of the patients who presented with ACD over the lower extremities were farmers followed by homemakers and students. Farmers are more engaged in outdoor activities in fields. They are more prone to skin trauma that leads to skin barrier dysfunction and increased chances of sensitization to environmental allergens causing ACD. The results are consistent with Chougule and Thappa,[8] who observed similar occupation profile. However, few Indian studies noticed homemakers were mostly affected.[2] This may be due to increased exposure to water, household detergents, and cleansing agents

that may result in a higher frequency of penetration of allergens. In our study, patients who had disease duration <1 year (55%) were more among those who underwent patch test. This shows that awareness of the problem and need for early treatment have increased among the community.

The most common clinical presentation was itchy hyperpigmented scaly plaques over the dorsa of the feet. This is similar to studies done on foot eczema in which the most common site involved was the dorsa of the feet, and dry scaly plaques were the common presentation.[\[7,8\]](#)

Topical steroids are available and used in combination with antibiotics and/or antifungals. It is prescribed by pharmacists and general practitioners. Self-medications make patients more prone to dermatitis medicamentosa. The prevalence of ACD to topical medicaments varied from 14% to 40% in the literature. [\[10\]](#)

Spring *et al.* observed that steroids constituted 30% of the common sensitizers.[\[11\]](#) In our study, we noticed 63% ($n=49$) used topical steroids alone or in combination. Majority of patients used steroids with antibiotic combination. However, in our study, suspected corticosteroid allergy was not taken into account because we used ISS, in which corticosteroids were not included.

One or more positive results were observed in 57% of patients. Tufail *et al.*[\[9\]](#) (52%) and Bajaj *et al.*[\[1\]](#) (59%) showed almost similar positive results. Late reactions were not included because most of the patients were from rural areas and majority were farmers and repeated hospital attendance might lead to loss of daily wages.

The most common allergen identified in our study was potassium dichromate (35.3%). This is similar to an Indian study by Bajaj *et al.*[\[1\]](#) In that study, of the 310 patients with suspected footwear dermatitis, 190 showed positivity to one or more allergens, and potassium dichromate (34.2%) was the common allergen reported. Another Indian study by Chowdhuri and Ghosh[\[2\]](#) on footwear dermatitis showed that potassium dichromate (45.8%) was found to be the most common allergen. In India, chrome-free leather is not much in use due to its nonavailability and high cost. Western countries have reported a sharp decline in chromate positivity since the addition of ferrous sulfate to cement, which converts the easily absorbable hexavalent chromium to the less-sensitizing trivalent form.[\[12\]](#)

A study of sex predilection of allergens showed that potassium dichromate was the predominant allergen among male and nickel among female. These results are similar to previous Indian studies.[\[1,13\]](#) This may be attributed to the usage of leather footwear and contact with cement in case of males and usage of variety of footwear in females. Traditional customs, religious practices, and body piercing in Indian women lead to increased usage of jewelry, which is a risk factor for nickel allergy. Nickel is also present in shoe buckles, eyelets, and as ornamental agents in designer footwear.

Nickel was the second most common allergen found in our study (23.5%), followed by rubber allergens. However, few studies have showed that rubber chemicals were the most common allergens.[\[7,14\]](#) Fragrance mix and colophony are the next common allergens reported in our study. Fragrances are an important cause of ACD and are generally recognized as one of the five most common causes of contact sensitization. The prevalence of fragrance ranges from 5% to 14%.[\[15,16\]](#)

In our study, we observed that all the patients who showed a positive reaction to neomycin (4/4) gave a history of prior topical application. In neomycin sensitive patients, positive reactions to gentamycin can occur.[\[17\]](#)

The overall prevalence of multiple contact allergies ranges from 15% in general populations to 28%–37% in hospital patch test populations.[\[18,19,20,21\]](#) Multiple patch test reactions may occur due to nonspecific hyperreactivity, multiple primary hypersensitivities, or cross-reactions. Multiple primary hypersensitivities to substances that are unrelated chemically are frequent among patients with contact dermatitis. Patients with a long history of dermatitis, leg ulcer, and application of topical medicaments are more liable for several primary sensitivities.[\[22\]](#) Cross-sensitization is defined as the phenomenon where sensitization caused by one compound (primary allergen) extends to one or more other compounds (secondary allergens) because of structural resemblance.

There is generally no accepted number of allergens for polysensitization. Few authors consider two or more; however, some consider three or more contact allergies as cutoff point.[18] The lack of uniform definition contributes to the uncertainty regarding patients with multiple contact allergies. In our series, we considered two or more allergen positivity as the cutoff for polysensitization. More than one positive reaction was observed in 13 patients (38%) in our study. Majority of patients ($n=5$) showed sensitization to both mercapto mix and mercaptobenzothiazole. In our study, all the patients who showed a positive reaction to fragrance mix are associated with polysensitization. A study done in Denmark with the European standard series showed that nickel sulfate, fragrance mix, and Balsam of Peru were the three allergens having more association with other allergens.[23]

Our study suffered from certain limitations the most important of which is the absence of footwear material testing which we could not procure because of practical problem. Also the number of subjects were small and not all patients included in the study agreed to undergo patch testing.

Conclusion

Potassium dichromate and nickel were the common allergens responsible for ACD over the lower extremities, and neomycin was the common sensitizer to cause dermatitis medicamentosa. Polysensitization was seen with mercapto mix, mercaptobenzothiazole, and fragrance mix.

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Conflicts of interest There are no conflicts of interest.

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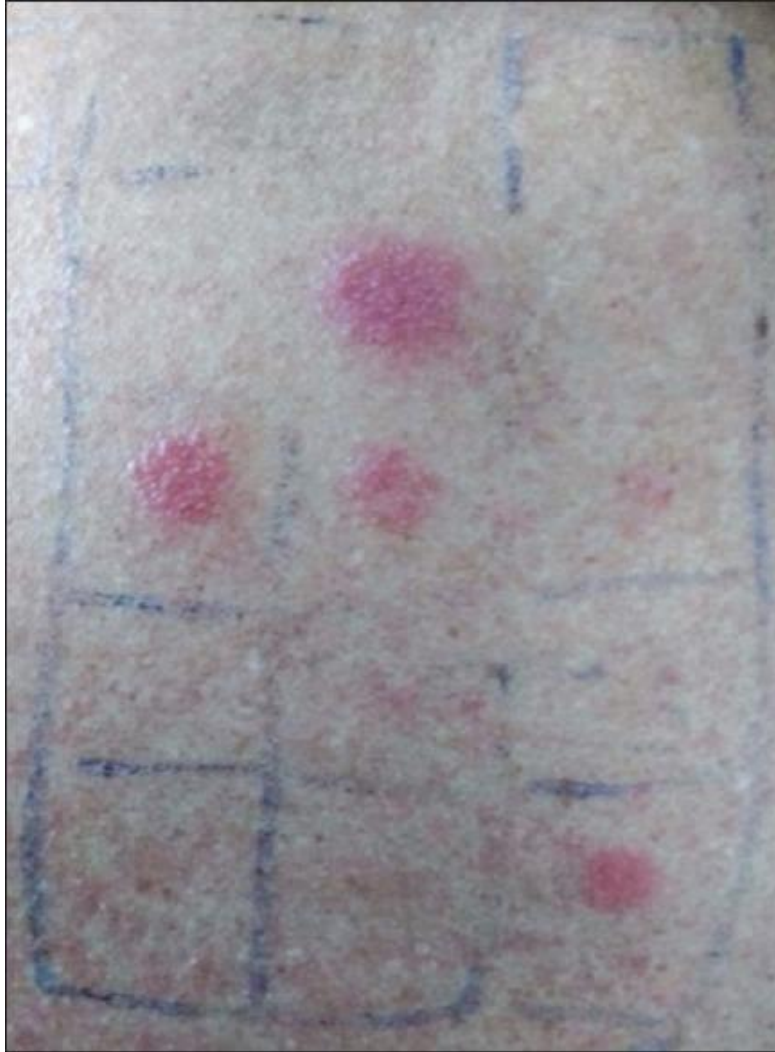
Figures and Tables

Figure 1

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Strong reaction to colophony and weak reaction to cobalt chloride

Figure 2



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Polysensitization

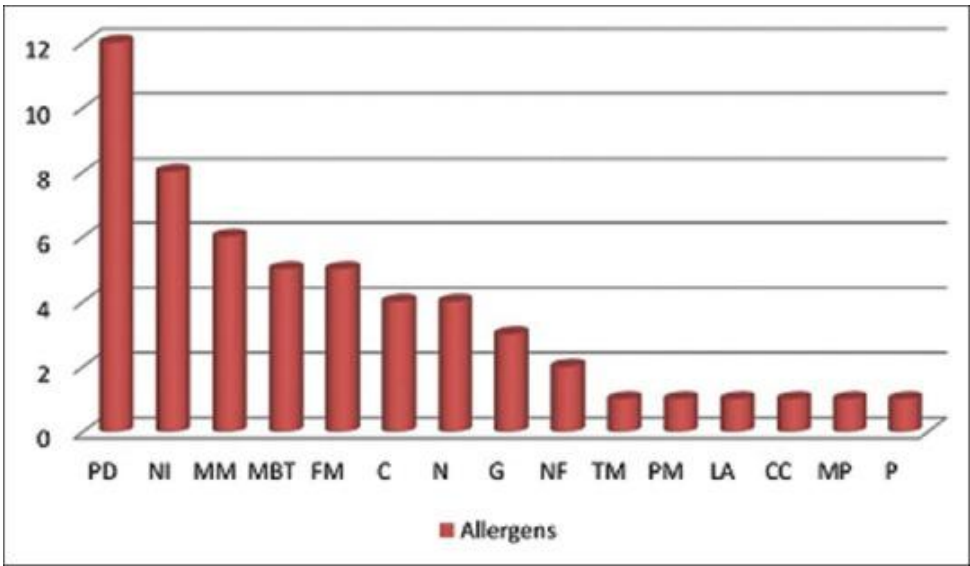
Table 1

Patch test results after 48 and 96 h

ICDRG criteria	48 h reading (Day 3)	96 h reading (Day 5)	Test statistics
-ve	26	26	Cramer’s V Test=0.981, <i>P</i> =0.000
+	18	21	
++	9	10	
+++	3	3	
?	4	0	
Total	60	60	

-ve=Negative, + = Weak reaction, ++ = Strong reaction, +++ = Very strong reaction, ? = Doubtful

Figure 3



Allergens identified in patch test. PD: Potassium dichromate, NI: Nickel, MM: Mercapto mix, MBT: Mercaptobenzothiazole, FM: Fragrance mix, C: Colophony, N: Neomycin, G: Gentamycin, NF: Nitrofurazone, TM: Thiuram mix, PM: Paraben mix, LA: Lanolin alcohol, CC: Cobalt chloride, MP: Myroxylon pereirae, P: Parthenolide

Table 2

Gender-wise distribution of single allergen positivity

Allergen	Male	Female	Total
Potassium dichromate	9 (90%)	1 (10%)	10 (100.0%)
Neomycin	1 (100.0%)	0	1 (100.0%)
Nickel	0	6 (100.0%)	6 (100.0%)
Colophony	1 (50%)	1 (50%)	2 (100.0%)
Mercaptomix	0	1 (100.0%)	1 (100.0%)
Lanolin alcohol	1 (100.0%)	0	1 (100.0%)
Total	12 (57.1%)	9 (42.9%)	21 (100.0%)

Table 3

Gender-wise distribution of polysensitization

Combination of allergens	Males	Females	Total
MM + MBT	2 (40%)	3 (60%)	5 (100.0%)
N + G	1 (100.0%)	0	1 (100.0%)
FM + NF	0	1 (100.0%)	1 (100.0%)
PD + FM	1 (100.0%)	0	1 (100.0%)
N + NI + G	0	1 (100.0%)	1 (100.0%)
N + NF	1 (100.0%)	0	1 (100.0%)
PD + PM + NI + FM	1 (100.0%)	0	1 (100.0%)
C + FM	1 (100.0%)	0	1 (100.0%)
C + FM + TM + P + CC + G + MP	1 (100.0%)	0	1 (100.0%)
Total	8 (62.5%)	5 (37.5%)	13 (100.0%)

MM – Mercaptomix, MBT – Mercaptobenzthiazole, N- Neomycin, G- Gentamycin, PD - Potassium dichromate, FM – Fragrance mix, NI –Nickel, NF – Nitrofurazone, PM – Paraben mix, C- Colophony, TM –Thiuram mix, P – Parthenolide, CC –Cobalt chloride, MP - MyroxylonPereirae

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