



Identification of Allergen Pattern in Allergic Contact Dermatitis in Leg Ulcer Patients: A Saims Experience

KEYWORDS

Allergic Contact Dermatitis, Leg Ulcers, Patch Test

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ABSTRACT *Introduction: Contact allergic dermatitis poses a significant impediment to healing of leg ulcers and local skin care. This study was designed to determine the frequency of contact sensitivity, prevalence of individual allergens, polyvalent sensitization and/or their relationship to ulcer duration in population of chronic leg ulcer patients.*

Material and Method: Forty patients (36 male and 4 females) were patch tested to determine the prevalence of contact hypersensitivity in chronic leg ulcers. Patients were patch tested with a battery of 34 allergens from Indian standard patch test series and medicament series.

Results: Twenty (50%) patients showed positive patch test reactions to one or more allergen. Polyvalent sensitization was found in 14 (35%) patients. Antimicrobial group of allergens ranked highest in causing contact sensitization with 62.3% positive patch test reaction, followed by topical excipient group with 13.2% positive patch test reaction. Frequency of sensitization was found to be high in chronic leg ulcer patients.

Conclusion: Patch test should be used to identify the topical agents that maybe responsible for perpetuation or aggravation of ulcer and surrounding eczema, especially in patients who do not improve despite adequate treatment of other underlying cause

Introduction:

Allergic Contact Dermatitis is a common inflammatory skin disease caused by exogenous substances such as plants, chemical compounds or topical medications [1]. This allergic reaction causes inflammation of the skin manifested by varying degrees of erythema, edema and vesiculation.

Chronic leg ulcers are a common condition affecting 0.12%-1.1% of the population worldwide [2]. It most commonly occurs after a minor injury in association with chronic venous insufficiency (CVI), peripheral arterial occlusive disease (PAOD), combined CVI and PAOD, post-surgical wounds, neurotrophic ulcers and diabetes. There are also many less common causes of leg ulcers such as systemic sclerosis, vasculitis and various skin conditions especially pyoderma gangrenosum.

Frequent use of potential sensitizing topical preparations may lead to rising incidence of sensitization in leg ulcer patients. Local contact allergic dermatitis poses a significant setback to healing of leg ulcers and local skin care. It is suspected that high incidence of sensitization in leg ulcer population is influenced by factors like intrinsic genetic predisposition, use of occlusion and the disrupted skin barrier with an increase permeability and inflammation of the skin upon which the wound care products are applied. Patients with chronic wounds acquire often sensitizations even against otherwise weak allergens[3]. The frequency of positive patch test results found in this patient population has ranged from 40% to 82.5% and sensitivities have involved one or multiple allergens[4-8].

This study was undertaken to identify allergens that commonly cause allergic sensitization in this subset of patients in our region. This will allow patients and treating physicians to avoid products that contain these allergens or related cross reacting substances.

Material and Methods:

This prospective study was conducted during 18 month period from Nov 2011 to April 2013 including forty consecutive patients with chronic leg ulcers of more than 2 months duration, attending the Outpatient department of Dermatology, Sri Aurobindo Medical College and PG Institute, Indore. Patients with acute dermatitis or on oral prednisolone dosage of more than 20 mg/day and receiving any topical or oral immunosuppressive therapy (i.e. cyclosporine, azathioprine, methotrexate, mycophenolate mofetil, or cyclophosphamide) and who had received therapeutic ultraviolet light exposure within last 3 months were excluded from the study.

Patient Evaluation:

A comprehensive questionnaire was filled out for all the patients, which included their demographic details, a detailed history of ulcer duration, healing times, frequencies of ulcer recurrence, past and present ulcer treatment in form of local or oral medicaments, any associated dermatitis, and allergic reactions. A thorough physical examination was performed at the initial evaluation which consisted of the following: general appearance, evaluation of skin disease and presence and severity of any dermatitis, description of lower extremity ulcerations, and evaluation of the distal vascular status. The details about patch testing and methodology were explained to each patient and written informed consent was obtained in each case.

Patch test:

The patch test relies on the principle of type IV hypersensitivity. A total of 34 patch test antigens comprising of Indian standard patch test series purchased from Systopic Laboratory Pvt. Ltd., New Delhi, India and Medicament series purchased from Chemotechnique Diagnostics, Sweden were patch tested by the Finn Chamber method. Approximately 0.2ml of each antigen was carefully pushed out of the syringe

onto the chambers and then Finn Chambers containing the allergen were applied and taped in a standardized order on the upper back of the patients. The patients were instructed not to wet or remove the patches during this period and to avoid excessive physical exertion and sweating. At the end of 48 hours the patches were removed and readings were taken 30 minutes after removal of patches. Patients were instructed to avoid scratching the sites during this period. The patients were re-examined for determination of results after 72 hours. Results were graded as per the International Contact Dermatitis Research Group criteria (ICDRG)[9].

Results:

Clinical & Demographic data:

A total of forty patients with chronic leg ulcers were enrolled in the study, 36 (90%) were male and 4 (10%) were female patient. The mean age at presentation was 48.7 years (16 years to 72 years). The mean duration of leg ulcers was 17.6 months (2 months to 120 months). Most common cause of leg ulcer in study population was found to be venous or arteriovenous etiology in 25 (62.5%) cases, post-surgical ulcers were found in 6(15%) cases, neuropathic ulcers were present in 2 (5%) cases and 7 (17.5%) cases had other causes of leg ulcer. Most common location of chronic ulcer was found to be malleolar region in 60% (n=24) cases, leg in 25% (n=10) and foot in 15% (n=6) cases. The duration of ulcers when the patch tests were carried out was < 2 years in 32 cases, 2 – 5 years in 6 cases and > 5 years in 2 cases.

Patch test results:

The result of our study showed that 50% (n=20) patients had 1 or more allergen sensitizations (Table 5). Thirty five percent (n=14) of patients had more than 1 allergen sensitization, and 15% (n=6) had only 1 positive allergen sensitization (figure 1).

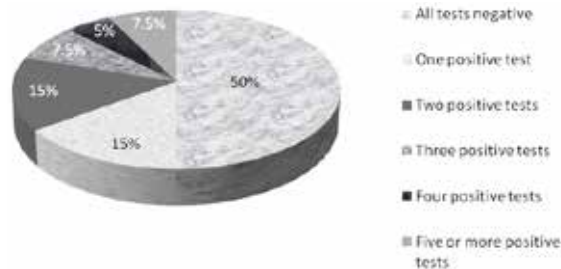


Figure 1: Distribution of Monosensitization and Polysensitization in Patients Tested

Sensitized patients:

Average age of patients with positive patch test results was found to be 49.5 years. The mean number of positive patch tests per patient among the 20 sensitized patients was 2.65 tests per patient. The mean number of positive patch tests per patient in the total population (no allergy and at least one allergy detected) was 1.32. On evaluating the dependence between leg ulcer duration and rate of sensitization, linear increase in positivity was observed in average number of positive results on comparing < 2 years duration with an average of 1.21 positive reactions with > 5 years duration with an average of 2.5 positive reactions.

Involved allergens:

Antimicrobial group of allergens were the most frequent sensitizers with overall sensitivity rate of 62.3%, next group of allergens with maximum positive reactions were the topical excipients and fragrances with 13.2% positivity. Rubber accelerators and topical anesthetics showed a similar rate of sensitization of 3.8%, similarly alloys and preservatives had a very low rate of sensitization of 1.9%. Individually the most frequently positive allergens were Miconazole (20%), chlorocresol (17.5%), framycetin sulphate (15%), sulphaniilamide (10%), nitrofurazone(10%) and econazole (10%) (Table 1).

Table1: The most common allergens in sensitized subjects

Rank	Allergen	Percentage of positive reaction % (n)
1	Miconazole	20% (8)
2	Chlorocresol	17.5% (7)
3	Framycetin sulphate	15% (6)
4	Nitrofurazone	10% (4)
4	Econazole	10% (4)
4	Sulphanilamide	10% (4)
5	Fragrance mix	7.5% (3)
5	Quinine sulphate	7.5% (3)
6	Balsam of peru	5% (2)
6	Colophony	5% (2)
6	Gentamycin sulphate	5% (2)

Discussion:

Chronic leg ulcers usually affect the elderly or middle aged individuals without any predilection for gender. The majority of chronic leg ulcer patients attending specialist hospital and community clinics have positive patch test reactions[10,11]. The risk of developing stasis dermatitis increases with each passing decade owing to the presence of chronic skin disorders like stasis eczema, asteatotic eczema and leg ulcers requiring long term topical therapy that may cause contact sensitivity, and its reported prevalence in adults older than 70 years exceeds 20%[12]. Prolonged standing is another risk factor for developing venous insufficiency/ venous eczema or its chronicity[13].

Allergy to components of topical preparations is common in patients of chronic dermatitis and leg ulcers that often complicates and prolongs the treatment. The reported prevalence of contact sensitivity in these patients is 57.8% - 71.5% [4, 14-16]. In agreement with prior studies, our results showed a high frequency of allergen sensitivity in our population of leg ulcer patients with 50% (n=20) of all the patients being sensitized to one or more allergen.

Prevalence of contact hypersensitivity in our patients with chronic leg ulcers (50%) is in accordance with results of previous studies[17-22]. A recent Serbian series of 75 patients with chronic leg ulcers, found 73% subjects with atleast one positive patch test[23]. In an Indian study conducted by Jindal et al[18] on 34 patients, the rate of sensitization was found to be 50% in chronic venous eczema patients which is almost similar to our findings in Indian population. Similarly in an Asian study conducted by Lim et al[21] reported an overall rate of contact sensitization of 61.4% in patients with chronic venous leg ulcers. Population based studies in Denmark [24], Israel [25] and Norway [26] detected hypersensitivity to at least one allergen in 44%, 19% and 26% of their sample population, respectively.

The rate of sensitivity to more than two allergens (polyvalent sensitization) in our patients (35%) is less in comparison to data from North America(52%), Poland(56%), Croatia(48%) and Serbia(53%)[23,27-29]. The most common allergens (>10%) sensitized subjects in our leg ulcer patients were miconazole (20%), chlorocresol (17.5%), framycetin sulphate (15%), nitrofurazone (10%), econazole (10%) and sulphaniilamide (10%). These numbers reflect local management practices for chronic leg ulcers, particularly the use of topical antimicrobials.

The longer the duration of the ulcer is, the more frequent is the contact sensitization[29]. There is a link between the number of sensitizations per patient and the duration of the

ulcer, suggesting that topical drugs and dressings used for chronic leg ulcers are responsible in inducing the sensitization. We confirm that sensitization is frequent in patients with chronic leg ulcers as 2.65 tests per patient were positive among the 20 sensitized patients. The North American study[27] and Serbian[23] study could not confirm this association, but a number of European studies showed a statistically significant correlation between leg ulcer duration and contact sensitization[6,29].

In conclusion, contact sensitization to active drugs or to their constituents is a continuously operating factor and is one of the factors responsible for the chronicity and deterioration in chronic leg ulcer patients. In patients with chronic leg ulcer need to be patch tested as they have a very high risk of contact allergy.

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