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Original Contribution

CONTACT DERMATITIS IN PATIENTS WITH CHRONIC VENOUS INSUFFICIENCY

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ABSTRACT

Leg ulcers are major clinical features of chronic venous insufficiency (CVI) morbidity, increasing rapidly with age. A key factor in therapy is the promotion of wound healing. Allergic contact hypersensitivity to topical treatments which are used in leg ulcers is common.

In the current study we determined the clinical type of contact dermatitis (allergic or irritant) and the most common allergens which are responsible for the occurrence of allergic contact dermatitis among patients with chronic venous insufficiency state III. We used epicutaneously (Patch) testing technique with Standard European series on 10 patients with chronic venous insufficiency. It was found that 7 patients were with irritating or positive allergic reaction and 3 patients without reaction inside of the Patch tested 10 patients.

In conclusion our results established high frequency of allergic reactions to parabens, topical antibiotics, adhesives inside of the study group patients. We observed poly-sensitization – more than one positive allergic reaction on 4 patients.

Proper therapy procedures for manifesting contact dermatitis and exclusions of potential contact allergens from local treatment would help for two directions: reduce the cases of contact dermatitis of surrounding skin and fast healing of leg ulcers and stasis dermatitis.

Key words: chronic venous insufficiency, leg ulcers, allergic contact dermatitis, irritant contact dermatitis, parabens, nickel

INTRODUCTION

Chronic venous insufficiency (CVI) is a common debilitating disorder which represents as a result of superficial and/or deep origin chronic venous disease and characterized by the retrograde flow of blood in the lower extremity, with its prevalence increasing in age and affects about 15-20% of the total population in Western countries. Although varicose veins are more likely to develop in women due to pregnancy and men more commonly have venous ulcers.

Venous ulcers are usually long-lasting (chronic) wounds and may persist for years or even decades. Those cases require a great deal of work on doctors' side and patients have to consume days, even weeks in hospital (1).

A key factor in therapy is the promotion of wound healing. New types of wound dressings, topical and systemic therapeutic agents, compression, surgical modalities, bioengineered tissue, matrix materials and growth factors are all novel therapeutic options and they might be presented as "golden standard" of venous ulcers treatment (2).

Contact sensibility to topical treatments which are used in leg ulcers is common and should be suspected in patients showing resistant to therapy. The incidence of secondary allergic contact dermatitis is very high in this population.

The most common positive allergens from Standard European Series among patients with CVI are Balsam of Peru, lanolin, fragrance mix, colophony, neomycin sulfate, benzocaine and parabens according to published data (3-5).

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The rate of sensibility to parabens on patients with chronic leg ulcers is higher than the general population. Machet and all reported that from 3043 patients with leg ulcers, 8,5% of them had contact sensitivity to any allergen and 5,7% of them were sensible to the paraben mixture (6). Parabens are class of chemicals, widely used as preservatives by cosmetic and pharmaceutical industries due to their bactericidal and fungicidal properties. Allergic contact dermatitis is most commonly reported with the paraben-containing topical products, even when preparations with low paraben concentrations of 0,1 to 0,3%, are applied on damaged skin (7-10).

The aim of our study is to determine the type of contact dermatitis and the most common allergens from Standard European Series which are responsible for the occurrence of contact dermatitis among patients with chronic venous insufficiency.

MATERIALS AND METHODS

We performed epicutaneous (Patch) test with Standard European series on patients with chronic venous insufficiency.

Patch testing is a method for in vivo visualization of a type IV allergic reaction and is intended to reproduce "in miniature" eczematous reaction by applying an allergen on intact skin of the patients who are suspected to have a certain allergen sensitivity. The technique was first created by Jadasson and Bloch in 1895. Now it is the standard of diagnosing allergic contact dermatitis (11).

The Standard European set contains 28 most common allergens in given concentration fixed in Vehiculum (Vaselinum album or Aqua destillata). **(Table 1)**

Table 1. *Standard European set*

No.	Allergen	Conc.(%)	Vehiculum
1	Kalium bichromas	0.5	Vaselinum album
2	4- phenylendiamininum	1.0	Vaselinum album
3	Thiuram mix	1.0	Vaselinum album
4	Neomycinum sulfas	20.0	Vaselinum album
5	Cobaltum (II) chloridum	1.0	Vaselinum album
6	Benzocainum	5.0	Vaselinum album
7	Nickelum (II) sulfas	5.0	Vaselinum album
8	Clioquinol (Vioform)	5.0	Vaselinum album
9	Colophonium	20.0	Vaselinum album
10	Paraben mix	16.0	Vaselinum album
11	N-isopropyl-N-phenyl-4-phenylendiaminum	0.1	Vaselinum album
12	Lanolin alcohol	30.0	Vaselinum album
13	Mercapto mix	2.0	Vaselinum album
14	Epoxy resin	1.0	Vaselinum album
15	Balsamun peruvianum	25.0	Vaselinum album
16	4-tert-Butylphenol formaldehydum	1.0	Vaselinum album
17	2-Mercaptobenzothiazolum (MBT)	2.0	Vaselinum album
18	Formaldehydum	1.0	Aqua destillata
19	Parfum mix	8.0	Vaselinum album
20	Sesquiterpenum mix	0.1	Vaselinum album
21	Quaternium 15	1.0	Vaselinum album
22	Primin	0.01	Vaselinum album
23	Kathon CG (Cl+Me-isothiazolinonum)	0.01	Aqua destillata
24	Budesonidum	0.1	Vaselinum album
25	Tixocortol-21-pivalatum	0.1	Vaselinum album
26	Methyldibromoglutaronitrilum	0.5	Vaselinum album
27	Fragrance mix II	14,0	Vaselinum album
28	Lyral	5,0	Vaselinum album

The allergens of the standard sets or additional target sets, in volume of 20µl, are placed in aluminum chambers and applied with hypo allergic tape onto pre-cleaned skin. The tests are fixed on the patient's back, places with biggest occlusion from lateral to the spine. All the patients should be educated that the tested area has to be kept dry.

The results can be read on the 2nd and 3rd day (at the 48th and 72nd hour) by the Wilkinson et all scale The scale is interpreted as so: **Table 2.**

Table 2. *Interpretation of Wilkinson et all scale*

(-)	Negative
(?+)	Doubtful reaction (slightly infiltrated erythema)
(+)	Weak positive reaction (slightly infiltrated erythema)
(++)	Strong positive reaction (erythema, edema or vesicular reaction)
(+++)	Extreme positive reaction (vesicular or ulcerative reaction)
IR	Irritant reaction (discrete erythema, no infiltration)

The results that can be read false positive and false negative should be taken into account.

The study was conducted in 10 patients with chronic venous insufficiency with/or without leg ulcer who were clinical examined and treated at the University Clinic of Dermatology and Venereology Diseases, Stara Zagora in a year of period. The diagnosis Contact Dermatitis was based on detailed professional and habitual anamnesis, clinical features, localization of the rash and positive Patch Test results.

Clinical data were present in **Table 3** as follows:

Table 3. *Clinical date*

- 10 patients with chronic venous insufficiency - CEAP classes C4-C6
- Average duration of CVI –7,2 years
- Open venous ulcers on 5 patients during the study
- History and clinical manifestations of irritant and/or allergic contact leg dermatitis repeating more than twice a year
- No evidence of atopic dermatitis
- Middle-age of patients -over 55 years
- Predominance of female (6:4)

Exclusion criteria of participations in study were administration of systemic corticosteroids and/or antihistamines, topical steroid therapy, active exposure to sunlight for at least four weeks prior to the test and the lack of acute autoimmune or neoplastic diseases.

An important exclusion criteria was the absence of acute eczematous reaction during the testing procedure.

RESULTS

In epicutaneously tested 10 patients, we had 7 patients with irritant and/or positive allergic reaction and 3 patients with no reaction.

We recorded 2 irritant and 11 positive allergic reactions with prevalence of paraben mix (30%) and balsam of Peru (30%), followed by colophony (20%) and neomycin sulfas (20%) **(Figure 1)**.

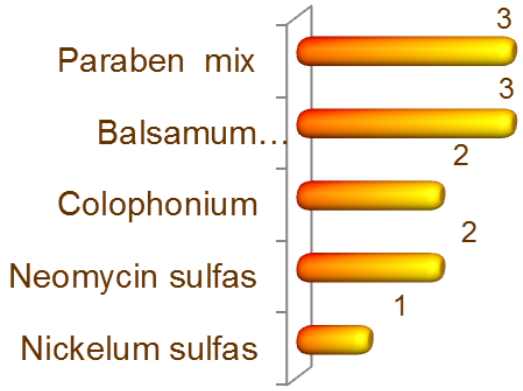

Figure 1. Positive allergic reactions

In 4 patients we had poly-sensitization with more than one positive allergic reaction. **(Figure 2)**

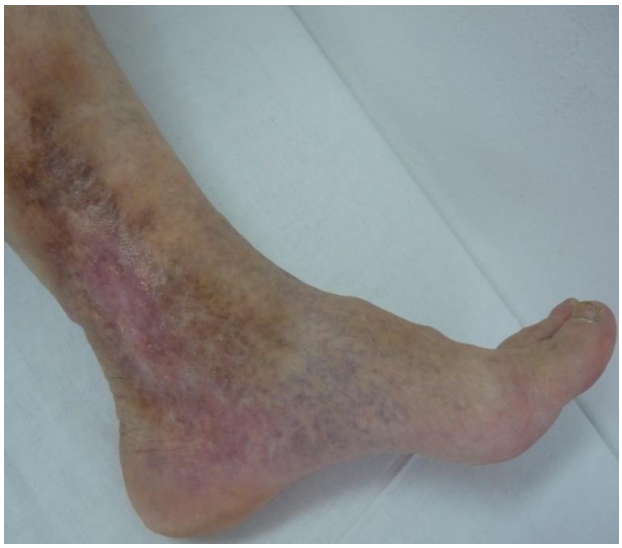

Figure 2 a. 57 years old woman with 7 years duration of CVI

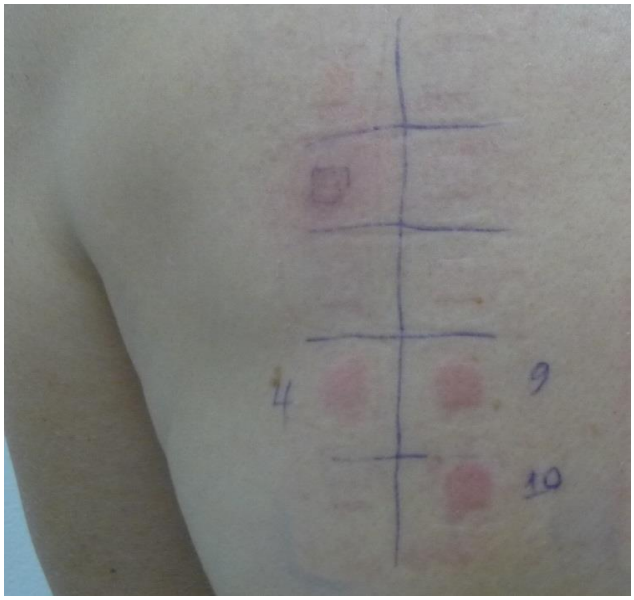

Figure 2 b. Positive allergic reactions to neomycin sulfas, colophony and paraben mix and irritant reactions to 4-phenylendiamin.

Balsam of Peru is a sticky aromatic liquid that is used as fragrance in perfumes and toiletries, flavoring in food and drink, healing properties in medical products. Colophony is sticky substance that comes from pine and spruce trees. It is used in wide range of products as adhesives (sticking plasters) and cosmetic medicine products [12]. Neomycin is an aminoglycoside antibiotic found in many topical medications such as creams, ointments, and eye drops. Paraben is a mixture of 5 different paraben esters which are the most commonly used as preservatives in topical pharmaceutical preparations (13).

CONCLUSIONS

The results in our study confirm a high rate of contact (poly) sensitization in patients with chronic venous insufficiency due to impaired barrier function of the skin and frequent reapplication of topical products. We established high frequency of allergic reactions to parabens, topical antibiotics, adhesives inside of the study group patients. In general population allergic reactions to nickel are higher when it is compared with the study group. The results are similar to previous our reports (14).

For patients with (CVI) in our study group, it is well to keep in mind the term of "paraben paradox", that first described by Fisher in 1973. Paraben sensitive people react to paraben mix when paraben containing products are applied on damaged skin surface, but there is no reaction when paraben containing products are applied on the other areas of body that have intact skin barrier (15).

We did not find any relationship between the duration, severity of CVI (classesC4-C6) and expression of positive allergic reaction. Some cases need additional allergy tests with corticosteroids, antibiotics and vehicles to find relation between the possibly contact allergens in the treatment of CVI and appearance of the contact dermatitis.

Allergic contact hypersensitivity is common in patients with CVI and highly relevant for dermatologist, since it is the pathogenic basis for allergic contact dermatitis, a frequent inflammatory dermatoses. Once allergens are positively identified the patients should be given written information on all of these chemicals (16). Proper therapy procedures and exclusion of potential contact allergens from local treatment have an important role for the treatment of patients. They can help for two directions: reduce the cases of contact dermatitis of surrounding skin and fast healing of leg ulcers and stasis dermatitis. We recommend patch testing for all patients with CVI, especially on the patients showing treatment resistance.

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