THE ROLE OF TOPICAL MEDICATIONS IN THE MANAGEMENT OF STASIS ULCERS

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Topical medications applied to stasis ulcers must be used with some circumspection. Personal experience, and a review of the European and American literature, indicates a general agreement that topical therapy for stasis ulcers produces far more instances of sensitization than from any other condition.

Thus, Laubstein[1], a German investigator, calls attention to the frequent drug-induced sensitization in the course of topical treatment of stasis ulcers. In his series, out of 100 patients examined, 51 exhibited a sensitization to one of several topical agents and the incidence of sensitization increased with the duration of the therapy.

Hjorth and Trolle-Lassen,[2] from Scandinavia, report that most allergic reactions to ointment bases, including lanolin, occur following sensitization at the site of leg ulcers.

Wilkinson[3] in a British text, states that the use of paste bandages by reducing the number of local applications and the prevention of self-treatment reduces the chances of sensitization reactions. However, this author warns that sensitization to elastic adherent bandages and to "parabens" (preservatives) in paste bandages can occur.

Schorr,[4] in this country, confirms Wilkinson's findings stating that the risks of paraben-sensitivity is greatest in stasis ulcers and further states that other common sensitizers in stasis ulcers are neomycin, lanolin and the "caine" group of local anesthetics.

As far as paraben-sensitivity is concerned, there are numberous reports both in this country and abroad that these popular preservatives, present in a great many topical medications and in paste bandages used in the treatment of stasis ulcers, are frequent causes of allergic contact sensitizations.[5-11]

Bielicky and Novak[12] from Prague, reported that in all eleven cases of allergic hypersensitivity to gentian violet, the primary disease was an ulcer or eczema of the leg. Epstein,[13] in this country, has also reported allergic hypersensitivity to gentian violet. It should be noted that a triphenylmethane dye, alphazurin, related to gentian violet, has produced anaphylactic reactions when used during lymphography.[14] These authors also noted frequent sensitization to neomycin and the constituents of ointment bases used on stasis ulcers.

Salo et al.,[15] Scandinavian investigators, state that sensitivity to dequalinium chloride (a quaternary ammonium antibacterial compound) was more frequent

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among patients with leg ulcers and/or varicose eczema than in other dermatologic conditions.

Ethylenediamine hydrochloride, a stabilizing preservative in Mycolog cream, has produced numerous instances of allergic sensitization when this medicament has been applied to stasis ulcers and eczemas.[16, 17]

Schorr[18] reports three patients who acquired an allergic contact dermatitis from the application of Gelocast "Unna Boots" to stasis ulcers. The actual sensitizer in the boot was dichlorophene (G-4), a preservative present in the boot.

Complications of the Use of Sensitizing Topical Medications. Not only does an allergic contact dermatitis occur around the stasis ulcer, but widespread "auto allergy" dermatitis requiring hospitalization may occur in the sensitized individual.[19]

Furthermore, sensitization to certain topical medications may cause the patient to suffer a "systemically" produced dermatitis should the sensitizing medication or an immunologically related drug be ingested or injected. Thus, once sensitization to neomycin occurs, the systemic administration of either streptomycin or kanamycin, both of which may cross-react with neomycin, may produce a widespread eczematous dermatitis medicamentosa.[20]

In addition, although neomycin and bacitracin are not chemically related, in many instances there is a combined sensitivity to these two drugs. Such occurrences represent coincidental simultaneous sensitization rather than true cross-sensitivity.[21]

Senitization to ethylenediamine brings with it the hazard that the administration of aminophylline (which consists of ethylenediamine and theophylline) will produce a widespread dermatitis. In addition, ethylenediamine is the parent substance of the antihistamines, antistine, phenergan and pyribenzamine. The administration of these antihistamines to an ethylenediamine-sensitive patient may produce a generalized contact-type dermatitis medicamentosa.[22]

Benzocaine, also known as anesthesin and ethylaminobenzoate, is such a notorious sensitizer that it should never be applied to stasis ulcers. Sensitization to benzocaine brings with it the hazard of cross-reactions to procaine (Novocaine) and other local anesthetics which are based on paraaminobenzoic acid (PABA).[23] Benzocaine may also cross-react with sunscreens based on PABA and with the hair dye paraphenylenediamine. In addition, the following drugs which may be ingested or injected which cross-react with benzocaine may produce a "systemic" dermatitis: azo dyes in foods and drugs, Dymelor, Orinase, Diabinese, Sulfonamides, Diuril, Hydrodiuril, Saluron, Renese, and Para-aminosalicylic acid (PAS).

Furacin. Furacin is a brand of nitrofurazone (5-nitro-2-furaldehyde semicarbazone). In spite of the fact that it not infrequently causes a severe allergic contact dermatitis, it remains a favorite topical medication among surgeons for use on burns and cutaneous ulcers. Furacin soluble dressing is doubly hazardous since it is composed of Furacin 0.2 per cent in water-soluble ointment-like base of polyethylene glycols in which base Furacin is particularly troublesome as a sensitizer. It is felt in some quarters that Furacin is such a potent sensitizer that it should not be used on the skin (or at least not on diseased skin) because of its high sensitizing properties particularly on stasis ulcers.[24]

The Use of Patch Tests in the Management of Stasis Ulcers. Patients who have suffered one or more attacks of allergic contact dermatitis super-imposed upon stasis ulcer, should have patch tests performed with previously applied medications and with the following chemicals in order to avoid recurrences and widespread disabling dermatitis.

The "Parabens". The methyl-, ethyl-, propyl-, and butyl-esters of p-hydroxybenzoic acid are the most frequently occurring preservatives in topical medications. A positive reaction to the "parabens" contraindicates the use of all corticosteroid *creams* except Hytone (Dermik) and Valisone (Schering). The following corticosteroid ointments contain the parabens: Aristocort, Cortril and Medrol. Many antibacterial preparations contain the parabens except Ilotycin, Terracortril, Polysporin, and Neosporin. Dome-Paste bandage contains the parabens. Medico Paste bandage (Graham Field) also contains this preservative.

Dichlorophene (G-4). This chlorinated phenol is used in Gelocast "Unna Boot" (Duke). A positive reaction to G-4 contraindicates the use of this paste bandage.

Hexachlorophene (G-11). This chlorinated phenol is closely related to dichlorophene with which it may cross-react. Allergic reaction to this preservative is rare. A positive reaction to this chemical contraindicates the use of such soaps as Dial and numerous proprietary medications.

Lanolin. Although this constituent of many ointments is not a common sensitizer, the frequency of lanolin-sensitivity among patients with stasis eczema and ulcer is quite high.[25] On occasion lanolin cross-reacts with such "hydrophilic" ointments as Aquaphor (Duke), Polysorb (Fougera) and Qualatum (Schieffelin).

Effective Non-Sensitizing Topical Medications

Acute Stasis Ulcer and Dermatitis. The weeping acute eczematous dermatitis super-imposed on a stasis ulcer is best treated with wet compresses of either normal saline solution (1 teaspoon of salt to a pint of water) or a 1 to 10,000 potassium permanganate solution. In the presence of infection, a ½ percent silver nitrate solution may be used. A silver nitrate solution must be kept thoroughly wet to prevent concentration by evaporation and must be handled carefully since the solution leaves long-lasting dirty gray and black stains on the skin, nails and utensils. (Note: Stains may be partially removed with tincture of iodine followed by "hypo" solution.) Between the compresses plain Lassar's paste may be applied. If there is considerable pruritis a "paraben-free" corticosteroid cream may be applied around the ulcer but not *on* the ulcer, since corticosteroid creams have a vasoconstricting effect and may further impair the circulation to the ulcer. Hyt́ ne cream (Dermik) which contains sorbic acid as a preservative has, in our experience, never produced allergic contact dermatitis. Valisone cream (Schering) which contains chlorocresol as a preservative, is also relatively non-sensitizing. We have observed only one instance of allergic reaction to Valisone cream.

Subacute and Chronic Phase of Stasis Ulcers. One-half per cent silver nitrate in Aquaphor has proved to be a non-sensitizing, antiseptic and effective re-epithelializing medicament. We have not yet encountered allergic sensitization to this mixture, although it is theoretically possible for Aquaphor to cross-react with lanolin. In the rare event of sensitization to Aquaphor, hydrophylic ointment (U.S.P.) may be used provided the patient is not allergic to the parabens.

In this stage, for pruritus and peri-ulcer eczema the paraben-free corticosteroid creams may be used *around* the ulcer. Direct contact of the ulcer with gauze should be avoided. A non-adhering Surgical Dressing (Johnson and Johnson) or sterilized linen cloth should be used instead. If there is some oozing, Lassar's paste may be used super-imposed upon the corticosteroid cream but not over the silver nitrate ointment. In the event that the chronic ulcer and/or the skin is infected or impetiginized, a paraben-free ointment may be applied. Of the antibacterial ointments which are paraben-free, Ilotycin ointment is the least sensitizing and most efficient.

The Use of Modified Unna Paste Dressing. To prevent edema of the ambulatory patient with stasis ulcers an "Unna Paste Boot" may be applied. There are three "Paste Boots" available; Gelocast, Medico Paste and Dome Paste bandage. The patient with paraben sensitivity must avoid both the Medico Paste and Dome Paste bandage. The patient with dichlorophene sensitivity must avoid the Gelocast and use the other paste bandages. In the event of sensitivity to both these types of bandages, a non-rubber spandex Ace bandage should be used. The Becton and Dickinson Ace Bandage is made of 85 percent spandex and 15 percent polyester fibres, is free of rubber chemicals and is virtually nonsensitizing.

The Use of Gold Foil. When there is marked ischemia with indurated edges to the ulcer, the use of autoclaved 23 K deep gold leaf obtained in a paint or art store may be helpful in epithelialization.[26] Allergic reaction to metallic gold may occur.[27, 28]

Summary and Conclusion

There is general agreement that topical therapy for stasis ulcers produces far more instances of sensitization than from any other condition. One-half percent silver nitrate in Aquaphor, paraben-free corticosteroid *creams* such as Hytone cream (Dermik) and Valisone cream (Schering), most corticosteroid *ointments,* and Ilotycin ointment are the safest effective topical medications. Unna paste bandage may contain paraben preservatives or dichlorophene (G-4) which can readily produce sensitization.

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