

Contact Sensitization to Modern Wound Dressings in 70 Patients With Chronic Leg Ulcers

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Background: Patients with chronic leg ulcers typically experience contact allergy to topical treatments. Although declared as hypoallergenic, modern wound dressings have caused several reported cases of contact allergy.

Objective: The aim of the study was to evaluate any allergenic potential of modern wound dressings in patients with leg ulcers.

Methods: Seventy-one patients were included in our prospective observation. Patch tests were performed with a selection of 10 modern wound dressings and with selected allergens according to series of the German Contact Dermatitis Research Group (DKG).

Results: Of 70 patients eligible for evaluation, 12 (17%) were positive for the hydrogel NuGel, followed by the hydrocolloid NuDerm (n = 7/70, 10%) and the ionic silver-containing wound dressing Aquacel Ag and the gauze Adaptic (both n = 4/70, 5%). Patients with recalcitrant ulcers of prolonged duration showed a significant higher number of epicutaneous sensitizations to wound dressings than patients with shorter ulcer duration.

Conclusions: The allergenic potential of modern wound dressings should not be underestimated. There is need for precise declaration of all ingredients.

APPROXIMATELY 40% to 80% of all patients with chronic leg ulcers experience different epicutaneous sensitizations to wound treatment products, that is, ointments, creams, antiseptics, or scented products.^{1–3} Analyses identified approximately 2 to 3 sensitizations per patient, and polysensitization is associated with longer duration of chronic wounds.^{4–7} With the introduction of modern so-called hypoallergenic wound dressings, there was hope that the burden of allergies would decrease in those patients. However, recent reports pointed out the allergenic potential of modern wound dressings.^{1,6,8,9} In 2011, we reported 39 patients¹⁰ of whom 13 (33.3%) had shown any sensitization, and several of them to modern wound dressings such as NuGel (Systagenix Wound Management GmbH, Hamburg, Germany; 8/39, 20%).

The aim of our follow-up study was to get data from a larger cohort of patients with leg ulcers of different duration to better understand the allergenic potential of modern wound dressings.

PATIENTS

Between July 2008 and August 2011, we included 71 consecutive patients (22 males, 49 females) with chronic leg ulcers (mean

wound duration, 33.18 months; median, 10 months) who ever had been treated with at least 2 different modern wound dressings. The median age of the patients was 72 years (range, 47–90 years). Clinical characteristics of the first 39 patients had been reported previously.¹⁰ They presented in our university department of dermatology either as inpatients or as outpatients for treatment of their leg ulcer. Overall, we registered the main primary causes for their ulcerations (see Fig. 1). “Stasis dermatitis” in this figure was defined as caused by other diagnoses, for example, secondary to edema due to heart failure. Sixty-five patients were also tested with the following series of the German Contact Dermatitis Research Group (DKG) (10): number 1, standard; number 18, ingredients of topical preparations; number 38, preservatives (Hermal Reinbeck, Germany).

METHODS

Patch tests were performed according to guidelines of the DKG with an application time of 2 days and final standardized reading on day 3.¹¹ For data analysis, reactions with “+” to “+++” were evaluated, and only stable or crescendo reactions were considered as positive. In all 71 patients, patch tests were performed with a selected series of 10 modern wound dressings (see Table 1). Patch tests were performed with the wound dressing “as is” in Finn chambers, but polyurethane foams and collagen were moistened with 0.9% saline solution. Statistical analysis was performed with the χ^2 test.

RESULTS

One patient was excluded under the diagnosis of an angry back reaction.

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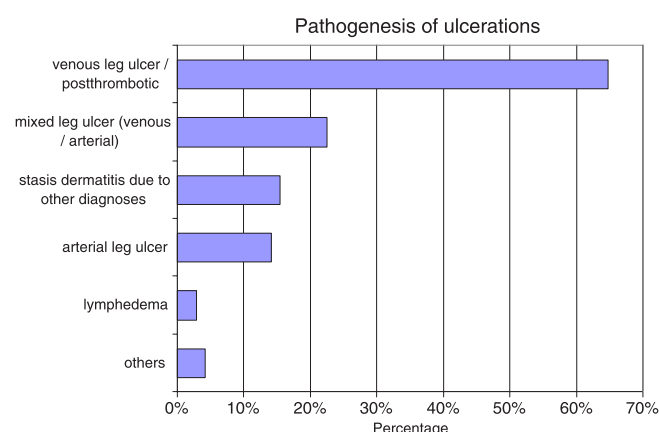


Figure 1. Pathogenesis of the leg ulcerations.

Wound Dressing Series

Of 70 patients, 51 (72.9%) showed no reaction, and 19 (27.1%) showed in total 35 positive reactions.

On average, 12 patients showed 1 sensitization, 3 patients showed 2 sensitizations each, 3 patients showed 4, and 1 patient showed 5 sensitizations each to different wound dressings.

Most reactions were documented for the hydrogel NuGel ($n = 12$), followed by the hydrocolloid NuDerm (Systagenix Wound Management GmbH, Hamburg, Germany; $n = 7$) and the ionic silver containing wound dressing Aquacel Ag (Convatec, Munich, Germany) and the gauze Adaptic (Systagenix Wound Management GmbH, Hamburg, Germany; both $n = 4$; see Fig. 2). Double sensitization to NuGel and propylene glycol was observed only in 2 patients, and to NuDerm and colophonium, in 3 patients.

Results of the DKG Test Series

In the DKG test series, 10 (15.4%) of 65 patients reacted to Amerchol (Edison, NJ), fragrance mix II [consisting of alpha-hexyl cinnamaldehyde, citral, citronellol, farnesol, coumarin, and hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyrall, International Flavors & Fragrances Inc., NY)], and *Myroxylon pereirae* (according to the

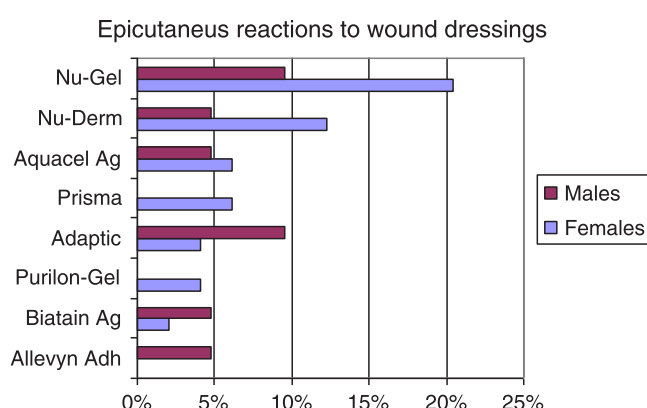


Figure 2. Detailed distribution for patch test results for different wound dressings.

International Nomenclature of Cosmetic Ingredients classification, or balsam of Peru; see Fig. 3). Nine (13.8%) patients showed positive reactions to lanolin alcohol and *tert*-Butylhydroquinone. Seven (10.8%) patients reacted to potassium dichromate, and 4 patients (6.2%) reacted to propylene glycol.

Correlation of Ulcer Duration and Patch Test Results

Mean wound duration of all patients was 33.18 months, but with a median of 10 months, so for better analysis, we divided the patients in 3 groups of ulcer duration: up to 19 months, 20 to 39 months, and more than 40 months (see Table 2). If we summarized all reactions to all test series, there was no correlation for number of sensitizations and wound duration (see Table 2).

However, when analyzing only the wound dressing series, there was a significant correlation between number of sensitizations to wound dressings and wound duration ($P < 0.05$, see Table 2).

DISCUSSION

Patients having chronic wounds have an increased risk to develop contact sensitization. This is because patients and practitioners tend to treat chronic wounds with a plethora of ointments or impregnated gauzes, containing ingredients such as antibiotics,

TABLE 1. Overview of the Tested Wound Dressings

Dressing	Labelling	Manufacturer
Ointment-impregnated gauze	Adaptic	Systagenix Wound Management GmbH, West Sussex, UK
Polyurethane foam with adhesive borders	Allevyn adhesive	Smith & Nephew GmbH, Hamburg, Germany
Polyurethane foam with adhesive borders and Ibuprofene	Biatain Ibu	Coloplast GmbH, Hamburg, Germany
Polyurethane foam without adhesive border	Biatain	Coloplast GmbH, Hamburg, Germany
Polyurethane foam with silver	Biatain Ag, formerly known as Contreet (Ag)	Coloplast GmbH, Hamburg, Germany
Collagen with silver	Prisma	Systagenix Wound Management GmbH, West Sussex, UK
Hydrogel with propylene glycol	NuGel	Systagenix Wound Management GmbH, West Sussex, UK
Hydrogel without propylene glycol	PurilonGel	Coloplast GmbH, Hamburg, Germany
Hydrofiber containing silver	Aquacel Ag	Convatec, Munich, Germany
Hydrocolloid dressing	NuDerm	Systagenix Wound Management GmbH, West Sussex, UK

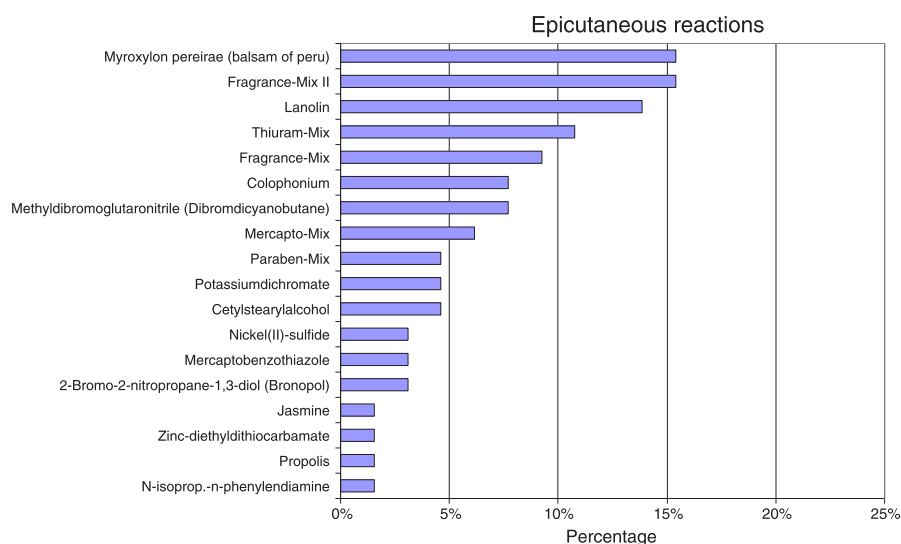


Figure 3. Results of the additional DKG series testing (standard, ingredients of topical preparations, preservatives).

antiseptics, or preservatives. The introduction of modern wound dressings provided several advantages such as atraumatic and fewer dressing changes, less pain, or lower nursing costs. However, after their introduction, some of these wound dressings also revealed their allergenic potential. Investigation in patient groups of 25 to 36 patients showed sensitization to wound dressings in 8% to 35% ($n = 3/36$, $n = 8/25$, and $n = 13/25$).^{1,12,13} Sensitizations to hydrogels seem to be most common with 9% to 23% of the tested patients reported to be patch test positive.^{8,14}

Here, we confirm a sensitization rate to hydrogels of 20% [NuGel + PurilonGel (Coloplast GmbH, Hamburg, Germany), $n = 14/70$], which turns out to be comparable with our previous data on 39 patients of this group who had a sensitization rate of 23% (NuGel + PurilonGel, $n = 9/39$). Most authors ascribe this sensitization to hydrogels to propylene glycol, which is a common preservative in hydrogels but not in all.^{1,8,9,14} Indeed, we observed most positive patch test reactions to the propylene glycol containing hydrogel NuGel but not to the (according to the manufacturer) propylene glycol-free hydrogel Purilon. On the other hand, most patients with sensitization to NuGel did not react to propylene glycol, so maybe this is not the causative allergen in our patients.

Further common sensitizers reported are the hydrocolloids in approximately 11% to 52% of patients.¹⁵ This can be caused by sensitization to Pentalyn (Eastman Corp., Kingsport, TN), the pentaerythritol ester of hydrogenated rosin,^{12,16} to other ester gum

rosins, for example, glyceryl rosinate,¹⁴ or to polyisobutylene derivatives (Vistanex, BASF Corp., Florham Park, NJ).¹⁷ These substances act like tackifying agents. Patients with positive reactions to hydrocolloid dressings might show cross-reactions also to unmodified colophonium, but often they do not because the described allergens are processed and modified. In our case, only 3 of 7 patients showed combined sensitization to hydrocolloid and unmodified colophonium.

It will be interesting to see if sensitization to hydrocolloids will decrease over the years as they are gradually replaced by more convenient wound dressings. In our case, there is a slight increasing rate of 10% (7/70 patients) versus 7% (in previous 3/39 patients).

We still observed many positive reactions to the silver-containing wound dressings (total $n = 9/70$, 12.8%). The allergen responsible is not known. Regarding polyurethane foams, sensitization may arise because of the butyl methacrylate/methyl methacrylate-containing adhesive borders.⁸ In our cases, this could not be proved because patients showed positive reactions to the foam without adhesive borders itself, and we did not test butyl methacrylate/methyl methacrylate or the adhesive borders separately, so the allergen remains unclear until yet. In addition, there exists only 1 case report describing sensitization to regenerated oxidized cellulose contained in Promogran,¹⁸ a very similar product to the product Prisma (Systagenix Wound Management GmbH, West Sussex, United Kingdom) that additionally contains silver. Sensitization to silver is observed only very rarely.¹⁹

TABLE 2. Positive Patch Test Reactions per Patient in Correlation to Ulcer Duration

Ulcer Duration, mo	Ulcer Duration, Mean/Median, mo	All Reactions (per Patient)	Reactions to Wound Dressing Series (per Patient)
<19	7.3/6	0.53	1.4
20–39	30.3/28.5	0.39	1.6
>40	134.8/108	0.5	2.3

Very few case reports exist about sensitization to Adaptic gauze. In these cases, sensitization was caused by a mixture of monoesters and diesters of sorbitol and its monoanhydrides and dianhydrides with oleic acid (Arlacel C, Croda International Plc, East Yorkshire, United Kingdom).²⁰ However, Adaptic seems to have a relevant potential for contact sensitization because we observed consistent sensitization levels (5% in only 39 patients vs 6% in all 70 patients). In our cases, no additional sensitization of these patients to sorbitan sesquioleate could be found. Sorbitan sesquioleate was tested as part of the fragrance mix.

In our patients with positive reactions to wound dressings, it was not always possible to verify if and how long they had been exposed to these wound dressings and if there was any clinical relevance. We therefore advocate that practitioners document all prescribed wound dressings as well as possible adverse or allergic reactions. Often, practitioners only try to change wound dressings in case of possible contact dermatitis and do not perform patch testing.

In our population, we could demonstrate a correlation between number of sensitizations to wound dressings and the duration of the ulceration. It is likely that this is due to the prolonged and repeated exposure to different wound dressings in nonhealing recalcitrant ulcers. Other sensitizations to common allergens with no direct relation to wound treatment might be acquired by the patients independently to their ulcer and therefore to their ulcer duration.

CONCLUSIONS

Of 71 patients, 19 (26.8%) showed in total 35 positive reactions in our wound dressing patch test series. Most reactions were documented for the hydrogel NuGel (n = 12), followed by the hydrocolloid NuDerm (n = 7) and the ionic silver-containing wound dressing Aquacel Ag as well as the ointment gauze Adaptic (n = 4). Those wound dressings seem to have their place within epicutaneous testing, but they should be selected according to local uses or patients history, respectively. There is still need for precise declaration of all ingredients of modern wound dressings so that specific and standardized patch tests can be performed. Patients with recalcitrant ulcers of prolonged duration (>40 months) show a higher number of sensitizations to wound dressings than patients with shorter ulcer duration (<19 months).

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