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Beneficial effect of resin salve in treatment of severe pressure ulcers: a prospective, randomized and controlled multicentre trial

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Conflicts of interest
A.S., J.J.J., J.L. and P.S. have now founded a company (Repolar Ltd) for developing the resin salve as a commercial product. P.S. is a shareholder and scientific advisor of Biohit Plc, a company that markets and develops laboratory equipment and tests. There are no other conflicts of interest.

A.S. and J.J.J. contributed equally to this study.

Summary

Background Resin salve of the Norway spruce (*Picea abies*) has been used in folk medicine to heal wounds and infections.
Objectives To study its clinical effectiveness in the treatment of pressure ulcers of the skin.
Methods A prospective, randomized, controlled multicentre trial involving 37 patients with grade II–IV pressure ulcers in 11 primary care hospitals was carried out between 2005 and 2007. The ulcers were randomly allocated to receive either resin salve or sodium carboxymethylcellulose hydrocolloid polymer treatment. The inclusion criterion was grade II–IV pressure ulcer. Exclusion criteria were a life expectancy of less than 6 months or a malignant disease. The primary outcome measure was complete healing of the ulcer within 6 months. Secondary outcome measures were partial healing of the ulcer, and successful eradication of bacterial strains cultured from the ulcers at study entry.
Results Thirteen patients of the resin group and nine patients of the control group completed the 6-month trial. All ulcers healed in 12 of the 13 patients (92%) in the resin group and in four of the nine patients (44%) in the control group ($P = 0{\cdot}003$; power 73%). Complete healing of the ulcers over time was significantly more common in the resin group than in the control group ($P = 0{\cdot}013$). Bacterial cultures from the ulcer area more often became negative within 1 month in the resin group.
Conclusions Traditional resin salve is significantly more effective in the treatment of infected and noninfected severe pressure ulcers than cellulose polymer gauzes.

Cutaneous pressure ulcers are areas of skin with superficial or deep tissue damage caused by pressure, shear, friction or a combination of these. The aetiology of pressure ulcers is multifactorial, but the most important predisposing factors are immobilization, malnutrition and ischaemia. Recovery is compromised and the susceptibility of the patient to pressure ulcers is enhanced by advanced age, diabetes, venous insufficiency, hepatic or renal failure, malignancies, certain drugs (e.g. corticosteroids and other immunosuppressive drugs), trauma, local endothelial dysfunction and smoking. The prevalence of pressure ulcers varies from 0·4% to 38% in patients in acute care, from 2·2% to 29% in those in long-term care, and from 0% to 17% in home care.[1–3]

Pressure ulcers are difficult to treat, and there is, as yet, no 'gold standard' for their treatment. Prevention involves recognition of the risk factors, reduction of pressure, assessment of the patient's nutritional status, avoidance of excessive immobilization, and preservation of skin integrity. The main treatment principles include reduction of pressure, friction and shear forces, local wound care, surgical debridement of necrotic tissue, management of bacterial contamination and infection, and optimizing the patient's nutritional status.[3,4]

Local wound care products are pivotal in the treatment of pressure ulcers and are usually the first and, occasionally, the only intervention that is required. The latter is particularly true when the wound is not severe enough to require surgery or when the patient is not fit for surgical treatment due to poor overall health or high anaesthetic risk. A large variety of local wound care products is currently available. Hydrogels, hydrocolloids, alginates, foams and films are frequently used but they are often ineffective and usually expensive.[4] To date, topical applications that are simultaneously protective, antibacterial and regenerative have not been developed.

Topical treatment of skin ulcers with a salve made from Norway spruce (*Picea abies*) resin mixed with butter has been folk medicine among the Lapp people in Northern Finland for decades, probably for centuries. Following some observations on the therapeutic value of this traditional Lapp resin salve[5] – some of which is related to the antimicrobial properties of the preparation[6] – we designed a randomized controlled trial to establish the efficacy and safety of resin therapy in the clinical setting. In this trial, comparison was made with a generally accepted control therapy in the treatment of severe, grade II–IV pressure ulcers of the skin.

Materials and methods

Patients and study objectives

This study was a prospective, randomized controlled multicentre trial designed to compare the effect of traditional resin salve treatment with a generally accepted control treatment of severe pressure ulcers (grade II–IV). We hypothesized that the resin salve treatment may have some beneficial effects on ulcer healing compared with control treatment. The primary outcome measures were the proportion of completely healed ulcers within 6 months, and the healing of the ulcers over time. The secondary outcome measures were improvement of ulcer grade during the 6-month follow-up period, and the successful eradication within 1 month of pathogenic bacteria cultured from the ulcers at study entry. Safety was followed by adverse event reports.

The study population was recruited in 11 primary care hospitals in Finland between June 2005 and March 2007. There were 37 consecutive patients with 45 pressure ulcers, and who were not considered suitable for surgical treatment. All patients were primarily recruited from the wards of primary care hospitals, where they were being either permanently or temporarily treated for an acute or a chronic illness. The inclusion criterion was one or several severe pressure ulcers (grade II–IV) with or without infection. The exclusion criteria were a life expectancy of less than 6 months, or an advanced malignant disease.

Eleven independent physicians, one in each primary care centre, collected the data during the study period (6 months). They confirmed the diagnoses and graded the pressure ulcers according to the European Pressure Ulcer Advisory Panel recommendations,[7] recorded clinical data, and evaluated the interim and final outcome. If a patient's status was ambiguous with regard to the diagnosis or definitive treatment (i.e. the patient could undergo surgical treatment), the physicians were recommended to consult the senior plastic surgeon (A.P.) of the study group. Trained nurses attended daily to the ulcers per study protocol under the supervision of the study physicians. At the beginning of the study, all physicians and nurses were personally interviewed and instructed by three members of the study group (A.S., J.J.J., J.L.) to verify that the diagnostic, treatment protocol and follow-up scheme were followed similarly in each centre.

Ethics, registration, and approvals

The study protocol was approved by the Ethics Committee of the Lapland Healthcare District. All patients gave written informed consent. The National Agency for Medicines was duly notified of the study on 24 March 2005 (clinical trial number 160/2004).

Randomization

Randomization was in permuted block sizes of four. The randomization protocol was designed by a specialist in biometrics (S.S.). The responsible physicians in the primary care hospitals allocated patients to receive either resin treatment or control treatment according to the randomization list (closed envelopes). As there are, by necessity, discernible properties of the resin salve (e.g. fragrance and consistency), the treatment could not be blinded.

Estimation of the sample sizes

Before the beginning of the study, the sample sizes were estimated as follows by a professional statistician (S.S.): a two-group χ^2 test with a 0·050 two-sided significance level will have 80% power to detect the difference between a group 1 proportion, π_1, of 0·900 and a group 2 proportion, π_2, of 0·500 (odds ratio 0·111) when the sample size in each group is 20.

Resin treatment

An even layer of resin approximately 1 mm thick was spread between loose sterile cotton gauze (Tyke HealthCare Ltd, Ulvila, Finland). The gauze was placed on both infected and non-infected areas of the pressure ulcer to cover the ulcer area with resin fully. The resin–gauze dressing was changed daily if the ulcer was infected or produced a discharge; if this were not the case, the dressing was changed every third day.[5]

Control treatment

Before the beginning of the study, clinical wound care experts, in a meeting specially arranged for this purpose, convened to agree on a control treatment consisting of sodium

carboxymethylcellulose hydrocolloid polymer without or with ionic silver (Aquacel® or Aquacel Ag®; ConvaTec Ltd, London, U.K.). Aquacel Ag was recommended for use on infected skin wounds or ulcers. The usage and results of the Aquacel products, which are universally available, are well documented in the scientific literature.[8–11] According to the manufacturer, Aquacel and Aquacel Ag are indicated for the treatment of acute and chronic wounds, including pressure and leg ulcers. The antibacterial spectrum of Aquacel Ag is broad, at least *in vitro*, and it has effect against methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE) and multiresistant *Pseudomonas aeruginosa*.[12] The Aquacel–hydrocolloid dressing was changed daily if the ulcer produced excessive discharge, but if there was no secretion the dressing was changed every third day, as for the resin–gauze. As stated in the manufacturer's instructions, Aquacel Ag was used if there was both clinical and laboratory confirmed evidence of infection (defined as a positive bacterial culture and a C-reactive protein concentration > 40 mg L^{-1}).

Bacterial cultures

Bacteria were cultured from all ulcers at the beginning of the study and after 1 month. Thereafter, cultures were taken selectively when clinically indicated. In both treatment groups, oral antibiotics were administered only if the wound was infected, and if there were both clinically and laboratory confirmed evidence of infection (body temperature over 38 °C, redness or suppuration of ulcer, and C-reactive protein concentration > 40 mg L^{-1}).

Follow-up

A clinical report form was completed by the responsible physician for every patient at the beginning of the study and thereafter monthly until study end 6 months later. The report included demographic, clinical and follow-up variables as follows: sex, age, height, weight, body mass index, smoking history, nutrition, albumin (P-albumin), mobilization, occupation, permanent medication, use of antibiotics, medical history, localization of pressure ulcer, grade of pressure ulcer, colour of pressure ulcer, width of pressure ulcer, depth of pressure ulcer, use of pressure ulcer mattress, bacterial cultures (at study start and after 1 month, and after 6 months if needed), need for wound revision, number of wound revisions during follow-up, and assessment of final outcome.

If the ulcer healed in less than 6 months, the last clinical report form was completed when the ulcer was considered fully healed (primary endpoint was achieved). If the ulcer had not healed in 6 months, the treatment was considered unsuccessful and follow-up was discontinued (primary endpoint was not achieved). All ulcers were photographed and planimetric analysis including the greatest width, length and depth from the bottom of the ulcer to surface of the skin were recorded on the forms at the beginning and monthly thereafter. The nurses recorded every dressing change into a logbook. Any notable improvement, deterioration, or any factor contributing to ulcer healing (like mechanical wound revision or cleansing), were recorded in the logbook. The clinical report forms and the logbooks of each patient were sent to the study group when the follow-up period was over. Finally, the forms were double-checked and all information was coded and entered into a computerized database by the two principal researchers (A.S., J.J.J.).

Preparation of spruce resin

The resin was collected in Kolari, Finnish Lapland, with sharp knives from the trunks of full-grown Norway spruce trees (*P. abies*) with permission of the landowners. Bark and other impurities were removed by mechanical cleaning and the resin was stored in a refrigerator (+4 °C) until further processed. The resin salve was prepared in the traditional way by mixing it with salt-free butter (Valio Ltd, Helsinki, Finland) by stirring, in an approximate weight proportion of 1 : 3 (w/w), and boiling the mixture at around +100 °C. After cooling, the resin salve was packed aseptically into aluminum salve tubes by the Pharmacy of the University of Helsinki, and was kept in a refrigerator until used. Minimal inhibitory concentration (MIC) values were determined for pure spruce resin in order to define MIC breakpoints and antibacterial effects of resin against bacteria. The detailed results of the antibacterial effects of resin salve have been published previously.[6]

Statistical analyses

Data analyses and reporting were based on the CONSORT statement.[13] Differences between parallel groups were compared with the χ^2 test or Fisher's exact test, as appropriate. Mean and SD were computed for continuous variables and proportions were compared after distribution analysis with the nonparametric Mann–Whitney U-test or Student's t-test, as appropriate. The healing of the ulcers over time was assessed by Kaplan–Meier analysis and the log-rank test was used to estimate the differences in the final outcome and healing time between the parallel groups. $P < 0{\cdot}05$ was considered statistically significant. SPSS 14.0 was used for the statistical calculations (SPSS, Chicago, IL, U.S.A.).

Results

After exclusion of the dropout patients, the final analysis included 13 patients in the resin group and nine patients in the control group. The corresponding numbers of ulcers were 18 and 11 (Fig. 1). Five patients presented with more than one ulcer. In the resin group, two patients had two ulcers, and one patient had four ulcers. In the control group, two patients had two ulcers.

At baseline, there were no significant differences in terms of patient demographics and clinical characteristics (age, body mass index, mobility, nutritional status, smoking, chronic diseases, or use of pressure ulcer mattress) between the treatment

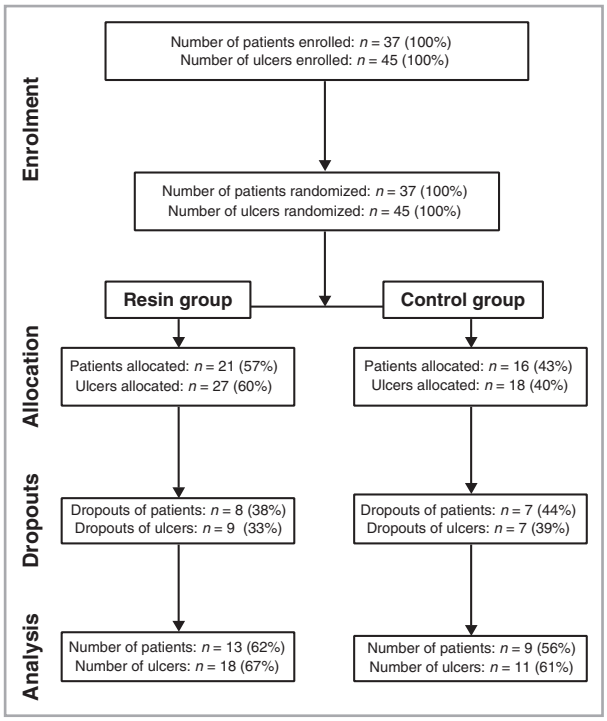

Fig 1. Flow diagram of trial.

groups (Table 1), nor were there any statistical differences at baseline regarding the ulcer variables localization, grade, dimension, or number of wound revisions.

Primary outcome measures

All ulcers healed in 12 of 13 patients in the resin group and in four of nine patients in the control group (92% vs. 44%, P = 0·003; power 73%) during the 6-month treatment period. The speed of ulcer healing was significantly faster in the resin group than in the control group (Fig. 2; log-rank test, P = 0·013). Complete healing of the pressure ulcers was significantly more common in the resin group (94% of the ulcers healed within 6 months) than in the control group (36%, P = 0·003) (Table 2).

Secondary outcome measures

In both groups, ulcers that did not heal completely during the 6-month treatment period did, however, tend to became smaller (Table 2). During the 6-month therapy period, only one ulcer (6% of all ulcers) was not healed in the resin group, although there was much improvement. Correspondingly, in the control treatment group, six ulcers (55% of all ulcers) were not healed. One ulcer (9%) in the control group became worse during the follow-up (Table 2).

The results of the bacterial cultures and concomitant oral antibiotic treatment during the follow-up are shown in Table 3. At baseline, 10 different bacterial strains were cultured in each group. One patient in the resin group and one

Table 1 Demographic data at baseline. Dropouts are not included. n indicates number of patients. Data are shown as mean ± SD (range)

	Resin treatment (n = 13)	Control treatment (n = 9)	P-value
Follow-up time (days)	107 ± 54 (20–180)	123 ± 69 (13–180)	0·589
Sex			
Male	6 (46%)	3 (33%)	
Female	7 (54%)	6 (67%)	0·674
Age (years)	80 ± 10 (58–98)	74 ± 8 (60–88)	0·110
BMI (kg m^{-2})	21·8 ± 7·1 (15·9–35·5)	21·9 ± 6·6 (16·9–34·7)	1·000
Mobility			
Normal	2 (15%)	1 (11%)	
Need for support	1 (8%)	1 (11%)	
Bedridden	10 (77%)	7 (78%)	0·932
Use of pressure ulcer mattress	1 (8%)	2 (22%)	0·544
P-albumin (g L^{-1})	31·4 ± 5·2 (22·0–39·0)	28·3 ± 4·5 (23·0–34·3)	0·157
Positive smoking history	1 (8%)	1 (11%)	0·342
Chronic diseases			
Diabetes	6 (46%)	1 (11%)	0·174
PAD	2 (15%)	1 (11%)	1·000
CAD	5 (39%)	2 (22%)	0·656
COPD	3 (23%)	–	0·257
Neurological disease	2 (15%)	1 (11%)	1·000
Alcoholism	1 (8%)	2 (22%)	0·531
Rheumatoid arthritis	–	2 (22%)	0·133

BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; PAD, peripheral arterial disease.

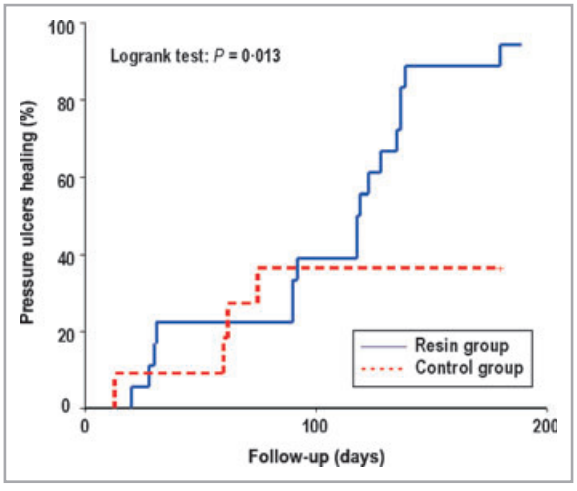

Fig 2. Kaplan–Meier analysis of the healing of ulcers over time. Comparison between resin and control treatment groups. Dropouts are not included.

Table 2 Clinical characteristics of pressure ulcers at study entry, after 1 month, and at endpoint (after 6 months). Dropouts are not included. n indicates number of ulcers. Data are shown as mean ± SD

	Resin (n = 18) vs. control (n = 11) [*P*-value]		
	At baseline	At 1-month follow-up	At endpoint
Localization			
Calcaneus	8 (44%)/2 (18%)	–	–
Trochanter	3 (16%)/1 (9%)	–	–
Sacrum	1 (6%)/2 (18%)	–	–
Ischium	1 (6%)/5 (46%)	–	–
Other	5 (28%)/1 (9%) [0·06]	–	–
Grade			
II	7 (39%)/5 (45%)	5 (28%)/6 (55%)	0 (–)/2 (18%)
III	9 (50%)/5 (45%)	8 (44%)/3 (27%)	1 (6%)/4 (36%)
IV	2 (11%)/1 (9%) [0·938]	1 (6%)/2 (18%)	0 (–)/1 (9%)
Fully healed	–	4 (22%)/0 (–) [0·150]	17 (94%)/4 (36%) [0·008]
Width (cm)	3·2 ± 2·4/4·2 ± 2·8 [0·387]	2·4 ± 1·6/3·7 ± 2·6 [0·207]	0·2 ± 0·7/1·8 ± 1·9 [0·011]
Depth (mm)	5·2 ± 10·3/5·3 ± 6·5 [0·580]	4·4 ± 7·8/4·9 ± 7·4 [0·955]	0·6 ± 2·4/5·4 ± 9·0 [0·011]
n of wound revisions	–	–	5 (28%)/7 (64%) [0·078]
Final outcome			
Fully healed	–	–	17 (94%)/4 (36%)
Significantly better	–	–	1 (6%)/6 (55%)
Unimproved	–	–	0 (–)/1 (9%) [0·003]

Table 3 Results of bacterial cultures. Numbers indicate the numbers of positive bacterial cultures (strains) obtained from separate ulcers. Letters in parentheses indicate antibiotics administered to the patients

	At baseline	At 1-month follow-up	At endpoint
Resin treatment (n = 18)			
Staphylococcus aureus	7 (D, H)	2 (E)	–
MRSA	1	–	–
Pseudomonas aeruginosa	6 (B, E, F, G, H)	3	1
Enterococcus faecalis	3	2	1
Escherichia coli	4	1	–
Streptococcus pyogenes	1	1	–
Diphteroides	2	–	–
Klebsiella pneumoniae	1	–	–
Bacteroides fragilis	2 (B, E, F, G)	–	–
Corynebacterium	1	1	–
Control treatment (n = 11)			
Staphylococcus aureus	3 (A, D)	5 (A, D, H)	–
MRSA	1	–	–
Pseudomonas aeruginosa	3 (A, B, D)	2 (A, D)	–
Enterococcus faecalis	5	3	–
Escherichia coli	2 (A)	1	–
Streptococcus pyogenes	2 (A, B)	–	–
Diphteroides	1	–	–
Bacteroides fragilis	2	3 (H)	–
Proteus mirabilis	1	–	–
Hafnia alvei	1	–	–

A, trimethoprim; B, ceftazidime; C, cefuroxime; D, nitrofurantoin; E, cefalexin; F, ciprofloxacin; G, pivmecillinam; H, methenamine hippurate; MRSA, methicillin-resistant *Staphylococcus aureus*.

in the control group had MRSA, but in both cases the culture was negative for MRSA 1 month later. *Staphylococcus aureus* seemed to be more susceptible to eradication with resin than with control treatment (Table 3).

Dropout analysis

There were eight (eight of 21; 38%) dropout patients in the resin group (one patient had two ulcers), and seven dropout patients (seven of 16; 44%) in the control group (Fig. 1). The reasons for dropping out from the resin group were three deaths (38% of all dropouts in the resin group), two admissions to operative treatment (25%), one allergic skin reaction (13%), one misdiagnosis (13%) and one patient-based refusal without any specific cause (13%). The reasons for dropping out from the control group were four deaths (57%), two patient-based refusals without any specific cause (29%) and one patient-based refusal because of randomization to the control group (14%). Subgroup analysis among the dropouts between the resin and control treatment groups regarding patient- and ulcer-related characteristics at baseline did not show statistical differences (data not shown).

Discussion

This study has documented a statistically significantly better healing rate of severe pressure ulcers among patients who were treated with a traditional resin salve than among those who were treated conventionally, when treatment and follow-up

lasted for 6 months. This finding underscores the efficacy of resin salve as a local treatment option for grade II–IV pressure ulcers compared with a 'modern' option that was considered to be the most available treatment at present. In addition, the resin salve had clear antimicrobial properties that seemed to be somewhat better than the antimicrobial properties of the locally administered polymeric-silver gauzes (Table 3).

Pressure ulcers are a significant clinical problem both in primary and in secondary health care. It has been estimated that the expenses allocated to the treatment of pressure ulcers in the U.S.A. are $1·335 billion annually.[14] The treatment of skin ulcers should be multidisciplinary and should include effective local wound care, surgical wound revision, and tissue reconstruction on an individual basis. The target of local wound care is to create preconditions for healing and to treat bacterial infections. There are many local wound care products on the market, but their efficacy, method of action, and their treatment outcomes are often questionable.[4,15,16] Lately, novel therapeutic options focusing on topical application of growth factors, and cell or tissue therapies, are being developed. Cytokine-derived growth factors (epidermal growth factor, platelet-derived growth factor and fibroblast growth factor), auto- or allogeneic materials in bioengineered human skin, and gene transfer have been suggested as answers to the problems of wound healing.[17,18]

Resin salve treatment has been used for centuries in Finnish Lapland as self-care in treatment of infected and noninfected wounds and skin ulcers.[19] There is no documentation on the results of this treatment in the literature. However, it is obvious that any treatment that has survived for centuries in competition with more modern treatment options, as the case is with the resin salve, might very well have an effect over and above the one of a placebo. Some of the authors (A.S., J.J.J., J.L.) had general practice in Lapland in 2001–2003 and made some empirical observations which were most encouraging regarding the effectiveness of resin salve.[5] The present randomized, prospective and controlled study supports these observations and supports the concept that resin salve is effective and constitutes an excellent tool for treating skin ulcers. Laboratory studies on resin have also shown that the resin salve has significant antibacterial activity against Gram-positive pathogenic skin bacteria, including MRSA and VRE.[6] The resin has also antifungal properties against some but not all strains of fungi. Our preliminary findings indicate that the resin has antifungal effects particularly against *Candida krusei* and *Acremonium falciforme*, and against some dermatophytes (unpublished observations).

The clinical efficacy of resin salve treatment was significantly better than that of the control treatment by each of the efficacy measures (complete healing of the ulcer or a decrease in grade; width and depth of the ulcer; and antimicrobial effect). Most importantly, however, the ulcers fully healed in the resin group significantly more often than in the control group within 6 months ($P = 0·013$). Figure 3 shows the progression in the ulcer healing of a patient who was randomized to the resin treatment group. During the 3 months of follow-up, a severe grade III pressure ulcer in the greater trochanter gradually ameliorated and eventually completely recovered.

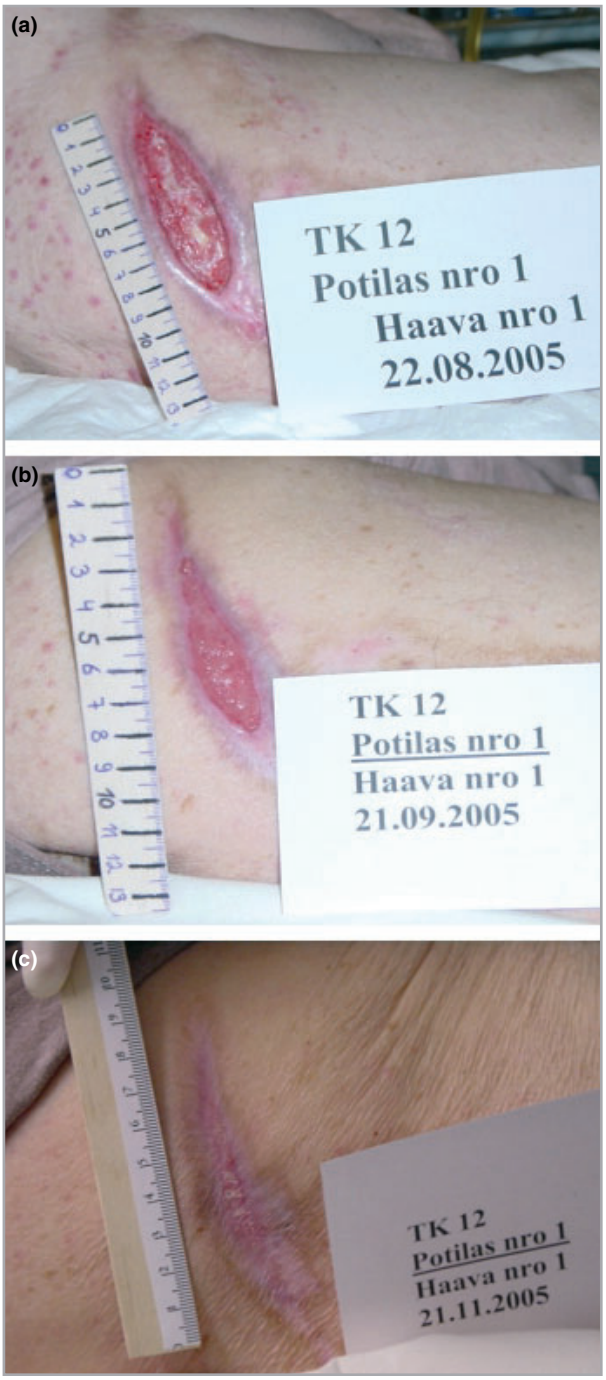

Fig 3. Picture series (a, b, c) of pressure ulcer in the greater trochanter. The patient was randomized to the resin treatment group and received 3 months of resin treatment according to the study protocol.

Interestingly, as compared with the control treatment, the superior effect of the resin salve treatment became evident after only 3 months of treatment (Fig. 2). This raises a question whether the resin salve has properties that induce wound healing by mechanisms that are unrelated to its antimicrobial

properties. Potential other effects of resin salve in wound healing may include induction of angiogenesis, epithelial migration and collagen synthesis. The antimicrobial effects (positive bacterial culture becoming negative in 1 month) occurred both in the resin and control groups even though this effect seemed to be somewhat better in the resin group than in the control group. The most important components of resin salve may be (preliminary observations) terpenoids (dehydroabietic, levopimaric, pimaric, palustric, isopimaric, sandracopimaric, abietic and neoabietic acids), lignans (lariciresinol, pinoresinol and matairesinol) and cinnamic acid. We assume that some of these components of the resin salve may also induce cell and tissue regeneration. Further experiments on this topic are in progress.

The only significant side-effect in the resin group was in one patient who had hypersensitivity to the preparation (contact dermatitis and eczema) and had to discontinue the treatment. The patient dropped out from the final analysis. It is known that resin has allergenic properties[20,21] and that one of its components, abietic acid, is commonly used as an antigen for resin allergy in epicutaneous tests. Allergic skin reactions to spruce or pine dusts are, however, rare, and in registries of the Finnish Institute of Occupational Health in 1976–1999 this allergy was found in only five patients.[22] The control treatment was not associated with local skin reactions.

In a preclinical evaluation done in collaboration with the National Public Health Institute, the Ames tests performed with the chemical components of the purified resin have thus far been negative.[23] This suggests that resin is probably neither mutagenic nor carcinogenic (unpublished data). Also, as the salve has been commonly used for several generations in folk medicine without any reports of harm, it seems as if the resin salve is a safe topical preparation.

This study recruited a modest number of patients and the final analysis revealed that more patients were randomized to the resin group than to the control group. However, the final power calculation showed that the power of the study was still quite high, 73% (initial power calculations targeted to a power of 80%; see Materials and methods). In particular, the number of dropouts was quite high, mainly due to several deaths of old and ill patients before the end of the 6-month treatment period. The skewed randomization of patients into the resin and control groups, in blocks of four, is presumably due to the large number of trial centres. From blocks of four in the randomization lists, more patients became randomized to the treatment groups in centres in which only one or two patients were recruited. It is likely that the treatment groups would have been more in balance if the number of centres had been lower, and/or if the number of patients in each centre had been higher (four or more). The treatment took several months in every patient and was tedious: careful data recording, measurements of ulcer dimensions, and regular photography of each ulcer were needed, and these were time consuming. In addition, not all subjects who were admitted to the trial hospitals during the study period could be recruited, often because of a lack of interest among many physicians. The study could not be blinded due to odour and consistency of the resin treatment. This might potentially decrease the reliability of the study.

In conclusion, this study strongly suggests that, in addition to our empirical observations and to folk tradition, resin salve treatment possesses objective, clinically measurable beneficial effects and may be used to enhance the healing of both infected and noninfected pressure ulcers of the skin.

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