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Original Contribution

A comparison of the prophylactic uses of topical mupirocin and nitrofurazone in murine crush contaminated wounds

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Abstract

Objectives: This work was conducted to study the prophylactic efficacy of 2 topical antibiotic ointments (mupirocin and nitrofurazone) against wound infection in experimental contaminated crush wounds.

Methods: Male Wistar rats underwent two 2-cm incisions at the back side and randomized into 3 groups—placebo (n = 14), mupirocin (n = 14), and nitrofurazone (n = 14)—and infected with either *Staphylococcus aureus* or *S pyogenes*. All wound edges were crushed for 5 seconds with hemostats to simulate crush injury before inoculation of the microorganisms. Half of the wounds were sutured and the other half left open. These wounds were treated 3 times daily for 6 days with topical mupirocin, nitrofurazone, or petrolatum (as placebo). At the end of 6 days, excisional biopsies were taken from wound edges and histopathologic assessments were made based on neutrophilic infiltration, edema formation, myofibroblastic proliferation, and granulation tissue formation. For the microbiologic assessments, quantitative tissue cultures were made.

Results: In *S aureus*-inoculated wounds, mupirocin showed higher antibacterial activity against bacterial colonization and reduced infection rates compared to placebo groups. The same effect was observed for the infection rates in *S pyogenes*-inoculated wounds. In *S pyogenes*-inoculated open wounds, nitrofurazone showed higher antibacterial activity against infection, but this effect was not observed in closed wounds. In *S pyogenes*- and *S aureus*-infected wounds, mupirocin treatment significantly lowered infection rates compared to nitrofurazone treatment. Histopathologic examination showed higher myofibroblastic proliferation and higher volume of granulation tissue in the nitrofurazon groups compared to the mupirocin groups.

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Conclusion: Topical mupirocin application was effective against crush wound infections inoculated with *S pyogenes* and *S aureus*. Nitrofurazone provides better granulation tissue formation, but did not effectively prevent bacterial colonization and infection in crush contaminated wounds.
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1. Introduction

Crush injuries are frequently encountered in emergency services and have a higher probability of becoming infected than lacerations without additional blunt trauma [1]. Some authors recommend routine use of antibiotics for prevention of wound infection after traumatic injury [2], whereas others restrict this practice to high-risk wounds [2-4]. Topical antibiotic use varies between hospitals and physicians. The mechanism and location of injury, degree and mode of contamination, the time interval between injury and treatment, and patient susceptibility among other factors determine the risk of wound infection [3,5-7]. Although it is not a common practice to suture contaminated crash injuries, suturing also makes crash wounds more prone to infections and enhance the need to administer systemic antibiotics [8]. All traumatic wounds are contaminated to some degree, and the infection causes cosmetic problems, increases the workload of the emergency department (ED), increases costs, and causes loss of work [9].

Mupirocin is a metabolite produced by submerged fermentation of *Pseudomonas flourescens*. Mupirocin potently inhibits bacterial protein and RNA synthesis, via inhibition of isoleucyl-transfer RNA synthetase [10-12]. The drug has excellent in vitro antibacterial activity against primary and secondary skin infections caused by such as *Staphylococcus aureus* and *Streptococcus pyogenes* [12,13]. Nitrofurazone is a synthetic nitrofuran with a broad antibacterial spectrum; it acts by inhibiting bacterial enzymes involved in carbohydrate metabolism [14]. Nitrofurazone is a topical anti-infective agent with a broad antibacterial spectrum; bactericidal against most bacteria commonly causing surface infections, including *S aureus*, *Streptococcus* [14].

Taking these data into consideration, we aimed to investigate the prophylactic efficacies of 2 local antibiotic ointments (mupirocin and nitrofurazone) in the treatment of experimental crush contaminated injuries.

2. Material and methods

2.1. Experimental animals

Adult Wistar albino rats (220-250 g) that are known to be susceptible to human pathogens were used [15]. The animals were obtained from Experimental Research Center of DoKuZEylul University; they were housed in a room with a 12:12-hour light/dark cycle and provided standard rat chow and water ad libitum. Forty-two animals were divided into 3 groups, and then further into subgroups of 7 animals each. The rats were housed individually. All equipment was modified to prevent the risk of infection to the personnel and all cages were kept in a separate room to prevent laboratory contamination. The use of anesthesia during the operative procedure and subsequent postoperative care were consistent with the guidelines in the National Institutes of Health's *Guide for the Care and Use of Laboratory Animals* (NIH publication No. 86-23, revised 1985; Bethesda, Md) and also approved by the experimental animal committee at Dokuz Eylül University Medical School.

2.2. Wound creation and management

Under ether anesthesia, the hair on the dorsal side of the rats were shortened with scissors and removed with depilatory cream. The exposed skin was wiped with 70% ethanol and then with povidone iodine. Two paravertebral linear incisions (2 cm long, 4 cm apart) reaching the deep fascial layer were made with no 15 scalpel; then incisions extended from the level of the fourth thoracic vertebrae caudally for a length of 4 vertebral bodies. To simulate a devitalized crush wound, 1.5-cm segments of the wound edges were crushed with hemostats for 5 seconds [11,16]. To establish infected wounds, main pathogens in wound infections of human beings *S aureus* (ATCC25923) and *S pyogenes* (an isolate from human wound infection) were used [11,13,17-20]. The bacteria were cultured in blood-brain-heart infusion agar for 1 night. The proliferating colonies were used to prepare a suspension of 10^8 col/mL in 0.9% NaCl. Aliquots of 0.2 ml were dripped into each wound and left for resorption without spilling from the wound edges [8,11,16].

After inoculation of the bacteria, 1 of the wounds was closed with three 4/0 separate polypropylene sutures and the other was left open. Both wounds were covered with sterile gauzes, which were fixed with adhesive tape (width, 4 cm) extending to the abdominal area. As described previously [11], the topical treatment was started after 4 hours. The inevitable delay between the injury and the treatment in the ED was simulated in this model [16]. Mupirocin, nitrofurazone, and placebo (0.1 mL) were applied to the wound surfaces. Next, all wounds were covered with sterile gauzes and fixed. The second treatment was performed 6 hours later and repeated 3 times per a day for 6 days [11].

Approximately 16 to 18 hours after the last topical treatment on the sixth day, the animals were killed under

ether anesthesia. The hairs around the wound were shortened with scissors and removed with depilatory cream. The skin outside the wound was wiped with 70% ethanol and povidone-iodine. The sutures in closed wounds were removed. With a no 15 scalpel, approximately 3 cm^2 rectangular tissue samples including epidermis, dermis, and subcutaneous tissue with 0.5 cm margin from wound edges and ends were taken [11,16]. Half of each tissue sample was sent immediately in Petri dishes to the laboratory of the microbiology department for quantitative bacteriological analysis; the other half was fixed in 10% formalin for histopathologic examination.

2.3. Bacteriologic analyses

Each biopsy specimen were weighed and placed in 10 mL sterile saline and then vortexed for 10 minutes to dislodge adherent organisms from the tissue. Next, the tube was diluted serially (10^{-2}, 10^{-4}, 10^{-6}). Inoculations were made in 10 μL of each tube on blood agar plates. They were incubated for 24 hours under aerobic conditions at 37°C. The quantitative culture plates were evaluated at 24 hours and the number of colony-forming units (CFU) per gram tissue was calculated. A bacterial count of 10^5 CFU/g was taken as a critical level for microbiologic infection [11,16].

2.4. Histopathologic examination

The biopsies taken for histopathologic evaluation were fixed in 10% formalin for 24 hours. Macroscopically, the specimens were sectioned at 2 mm and embedded in paraffin. Then 5-μm sections were taken. Sections for immunohistochemical staining were taken on poly-L-lysine–coated slides and kept at room temperature for 24 hours. For each biopsy specimen, 1 section was stained with hematoxylin-eosin (H&E), 1 with Masson's trichrome, and 1 with α-smooth muscle actin (SMA) monoclonal antibody. The degree of inflammation and edema were scored semiquantitatively in H&E-stained sections. In Masson's tichrome-stained sections, the volume of granulation tissue was assessed by stereologic methods. Immunostaining for SMA antibody was used to evaluate myofibroblastic proliferation.

2.5. Immunohistochemistry for -SMA

The streptavidin-biotin immunoperoxidase method was used for staining with the primary monoclonal antibody against α-SMA (prediluted; Dako Corp, Copenhagen, Denmark). Briefly, the sections were deparaffinized and rehydrated, then immersed in distillated water, and endogenous peroxidase activity was blocked by using a 0.3% solution of hydrogen peroxidase in phosphate-buffered saline (0.01 mol/L, pH 7.5) at room temperature for 10 minutes. Primary antibody was applied for 60 minutes at room temperature and washed in TRIS buffer. Biotinylated secondary antibodies and streptavidin-peroxidase complex (Dako Corp) were added consecutively for 10 minutes at room temperature and washed in TRIS buffer. Peroxidase activity was visualized with 0.03% 3-3′diaminobenzidine tetrahydrochloride (Sigma Chemical, St Louis, MO) applied for 5 minutes. After rinsing in deionized water and counterstaining in hematoxylin, the slides were dehydrated and mounted. Appropriate tissue sections as positive and negative controls for primary antibody were also labeled.

In granulation tissue areas, spindle cells not associated with vessel walls but expressing SMA were considered as myofibroblasts [21]. Myofibroblastic proliferation was scored semiquantitatively as follows: no staining with the SMA antibody (−), mild staining (+), moderate staining (+), and intense staining (++) [22].

2.6. Evaluation of inflammatory cell infiltration and edema

Edema and inflammatory cell infiltration were evaluated in H&E-stained sections and scored semiquantitatively as follows: no or minimal edema and inflammatory cell infiltration (−), mild edema and inflammatory cell infiltration (+), inflammatory cells form aggregates/moderate edema (++), confluent inflammatory cell aggregates/moderate edema (+++), multiple inflammatory cell aggregates/severe edema (++++) [23].

2.7. Evaluation of the neodermis (granulation tissue)

The volume of the granulation tissue was assessed by stereologic methods [24]. The biopsy material was cut vertically at 2-mm intervals. The sections were then stained with Masson's trichrome stain to enhance the granulation tissue areas. With Masson's trichrome stain, granulation tissue areas were observed in red color, which differentiated them from the healthy skin. All sections were examined under a light microscope and granulation tissue areas were marked with a permanent marker. Then a grid with 2-mm intervals was used; each section was randomly placed on the grid and the number of dots corresponding to granulation tissue areas was counted. Granulation tissue volume is calculated as follows:

$V_{(GD)} = ta(n)\cdot\sum N_{(GD)}$ mm^3
$V_{(GD)}$: granulation tissue volume
T: section thickness (2 mm)
$A(n)$: area of each grid square (4 mm^2)
$N_{(GD)}$: number of dots corresponding to granulation tissue areas

2.8. Statistical analysis

The $\log_{10}$ values of the bacterial counts are given in this study. Results were evaluated with one-way analysis of

Table 1 Evaluation parameters in groups infected with *S pyogenes*

Parameters		*S pyogenes*			
		Mupirocin (n = 12)	Nitrofurazon (n = 14)	Placebo (n = 14)	*P* [a]
Quantitative bacterial colony count (log_{10}) (+SD)	O	4.05 (±0.75)	3.20 (±0.44)	4.28 (±0.64)	>.05
	C	4.11 (±0.43)	4.37 (±0.28)	4.33 (±0.37)	>.05
Frequency of microbiologic infection (%)	O	16.7	14.3	71.4	.050 (M vs P); .031 (N vs P)
	C	28.6	71.4	57.1	>.05
Granulation tissue volume (±SD)	O	22.66 (±8.62)	38.85 (±5.90)	27.42 (±10.88)	>.05
	C	6.85 (±2.08)	914 (±2.08)	12.57 (±1.60)	>.05
SMA (median [min − max])	O	1.5 (0-3)	3 (2-3)	3 (2-3)	.532
	C	1 (0-3)	2 (1-3)	3 (1-3)	>.05
Inflammatory cell infiltration (median [min − max])	O	2 (1-2)	2 (2-2)	2 (1-2)	>.05
	C	1 (1-2)	1 (1-2)	2 (1-2)	>.05
Edema (median [min − max])	O	2 (1-2)	3 (2-4)	3 (2-4)	.28 (F = 1.2)
	C	3 (1-3)	3 (1-4)	3 (0-4)	>.05

O indicates open; C, closed; M, Mupirocin; N, Nitrofurazone; P, placebo.
[a] Analysis of variance, Mann-Whitney U test, and χ^2 test.

variance (ANOVA) and Duncan test was used as a posthoc test. The frequencies of clinical and microbiologic infection were evaluated by χ^2 test and Fisher exact test when necessary. Histopathologic results were evaluated with Kruskal-Wallis variance analysis and Mann-Whitney *U* test. Comparison of "closed" vs "open" wounds is made using paired tests (ie, paired *t* test, Wilcoxon paired test, McNemar's test as appropriate). A factorial repeated-measures ANOVA (with treatment, bacteria, and wound type as factors) was used for bacterial count. Results were considered statistically significant when $P < .05$. Data were analyzed by statistical software (SPSS for Windows 10.0; SPSS, Chicago, Ill).

3. Results

One rat was inoculated with *S pyogenes* and treated with mupirocin ointment-developed septicemia on the fifth day. Its condition deteriorated and it eventually died.

3.1. Effects of topical agents on all wounds inoculated with *S pyogenes*

3.1.1. Microbiologic assessment of the secondary healing

Table 1 summarizes results of the individual treatment groups. Neither mupirocin nor nitrofurazone treatment

Table 2 Evaluation parameters in groups infected with *S aureus*

Parameters		*S aureus*			
		Mupirocin (n = 14)	Nitrofurazon (n = 14)	Placebo (n = 14)	*P* [a]
Quantitative bacterial colony count (log_{10}) (±SD)	O	4.25 (±0.30)	6.48 (±0.50)	7.54 (±0.29)	.001 (M vs P)
	C	4.69 (±0.65)	5.99 (±0.31)	7.09 (±0.33)	.031 M vs P
Frequency of microbiologic infection (%)	O	42.9	100	100	.0001 (M vs N); .0001 (M vs P)
	C	28.6	100	100	.0001 (M vs N); .0001 (M vs P)
Granulation tissue volume (±SD)	O	22.85 (±6.15)	24.00 (±5.05)	35.42 (±8.7)	>.05
	C	10.28 (±3.79)	16.00 (±3.90)	30.85 (±6.15)	>.05
SMA (median [min − max])	O	1 (1-3)	3 (2-3)	3 (3-3)	.042 (M vs N); .006 (M vs P)
	C	1 (0-2)	2 (1-3)	3 (3-3)	.0001 M vs P
Inflammatory cell infiltration (median [min − max])	O	2 (1-3)	2 (2-2)	2 (1-4)	>.05
	C	1 (1-2)	2 (1-4)	2 (2-4)	>.05
Edema (median [min − max])	O	2 (2-4)	3 (2-3)	4 (2-4)	>.05
	C	3 (2-3)	2 (0-4)	3 (1-4)	>.05

[a] Analysis of variance, Mann-Whitney U test, and χ^2 test.

Table 3 Multivariable analysis in the evaluation of topical antibiotics on open and closed crush wounds

Parameters	F	P*
Treatment	21.8	<.001
Bacteria	20.5	<.001
Wound type	1.27	.26
Treatment × bacteria	5.9	.004
Treatment × wound type	0.67	.5
Bacteria × wound type	0.83	.36
Treatment × bacteria × wound type	0.8	.45

* *P* values are from a factorial repeated-measures ANOVA.

significantly affected bacterial colonization in *S pyogenes*-inoculated groups as compared to placebo treatment. However, mupirocin treatment significantly lowered microbiologic infection rates (a bacterial count of $>10^5$ CFU/g) and similar effect was observed with nitrofurazone treatment compared to placebo ($P \leq .05$).

3.1.2. Microbiologic assessment of the primary closure

Higher rates of microbiologic infection and increased bacterial colonization were observed in *S pyogenes*-inoculated, nitrofurazone-treated groups after primary closure. However, bacterial colonization and microbiologic infection rates did not significantly differ in *S pyogenes*-inoculated, mupirocin-treated groups.

3.1.3. Histopathologic assessment of the secondary healing

Granulation tissue volume, α-SMA activity, and edema were nonsignificantly lower in *S pyogenes*-inoculated, mupirocin-treated groups compared to nitrofurazone and placebo groups. There were no differences in groups in terms of inflammatory cell infiltration.

3.1.4. Histopathologic assessment of the primary closure

Granulation tissue volume, α-SMA activity, and inflammatory cell infiltration were nonsignificantly lower in *S pyogenes*-inoculated, mupirocin-treated groups. There were no differences between groups in terms of edema.

3.2. Effects of topical agents on all wounds inoculated with *S aureus*

3.2.1. Microbiologic assessment of the secondary healing

Table 2 summarizes the results of the individual treatment groups. There were statistically significant differences among the groups in terms of bacterial colonization inoculated with *S aureus* ($P = .0001$; $F = 9.95$). Animals treated with mupirocin demonstrated a significant decrease in *S aureus* counts compared to the placebo group ($P = .001$). Microbiologic infection rates in the mupirocin group showed significant attenuation compared to nitrofurazone and placebo groups ($P = .0001$).

3.2.2. Microbiologic assessment of the primary closure

Bacterial colonization and infection rates were significantly higher in *S aureus*-inoculated, nitrofurazone-treated groups after primary closure.

3.2.3. Histopathologic assessment of the secondary healing

Granulation tissue volume and edema were nonsignificantly lower in *S aureus*-inoculated, mupirocin-treated groups compared to the nitrofurazone and placebo groups. Animals treated with mupirocin demonstrated a significant decrease in α-SMA activity compared to the placebo and nitrofurazone groups ($P \leq .05$). There were no differences in groups in terms of inflammatory cell infiltration.

3.2.4. Histopathologic assessment of the primary closure

Granulation tissue volume and inflammatory cell infiltration were nonsignificantly lower in *S aureus*-inoculated, mupirocin-treated groups compared to the nitrofurazone and placebo groups. Again, edema was nonsignificantly lower in nitrofurazone-treated group. Animals treated with mupirocin demonstrated a significant decrease in α-SMA activity compared to the placebo and nitrofurazone groups ($P = .0001$).

Multivariable analysis using the bacterial count verified the findings from the bivariate analyses (Table 3). The multivariable model included type of antibiotics, bacteria, and wound, in addition to all interaction terms. After adjusting for the other factors, type of antibiotics and bacteria, and the first-degree interaction term between the 2 were found significant.

4. Discussion

In this study, the effectiveness of placebo-controlled mupirocin and nitrofurazon treatments were investigated in experimentally designed open and closed crush wound models contaminated by inoculation of *S aureus* and *S pyogenes*. Topical mupirocin application was effective against crush wound infections inoculated with *S pyogenes* and *S aureus*. In *S pyogenes*-inoculated open wounds, nitrofurazone showed higher antibacterial activity against infection, but this effect was not observed in closed wounds. Nitrofurazone provided better granulation tissue formation, but did not effectively prevent bacterial colonization and infection in the crush contaminated wounds. Our results demonstrated that the selection of a particular topical antibiotic can have a range of effects on a variety of wound healing characteristics, and were consistent with previously conducted studies on this topic [12,25-29].

A myriad of wound care methods have been developed to minimize wound site infections. The role of ointments in prophylaxis after the treatment of lacerations is controversial [7]. Although the efficacy of topical antimicrobial agents in the prevention of infections due to superficial contamination has not been established, these agents are widely used in wound care [7]. Depending on the source of the traumatic wound, particular pathogens are expected to be present. For most infections of traumatic wounds, antibiotic therapy should be directed against the most common skin pathogens, *S aureus* and *Streptococci* [30]. Nitrofurazon is 1 of the most easily provided and widely used topical antibacterial agents in emergency medicine departments in our country. Even it is extensively preferred for the treatment of burn and wound care including contaminated crush wounds, as far as we know this is the first study to report on this subject.

In our model, mupirocin was effective in reducing the infection rates of all open and closed wounds contaminated by *S aureus* and *S pyogenes*. In their experimental study, Ward and Campoli-Richards [12] documented that topical mupirocin has antibacterial effect against *S aureus* and *S pyogenes*, supporting the microbiologic results and conclusions of our study. In the study of Boon et al [25], designed to evaluate the efficacy of mupirocin against *S aureus*, both mupirocin and fucidic acid were effective on reducing bacterial counts compared to control groups, which also consistent with our findings. Rode et al [26] also showed that use of topical mupirocin in *S aureus*-inoculated wounds quantitatively reduced the bacteria ratio significantly when applied 2 times a day for 48 hours on rats. In a single-blind, multicenter clinical trial on 413 selected patients with commonly encountered superficial skin infections, White et al [27] compared the clinical and bacteriologic efficacies of topical mupirocin and sodium fusidate; the success rates of mupirocin and sodium fusidate were similar: 97% and 93%, respectively. *Staphylococci* and/or β-hemolytic streptococci comprised 96% and 88% of the isolated pathogens in the mupirocin and sodium fusidate groups, respectively. Documented effects of mupirocin against staphylococci and/or β-hemolytic streptococci, in the study of White et al [27], were in accordance with our experimental results and, bears practical effectiveness and clinical relevance in daily use against those agents.

Although nitrofurazone has been used to treat surface wounds involving all parts of the body and all kinds of injuries (surgical, accidental, military, and pathologic lesions), it is not efficacious in the treatment of minor burns or surface bacterial infections involving wounds, cutaneous ulcers, or pyodermas [14,31]. Also, there is no sufficient evidence of efficacy of nitrofurazone in treating surface bacterial infections involving wounds [32]. In the present study, nitrofurazone was not effective against infection in open and closed wounds contaminated with *S aureus*, and in closed wounds contaminated with *S pyogenes*. But it was effective against open wound infection contaminated with *S pyogenes* in our study. Faulkner et al [28] compared nitrofurazone and silver sulfadiazine in an experimental study and showed that nitrofurazone suppresses the bacterial concentration of *S aureus* to a greater degree in burn wounds. Rodgers [30] performed in vitro susceptibility tests using bacitracin, silver sulfadiazine, mafenide acetate, nitrofurazone, and mupirocin on 177 bacterial isolates from pediatric patients with burn wounds. They found that nitrofurazone had the broadest spectrum of activity, but mupirocin was the most potent antibacterial agent against *S aureus*. They concluded that clinical correlation is necessary for a complete evaluation of the results. Although nitrofurazone had been found to be effective against *S aureus* and *S pyogenes*, in the present study, it was effective against *S pyogenes*-inoculated open wounds but not in wounds inoculated by *S aureus*. Results of the study concerning mupirocin seem to show similar effectiveness as found in our study.

In our study, mupirocin, nitrofurazone, and placebo (petrolatum; vaseline) were also compared with respect to histopathologic parameters. Histopathologic examination showed higher myofibroblastic proliferation and higher volume of granulation tissue in the nitrofurazon groups compared to mupirocin groups in all wounds inoculated with *S aureus* and *S pyogenes*. The contractile forces produced by granulation tissue in wounds are derived from myofibroblasts that contain contractile proteins. Contraction gradually reduces the wound area by the centripetal movement of the wound margins. Wound contraction is thought to be a result of these actin-rich myofibroblasts, which are the most prominent cells in granulation tissue [33]. Webber et al [34] compared nitrofurazone, povidone-iodine, and silver sulfadiazine in the ED outpatient treatment of 84 patients with second-degree burns of less than 15% (adults) or 5% (children) of their total body surface area. Indices of healing were percent of healing, degree of dryness, crust separation, eschar separation, tissue granulation, and wound pain. Statistical analysis indicates that healing in nitrofurazone-treated patients was superior to that in sulfadiazine-treated patients: tissue granulation began sooner, crusts separated more rapidly, wounds were dryer, and the amount of healing at 2 weeks was greater. Watcher and Wheeland [35] induced full-thickness wounds and made daily macroscopic measurements until completion of wound healing. Topical bacitracin, silver sulfadiazine, and capsaicin were found to increase epithelialization, whereas mupirocin had no effect on reepithelialization but markedly decreased wound contraction (15% vs 30% for untreated controls). The observed decrease in wound contraction may be due to the decreased SMA activity as demonstrated in our study. This finding could perhaps be used advantageously to limit contraction in certain anatomic locations for certain types of wounds where contraction could have adverse effects (eg, after Mohs surgery or other ablative procedures). On the other hand, the volume of scar deposited in a healed wound is influenced by the wound's initial size and by the role wound contraction plays in its closure. The greater the role of wound contraction, the less residual scar deposited. Further studies

on the histopathologic effects of topical agents are warranted to elucidate the mechanisms of these effects.

As a conclusion, topical mupirocin application was effective against crush wound infections inoculated with *S pyogenes* and *S aureus*. Nitrofurazone provides better granulation tissue formation, but does not effectively prevent bacterial colonization and infection in crush contaminated wounds. Our findings show that topical mupirocin is effective in prophylaxis of infection in crushed and contaminated wounds. Effective use of topical antibiotics requires knowledge of the antimicrobial activity and effects of wound healing of various agents in wounds and the advantages and disadvantages of each. An awareness of topical agents on various aspects of wound healing permits the clinician to choose the most appropriate material to advantageously control the wound process and final results. For example, a large full-thickness defect might best be managed with a substance that retards contraction so as to minimize distortion, if the wound heals by second intention. Therefore, topical antibiotics should be considered as potential primary therapy in the ED. However, further studies are indicated in this important area of wound healing research to evaluate the clinical efficacy of these agents and to search for the mechanisms that explain their effects.

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