Review: Some but not all topical antimicrobial agents improve the rate of healing of chronic wounds


Question
Are systemic and topical antimicrobial agents effective for healing chronic wounds (venous leg ulcers, pressure ulcers, diabetic foot ulcers, and pilonidal sinuses)?

Data sources
Studies were identified by searching 19 electronic databases, including MEDLINE and CINAHL, from their inception to January 2000. Conference abstracts, journals, and bibliographies of included studies were hand searched, and experts were contacted.

Study selection
Randomized controlled trials (RCTs) and nonrandomized trials with a control group were selected if patients had or were at risk for developing diabetic foot ulcers, pressure ulcers, chronic leg ulcers, pilonidal sinuses, nonhealing surgical wounds, or chronic cavity wounds; systemic or topical antimicrobial preparations (antibiotic, antifungal, or antiviral agents) intended to prevent or heal wounds were studied; and objective measurement of wound healing, change in skin condition, or development of new lesions was reported.

Data extraction
Data were extracted on study quality and characteristics, participants, interventions, outcomes, and adverse events.

Main results
30 trials (25 RCTs) met the inclusion criteria. Trials were grouped according to wound type (Table); data were not combined because of study differences. For topical agents for venous ulcers, allopurinol powder, dimethyl sulfoxide powder, silver impregnated charcoal dressing, and tripeptide-copper or silver sulfadiazine improved complete healing of the ulcer area more than did placebo or other topical agents. Oxyquinolone ointment improved complete healing of pressure ulcers. Excision with insertion of a gentamicin-impregnated sponge and pressure dressing also showed improvement in wound healing for pilonidal sinuses.

Conclusion
Healing of chronic wounds is improved by some topical antimicrobial agents, but few systemic agents show improvements.

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Treatment of chronic wounds or ulcers with systemic antimicrobial or topical agents*

<table>
<thead>
<tr>
<th>Wound type</th>
<th>Intervention</th>
<th>Studies</th>
<th>Number of patients</th>
<th>Healing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous ulcers</td>
<td>Systemic agents</td>
<td>2 RCTs</td>
<td>84</td>
<td>No improvement</td>
</tr>
<tr>
<td></td>
<td>Topical agents</td>
<td>5 RCTs, 2 nRCTs</td>
<td>449</td>
<td>3 of 7 improved</td>
</tr>
<tr>
<td>Mixed causes</td>
<td>Systemic agents</td>
<td>2 RCTs</td>
<td>85</td>
<td>Both improved</td>
</tr>
<tr>
<td></td>
<td>Topical agents</td>
<td>3 RCTs, 2 nRCTs</td>
<td>128</td>
<td>3 of 5 improved</td>
</tr>
<tr>
<td>Pressure ulcers</td>
<td>Topical agents</td>
<td>3 RCTs</td>
<td>169</td>
<td>1 of 3 improved</td>
</tr>
<tr>
<td>Diabetic ulcers</td>
<td>Systemic agents</td>
<td>2 RCTs</td>
<td>104</td>
<td>No improvement</td>
</tr>
<tr>
<td></td>
<td>Topical agents</td>
<td>1 RCT</td>
<td>29</td>
<td>Improvement</td>
</tr>
<tr>
<td>Pilonidal sinuses</td>
<td>Systemic agents</td>
<td>2 RCTs, 1 nRCT</td>
<td>190</td>
<td>2 of 3 improved</td>
</tr>
<tr>
<td></td>
<td>Topical agents</td>
<td>3 RCTs</td>
<td>198</td>
<td>1 of 3 improved</td>
</tr>
</tbody>
</table>

* RCTs = randomized controlled trials; nRCTs = nonrandomized controlled trials.

Commentary
Chronic wounds are a common cause of morbidity, and their cost of care is high. For example, the annual incidence of foot ulcers in patients with diabetes is about 6%, and 16% of these patients require amputation (1). The incidence of pressure sores in a well-staffed internal medicine ward was 4% (2). The role of infection and colonization in preventing wound healing is uncertain, and so is the role of antimicrobial agents in promoting recuperation.

The systematic review by O’Meara and colleagues on antimicrobial agents for treatment of chronic wounds is excellent, with a well-defined clinical question, a comprehensive search strategy, and unambiguous criteria for inclusion of studies. The included studies are well described, which allows readers to form their own opinion. The discussion is relevant and comprehensive for both methods and pathophysiologic content. Unfortunately, the review offers few recommendations to change clinical practice because little can be learned from the original studies. Most of them had a small sample size, weak methodology, and unclear biologic hypotheses. The abstract cannot do justice to the review by enumeration of positive and negative results. To gain a true insight, the review itself should be read.

Nevertheless, several messages can be highlighted. Overall, systemic antibiotics did not promote healing. However, an effect of antibiotic treatment on healing might have been missed because of a small sample size in some studies. Given the potential to induce resistance, the possible adverse effects, and the lack of evidence for effect, systemic antibiotic treatment should be given only for clear indications of a systemic or local infection.

Topical antimicrobial agents show more promise, but the trial results are inconsistent and the trials have the same methodologic problems as do the trials of systemic agents. RCTs of topical antimicrobial agents that use clinically relevant outcomes, a sufficient sample size, and correct methods are urgently needed.

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References