



Canadian Agency for
Drugs and Technologies
in Health

RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS



TITLE: Topical Antimicrobials and Antimicrobial Dressings for the Management of Diabetic Foot Ulcers: Clinical Effectiveness and Guidelines

DATE: 15 September 2014

RESEARCH QUESTIONS

1. What is the clinical effectiveness of topical antimicrobial use without wound dressing application on both infected and non-infected diabetic foot ulcers (DFU)?
2. What is the clinical effectiveness of topical antimicrobial use with regular, non-antimicrobial wound dressing application on both infected and non-infected DFUs?
3. What is the clinical effectiveness of antimicrobial dressing application on both infected and non-infected DFUs?
4. What are the evidence-based guidelines regarding the use of antimicrobial products on DFUs in the absence of signs and symptoms of infection?
5. What are the evidence-based guidelines regarding the use of topical antimicrobials and antimicrobial dressings for the management of DFUs?

KEY FINDINGS

Six systematic reviews and meta-analyses, three randomized controlled trials, and three non-randomized studies were identified regarding the clinical effectiveness of topical antimicrobials or antimicrobial dressing application on both infected and non-infected DFUs. One evidence based guideline was identified regarding the use of topical antimicrobials and antimicrobial dressings for the management of DFUs.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 9), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused

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Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and September 8, 2014. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria	
Population	Patients with diabetic foot ulcers (DFU)
Intervention	Q1 and 2: Topical antimicrobials (included, but not limited to, silver, iodine, acticoat) Q3: Antimicrobial dressings Q4 and 5: Both topical antimicrobials and antimicrobial dressings
Comparator	Q1: No comparator, regular non-antimicrobial dressings, antimicrobial dressings Q2: No comparator, antimicrobial dressings Q3: No comparator, topical antimicrobials without regular dressings, topical antimicrobials with regular dressings
Outcomes	Clinical effectiveness (clinical benefit; including, but not limited to, impact on healing and harms)
Study Designs	Health technology assessment reports, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Six systematic reviews and meta-analyses, three randomized controlled trials, and three non-randomized studies were identified regarding the clinical effectiveness of topical antimicrobials or antimicrobial dressing application on both infected and non-infected DFUs. One evidence based guideline was identified regarding the use of topical antimicrobials and antimicrobial dressings for the management of DFUs. No health technology assessment reports were identified and no evidence-based guidelines were identified regarding the use of antimicrobial products on DFUs in the absence of signs and symptoms of infection.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Six systematic reviews and meta-analyses, three randomized controlled trials, and three non-randomized studies regarding the clinical effectiveness of topical antimicrobials or antimicrobial dressing application on both infected and non-infected DFUs were identified.

Evidence regarding a number of antimicrobial interventions was identified.¹⁻¹² Overall, there was inconsistent evidence regarding the effectiveness of topical antimicrobials and antimicrobial dressing application on both infected and non-infected DFUs. Detailed results are summarized in Table 2.

One evidence-based guideline¹³ regarding the use of topical antimicrobials and antimicrobial dressings for the management of DFUs was identified. This guideline reported the following:

- “topical antimicrobials may be used for non-limb threatening infections to reduce bacterial burden in superficial infections
- there is mixed evidence regarding silver containing dressings and creams for promoting wound healing and preventing wound infections in DFUs
- “If topical antimicrobial agents are used and increased superficial bacterial burden or delayed healing are noted, treatment should be supplemented with debridement and moisture balance.”
- “There is mixed comparative evidence on the effectiveness of any particular dressing to heal diabetic foot ulcers.”

No relevant evidence-based guidelines regarding the use of antimicrobial products on DFUs in the absence of signs and symptoms of infection were identified.

Table 2: Summary of Findings of Systematic Reviews, Meta-analyses, Randomized Controlled Trials and Non-Randomized Studies

First Author, Year	Population	Intervention	Comparator	Study Findings and Author Conclusions
<i>Systematic Reviews and Meta-Analyses</i>				
Dumville, 2013 ¹	<ul style="list-style-type: none"> Patients with DFUs 	<ul style="list-style-type: none"> Antimicrobial (silver) fibrous-hydrocolloid dressings 	<ul style="list-style-type: none"> Standard alginate dressing Iodine-impregnated antimicrobial dressing Standard fibrous hydrocolloid dressing with and without topical cream containing plant extracts 	<ul style="list-style-type: none"> No difference in healing between treatment and any comparators. Insufficient evidence to support use of the treatment over other types of dressings.
Dumville, 2013 ²	<ul style="list-style-type: none"> Patients with DFUs 	<ul style="list-style-type: none"> Alginate dressings 	<ul style="list-style-type: none"> Basic wound contact dressings Foam dressings Silver-containing fibrous-hydrocolloid dressing 	<ul style="list-style-type: none"> No difference in the number of healed DFUs when antimicrobial (silver) hydrocolloid dressings were compared to alginate dressings.
Greer, 2013 ³	<ul style="list-style-type: none"> Patients with DFUs (non-healing) 	<ul style="list-style-type: none"> Platelet-derived growth factors and silver cream 	<ul style="list-style-type: none"> Standard care 	<ul style="list-style-type: none"> There was low-strength evidence that the combination treatment improved healing compared to standard care.
Peters, 2012 ⁴	<ul style="list-style-type: none"> Patients with DFUs (with infections in soft tissue and bone) 	<ul style="list-style-type: none"> Superoxidized water 	<ul style="list-style-type: none"> Soap Povidone iodine 	<ul style="list-style-type: none"> Better outcomes (not specified) were observed for superoxidized water than soap or povidone iodine (high risk of bias). No evidence to justify the adoption of any particular therapy in diabetic patients with infection of soft tissue or bone.

Table 2: Summary of Findings of Systematic Reviews, Meta-analyses, Randomized Controlled Trials and Non-Randomized Studies

First Author, Year	Population	Intervention	Comparator	Study Findings and Author Conclusions
Hunt, 2010 ⁵	<ul style="list-style-type: none"> Patients with DFUs 	<ul style="list-style-type: none"> Dimethyl sulfoxide Cadexomer iodine, 	<ul style="list-style-type: none"> Conventional treatment (not specified) 	<ul style="list-style-type: none"> Dimethyl sulfoxide was associated with greater odds of healing than conventional treatment. Cadexomer iodine did not result in improved healing compared to conventional healing.
Storm-Versloot, 2010 ⁶	<ul style="list-style-type: none"> Patients with DFUs 	<ul style="list-style-type: none"> Silver-containing hydrofibre dressing 	<ul style="list-style-type: none"> Non-silver dressings 	<ul style="list-style-type: none"> One trial showed significant reduction in healing time with treatment. Insufficient evidence to establish whether silver treatments are effective at promoting wound healing.
<i>Randomized Controlled Trials</i>				
Belcaro, 2010 ⁷	<ul style="list-style-type: none"> Patients (n = 148) with venous or diabetic ulcers (location not specified) 	<ul style="list-style-type: none"> Multivalent silver oxide ointment 	<ul style="list-style-type: none"> Standard cleaning and compression management 	<ul style="list-style-type: none"> Observations in treatment group after four weeks of treatment: <ul style="list-style-type: none"> greater increase in skin PO2 and skin flux, greater reduction in total ulcer surface area, higher proportion of complete closure of ulceration.
Trial, 2010 ⁸	<ul style="list-style-type: none"> Patients (n = 42) with locally infected chronic wounds, including DFUs (29%) 	<ul style="list-style-type: none"> Ionic silver alginate matrix dressing (Askina Calgitrol Ag) 	<ul style="list-style-type: none"> Standard silver-free alginate dressing (Algosteril) 	<ul style="list-style-type: none"> Treatment not superior to comparator. Clinical scores of infection decreased in both groups after 15 days.

Table 2: Summary of Findings of Systematic Reviews, Meta-analyses, Randomized Controlled Trials and Non-Randomized Studies

First Author, Year	Population	Intervention	Comparator	Study Findings and Author Conclusions
Jeffcoate, 2009 ⁹	<ul style="list-style-type: none"> Patients (n = 229 after withdrawals, ≥ 18 years) with type 1 or 2 diabetes Chronic (> 6 weeks) full thickness DFU (area = 25-2500 mm²) 	<ul style="list-style-type: none"> Aquacel dressings 	<ul style="list-style-type: none"> Non-adherent, knitted, viscose filament gauze (N-A) Inadine (iodine-impregnated dressing) 	<ul style="list-style-type: none"> No difference in percentage of ulcers healed by 24 weeks, quality of healing (recurrence), and adverse events between the three groups.
<i>Non-Randomized Studies</i>				
Coutts, 2014 ¹⁰	<ul style="list-style-type: none"> Patients with DFUs (n = 8) and venous leg ulcers (n = 7) High mean body weight Extended wound durations 	<ul style="list-style-type: none"> Antibacterial foam (polyvinyl alcohol) dressing bound with gentian violet and methylene blue 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> At study end, improvements in surface critical colonization and pain scores were noted, especially for patients with DFUs
Schwartz, 2013 ¹¹	<ul style="list-style-type: none"> Patients (n = 15) with DFUs that were infected or had achieved a critical level of colonization 	<ul style="list-style-type: none"> Cadexomer iodine antibacterial dressing 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> Reductions in wound surface area, bacterial load (at 3 and 6 weeks), ulcer surface area, and ulcer depth were observed. No ulcers completely healed during the study period.
Nagoba, 2010 ¹²	<ul style="list-style-type: none"> Patients (n = 115) with DFUs (of different Wagner grades) 	<ul style="list-style-type: none"> Citric acid gel 	<ul style="list-style-type: none"> None 	<ul style="list-style-type: none"> Treatment was effective at controlling infection, especially in Wagner I and II grades (> 94% success rate), and Wagner III grades without deep osteomyelitis.

DFUs = diabetic foot ulcers.

REFERENCES SUMMARIZED

Health Technology Assessments

No literature identified.

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See: Infection Control – Non-limb-threatening infections, pages 41-43
Moisture Balance, page 44.

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APPENDIX – FURTHER INFORMATION:**Systematic Reviews – Topical Antimicrobials or Antimicrobial Dressings Not Specified**

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Randomized Controlled Trials*Combination Therapy*

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See: Management and Preventative Care, page s146

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