Evidence summary: Wound management-low resource communities: Citric acid as a topical antiseptic

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CLINICAL QUESTION

What is the best available evidence regarding the use of citric acid for wound management?

BEST PRACTICE RECOMMENDATIONS

All recommendations should be applied with consideration to the wound, the person, the health professional and the clinical context.

Citric acid as a 3% irrigation solution or ointment applied daily offers a low cost option for managing chronic clinically infected wounds in settings where there is limited or no access to antibiotic therapy or where conventional treatment has been ineffective (Grade B).

Citric acid 3% could also be considered for treatment of limb wounds caused by trauma with delayed presentation for care (Grade B).

Assess patient's level of pain and provide pain relief if required prior to commencing dressing (Grade A).

SOURCES OF EVIDENCE

This evidence summary is based on a structured search of the literature and selected evidence based healthcare databases (including WHO and WHO AFRO) for evidence published up to 2016 using the terms citric acid and wounds. The development of this evidence summary is based on the Joanna Briggs Institute methodology. Levels of evidence for intervention studies are reported in Table 1.

CLINICAL BOTTOM LINE

Citric acid has been used as a low-cost option for managing a wide range of chronic wounds which have not responded to conventional management. Sensitivity of a range of bacteria to 3% citric acid, including multiple antibiotic-resistant organisms, has been demonstrated through microscopy, culture and sensitivity (MC&S) (Level 5c evidence). Complete wound healing has been achieved in a high percentage of cases with daily application of 3% citric acid (Levels 2c, 4b, 4c, 4d evidence) and histological findings suggest that citric acid may not create an environment that is toxic to a healing wound (Level 5c evidence). Some patients report mild to moderate irritation for several minutes after application (Level 4b, 4c, 4d evidence, although with superficial burns and large raw areas the burning sensation can be severe (Level 2c evidence). Randomised controlled trials on the effectiveness and safety of citric acid as an antiseptic with large sample sizes are required.

Table 1: Sources of evidence and the level

Level 1 Evidence	Level 2 Evidence	Level 3 Evidence	Level 4 Evidence	Level 5 Evidence
Experimental Designs	**Quasi-experimental Designs**	**Observational – Analytic Designs**	**Observational –Descriptive Studies**	**Expert Opinion/ Bench Research**
1.c RCT[14]	2.c Quasi-experimental prospectively controlled study[1]		4.b Cross-sectional study[2-4,7,8,13] 4.c Case series[5,6,10,12] Case studies[9,16,17]	5.c Bench research[11,15]

Types of wounds

Evidence on the use of citric acid for wound irrigation and/or topical application has been reported for a range of wounds including burns,[1] foot ulcers,[2,3] traumatic wounds,[4] necrotising fasciitis,[5] bursitis,[6] lepromatous (Hansen's disease) ulcer[7] and surgical site infections.[8-10]

Microbiology and histology

A study tested the effectiveness of four topical antiseptics against multi-drug resistant Pseudomonas aeruginosa in full thickness burns in rats. Only two of the antiseptic dressings — nanocrystalline silver-coated and silver sulphadiazine 1% dressings — were effective ($p<0.05$), while the results for chlorhexidine acetate and citric acid 3% were not significant[11] (Level 5c).

In a study of patients with chronic wounds infected with multiple antibiotic-resistant Escherichia coli, the bacteria were eliminated and the wounds completed healed in all 34 patients following daily application of 3% citric acid (range 7–42), with diabetic foot and Hansen's disease ulcers taking the longest to heal [3] (Level 4b).

In two cases M&CS conducted before and after application of citric acid to non-diabetic foot ulcers showed eradication of multiple antibiotic-resistant Staphylococcus aureus after six treatments and E. coli after two treatments. The number of colonies cultured before the application of citric acid was unclear, although in the second case there was active pus discharge (i.e. the ulcer in the first case may not have been clinically infected) Histological findings from the same study showed development of blood vessels and proliferating fibroblasts after two to six days in the ulcers irrigated daily with 3% citric acid and dressed with a 3% citric acid soaked pad[12] (Level 4c evidence).

In cases in which MC&S had been performed, other organisms that were sensitive to 3% citric acid included streptococci, Klebsiella spp, Citrobactre spp, Staphylococcus albus and Proteus spp. In a number of cases the isolated organisms were found to be sensitive to citric acid while being resistant to a wide range of antibiotics[1,2,4,7,8,13] (Level 5c evidence).

The inhibition of bacterial growth is thought to be due to citric acid's reduction of the pH of the wound.[2,14] The minimum inhibitory concentration (MIC) ranged from 500 to 2500 µg/ml (the MIC being the lowest concentration to which citric acid can be diluted and still remain effective)[7,8] (Level 5c evidence).

Promising results have been obtained in in-vivo studies of a citric acid-based, biodegradable hydrogel dressing material in terms of antimicrobial effects and compatibility with human fibroblasts.[15]

Effectiveness in promoting healing

A small double blinded, randomised control trial (n= 50) compared the effectiveness of daily applications of 3% citric acid and Eusol in healing lower limb, muscle deep ulcers resulting from trauma more than 10 days before presentation. (NB. Eusol should no longer be used for any wound management.) The mean time to development of healthy granulation tissue in the citric acid group was 10.56 days compared to 20.04 days in the group treated with Eusol ($p=0.00$). The biopsied tissues from the citric acid group showed a substantial concentration of fibroblasts and neovascularisation at day 7 while these were sparse in the Eusol group tissues. The group treated with citric acid dressings consequently had much shorter hospital stays for approximately half the cost when compared to the group treated with Eusol. Forty percent of the participants were diabetics divided almost equally between the two groups. When compared with the non-diabetic patients in their group, the mean length of hospital stay for the diabetics in the citric acid group was almost the same as the non-diabetics (16.38 days vs 15.78 days). In the Eusol group the mean length of stay for the diabetics was 31 days compared to 24.04 days for non-diabetics in this group.[14] A quasi-experimental study was undertaken with 66 participants with clinically infected burns that had not responded to conventional treatment. In the intervention group (n=46, 5–60% superficial to deep burns) daily application of 3% citric acid in paraffin was associated with complete healing in 40 (87%) cases in 7–25 days, while healthy granulation tissue formed in the remaining six patients. There was no significant statistical difference ($p=0.145$) in overall healing compared with the control group (n=20, 10–70% superficial to deep burns) whose burns were treated with daily topical silver sulfadiazine and systemic antibiotics — 9 cases (45%). Participants in the antibiotics group had more severe burns in terms of depth and total body area coverage[1] (Level 2c evidence).

In a large prospective observational study (N= 259) of non-diabetic patients with traumatic wounds which had

not responded to antibiotics and daily povidone iodine dressings, 244 (94%) wounds healed completely with debridement followed by 5–25 days of daily normal saline

irrigation and application of 3% citric acid (the remaining six patients required skin grafting). A significant reduction in exudate and pain was observed after 2–3 applications of citric acid[4] (Level 4b).

In another uncontrolled observational study (N=115) of patients with clinically infected diabetic foot ulcers (Wagner grades I–III) not responding to conventional treatment, 94% (n=32) of grade I ulcers treated daily with 3% citric acid in paraffin healed in 5 to 30 days. Ninety four percent (n=49) of Wagner grade II ulcers and 86% (n=25) of Wagner grade III healed in 16 to 34 days. The majority of ulcers that did not completely heal developed healthy granulation and skin grafts were performed (Level 4b evidence). (Note: patients with peripheral vascular disease were excluded from the study[2]) (Level 4b).

Similar results were obtained in a study of 70 patients with surgical site infections that were not responding to conventional treatment. Daily application of 3% citric acid ointment for 6–25 days resulted in complete healing or formation of healthy granulating tissue allowing final suturing of gaps in the wound in all but one case[8] (Level 4b).

In a study of 34 patients with Hansen's disease and ulcers that were not responding to antibiotic therapy, daily applications of 3% citric acid eliminated the pathogens and completely healed all the ulcers in 25 patients (74%). In the remaining nine patients healthy granulation tissue formed but complete healing did not occur, possibly due to underlying nerve and blood vessel damage from the disease[7] (Level 4b).

Another small study trialled the use of citric acid to prepare the wound bed for grafting in five road trauma cases with large raw areas infected with multiple antibiotic-resistant bacteria. Healthy granulation tissue was generated in four patients (80%) but deep seated infection could not be eliminated in the fifth patient[13] (Level 4b).

In another ten case studies, a variety of clinically infected chronic wounds treated with 3% citric acid achieved complete healing (n=8)[6,9,10,16,17] or sufficient granulation tissue to allow skin grafting (n=2).[5] The number of applications of citric acid ranged from 8 to 50, mainly on a daily basis but in some were on alternate days (Levels 4c & 4d).

ADVERSE EVENTS

Application of citric acid to wounds can be associated with mild to moderate irritation for up to five minutes post application.[3,4,8,10] (Levels 4b, 4c & 4d) In superficial burns the effect can be more severe in the first 2–3 minutes after application[1] (Level 2b).

CONFLICTS OF INTEREST

The author declares no conflicts of interest in accordance with International Committee of Medical Journal Editors (ICMJE) standards.

ABOUT WHAM EVIDENCE SUMMARIES

WHAM evidence summaries are consistent with methodology published in

Munn Z, Lockwood C, Moola S. The development and use of evidence summaries for point of care information systems: A streamlined rapid review approach, Worldviews Evid Based Nurs. 2015;12(3):131-8.

Methods are provided in detail in resources published by the Joanna Briggs Institute as cited in this evidence summary. WHAM evidence summaries undergo peer-review by an international review panel.

WHAM evidence summaries provide a summary of the best available evidence on specific topics and make suggestions that can be used to inform clinical practice. Evidence contained within this summary should be evaluated by appropriately trained professionals with expertise in wound prevention and management, and the evidence should be considered in the context of the individual, the professional, the clinical setting and other relevant clinical information.

PUBLICATION

This evidence summary has been published in:

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