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| **Evidence Summary: Wound Management-low resource communities: Citric Acid as a Topical Antiseptic**  | **May 2016** |

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**CLINICAL QUESTION:** What is the best available evidence regarding the use of citric acid for wound management?

**SUMMARY**

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 rangeof bacteria to 3% citric acid, including multiple antibiotic- resistant organisms, has been demonstrated through microscopy, culture and sensitivity (MC&S). Complete wound healing has been achieved in a high percentage of cases with daily application of 3% citric acid and histological findings suggest that citric acid may not create an environment that is toxic to a healing wound. Some patients report mild to moderate irritation for several minutes after application, although with superficial burns and large raw areas the burning sensation can be severe. Randomised controlled trials on the effectiveness and safety of citric acid as an antiseptic with large sample sizes are required.

**BEST PRACTICE RECOMMENDATIONS**

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* 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)

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**SOURCES OF EVIDENCE**

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| **Level 1** | **Level 2** | **Level 3** | **Level 4** | **Level 5** |
| Experimentaldesigns | Quasi-experimentaldesigns | Observational – Analytic designs | Observational - descriptive studies | Expert opinion Bench research |
| RCT 14 |  One 1 | 2, 3, 4, 7,8,13  | Case series 5, 6, 10, 12 | Bench studies 11,15 |
|  |  |  | Case studies9, 16, 17 |  |

**EVIDENCE**

*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) ulcers7 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 5 evidence)

In a study of patients with chronic wounds infected with multiple antibiotic-resistant *E.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 4 evidence)

In two cases M&CS conducted before and after application of citric acid to non-diabetic foot ulcers showed eradication of multiple antibiotic-resistant *S. 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 4 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 5 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 2 500µg/ml (the MIC being the lowest concentration to which citric acid can be diluted and still remain effective).7, 8 (Level 5 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 2 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 4 evidence)

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 4 evidence)

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 4)

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 4 evidence)

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 4 evidence)

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 8-50, mainly on a daily basis but in some were on alternate days (Level 4 evidence).

*Adverse effects*

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 2 evidence)

**METHODOLOGY**

This evidence summary is based on a structured search of the literature and selected evidence based healthcare databases (including WHO and WHO AFRO) using the terms citric acid and wounds. The development of this evidence summary is based on the Joanna Briggs Institute methodology.18

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