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| **Evidence summary: Wound management: Antiseptics – acetic acid**  **Low Resource Communities** |

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**AUTHOR:** Wound Healing and Management Group – R. Watts, Curtin University

**CLINICAL QUESTION:** What is the efficacy of acetic acid in relation to anti-microbial action and wound healing?

**BEST PRACTICE RECOMMENDATIONS**

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* In adult patients with soft tissue wounds or burns infected with *Pseudomonas* *aeruginosa*, treatment with acetic acid 1-3% is likely to be effective. (Grade A)
* Acetic acid may also be useful in treating wound infections caused by other organisms, for example *A. baumannii* (Grade B)
* As with all antiseptics, acetic acid should only be used in the short term i.e. its use should be discontinued when signs of infection are no longer present. (Grade A)
* Daily application of acetic acid to the wound should be sufficient. (Grade B)
* The use of a polylacticacid- acetic acid matrix dressing may offset the slowing effect of acetic acid on some components of the healing process by the regenerative effects of the polylacticacid. (Grade B)
* If commercial dilutions of acetic acid are not available, detailed instructions on the method of dilution of glacial (pure) acetic acid must be provided; alert messages placed in the bottles; and independent double checking be done for the solutions used, calculations and measurements, and labelling. Orders for its use should be written, including the strength required. These instructions should be developed and implemented by a qualified pharmacist. (Grade A)

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**SOURCES OF EVIDENCE**

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| **Level 1** | **Level 2** | **Level 3** | **Level 4** | **Level 5** |
| Experimental designs | Quasi- experimental designs | Observational analytic designs | Observational descriptive designs | Expert opinion Bench research |
| 1 RCT 3 | None | 1 cohort study with controls 16  1 case controlled study 5\*  6 studies without control group 2, 4, 11, 14, 9 | 1 case series 13  1 case study 12 | 4 *in-vitro* study 1, 5\*,9,15,18  1 *in-vivo* study 10  1 *in-vitro+ in-vivo* study17 |

\*Study includes both a clinical component and a laboratory component

**BACKGROUND**

Acetic acid is a traditional antiseptic with an ancient history claimed to go back more than 6,000 years.1 Its more modern use in wound management dates from World War 1 when Taylor found that treating wounds with a 1% solution for two weeks resulted in the elimination of *Bacillus pyocyaneus* 2. There have been a number of studies conducted on the efficacy of acetic acid since that time.3, 4, 5, 2, 6, 7 Interest in traditional antiseptics, including acetic acid, has been rekindled with the rapidly increasing problem of antibiotic resistance. Acetic acid is readily available, inexpensive and does not have the systemic adverse effects of some modern antiseptics.8

**EVIDENCE**

*Anti-microbial effect*

A standardised *in-vitro* study9 compared the antimicrobial effect of acetic acid 3% with povidone-iodine 11%; polyhexanide 0.04%; mafenide 5%; and chlohexidine gluconate 1.5% cetramide 15% on a typical bacterial spectrum for a burns unit. Both Gram-positive and Gram negative bacterial strains were tested. In the acetic acid treated group all detectable colony forming units (CFUs) of *P. vulgaris, P. aeruginosa, A. baumannii* and β. haemolytic *Streptococci* B were eliminated after 5 minutes at the lowest dilution (10-2). In respect to *P. vulgaris,* acetic acidwas more effective than all but one of the other antiseptics (chlorhexidine gluconate 1.5% cetramide 15%). At 30 minutes all but one of the remaining five organisms had been eliminated by the acetic acid while it took 60 minutes for acetic acid at the lowest dilution to eliminate *E.Coli.* (Level 5)

In contrast, an *in-vivo* study10 using a weaker strength of acetic acid (0.25%) and employing a porcine model, found that all the wounds were clinically infected by day four of the study. Wound cultures showed >105 coloniesper gram of tissue at 4 and 7 days of treatment. (Level 5)

In an Indian study11 cultures taken from seven hospitalised patients with wound infections that had not responded to routine treatment for more than seven days, grew *P. aeruginosa.* These wounds included post-operative wound infections, abscesses and infected foot ulcers. Six of the patients were treated once daily with 3% acetic acid in the form of wound irrigation/wash followed by a gauze-soaked dressing until the wound healed completely and cultures yielded no growth. No antibiotics were given during this period to any of the patients. Five percent acetic acid was used to treat the remaining patient who had a chronic abscess which was non-responsive to antibiotics plus the causative bacterium was resistant to 15 other anti-microbial agents. In all seven patients *P. aeruginosa* was successfully eliminated from the wound with successful healing by secondary intention with between 2 -12 applications (mean = 9.1). (Level 3e) In the same hospital a patient with an abdominal surgical incision post hysterectomy infected by *P. aeruginosa* was treated, due to a local shortage of antibiotic options, with daily wound irrigation of 3% acetic acid for 10 days. On completion of treatment the wound had healed completely and cultures were negative.12 (Level 4)

Two other clinical studies13,14 also reported on the effectiveness of acetic acid in treating Pseudomonal wound infections. Salati and Rather13 treated eight patients over a period of 22 months with a variety of confirmed Pseudomonal soft tissue wound infections. The primary reason for this treatment was that the patients could not afford to buy the newer antibiotics required. Gauze soaked 5% acetic acid dressings were applied four hourly. Negative wound cultures were obtained in four to 16 days. (Level 4) Al-Ibran and Khan14 treated 72 cases over a period of four years. The adult patients all had confirmed cultures of *P. aeruginosa* and burns of between 15-35% of total body surface. Daily gauze dressings soaked in 1% acetic acid were applied for 10-14 days. Sixty five (90%) patients returned negative wound cultures three days after the dressings were discontinued. (Level 3)

Ryssell. et.al.1 also investigated the effectiveness of a polylacticacid-acetic acid (3%) matrix to treat burns. This combined the regenerative effects of polylacticacid with the antiseptic action of acetic acid. In the *in-vitro* study the same range of bacteria and antiseptics were tested, with H2O as the control, as in the study9 reported above. The matrix sheets were placed on top of the agar plates and incubated for 20 minutes. Acetic acid again demonstrated a wide range of antiseptic effectiveness. Acetic acid, in common with all but one of the antiseptics (mafenide acetate), was effective in eliminating CFU’s for all of the organisms tested. (Level 5c) The matrix dressing was also compared to the microbial effect of two commercially available nanocrystalline silver dressings, again using a 3% solution of acetic acid, in an *in vitro* study15  After 60 minutes of incubation the matrix eliminated *P. aeruginosa, A. baumannii* and *K.pneumoniae* while the other two dressings still showed >103 CFU, although this was not at a clinically significant level of infection. (Level 5)

These laboratory studies were accompanied by a matched pair study16 involving 20 patients with IIb0 or III0 burns. The polylacticacid-acetic acid matrix was compared to silver sulphadiazine (SD-Ag) as the topical treatment for the matched symmetric burns. Although the results were not statistically significant, there was a beneficial tendency to the acetic acid matrix treatment. Following surgery on days 4-5, invasive infection, i.e. bacterial loads greater than 105 bacteria/g of tissue, was present in seven of 20 SD-Ag treated areas (35%) compared to three of the twenty areas treated with the polylacticacid-acetic acid matrix (15%). Also there were lower numbers of Gram–negative bacteria (*P. aeruginosa* and *A. baumanii)* found in the burns treated with the acetic acid matrix*.* (Level 3)

*Wound healing*

One of the earlier studies17 of topical antimicrobial toxicity examined the effects of three antibiotics and four antiseptic agents, including acetic acid, on fibroblasts using both *in-vitro* and *in-vivo* (rats) methods. The rat wounds were irrigated three times a day with acetic acid 0.25%. On days four and eight the wounds were statistically significantly un-epithelialised. By day 12 there was no statistically significant difference between the wounds treated with acetic acid 0.25% and the controls irrigated with saline. At four days the tensile strength of the open wounds treated with acetic acid was comparable with those irrigated with normal saline and by day eight exceeded those of the two control groups (saline and no treatment). The method of reporting and analysing bacterial counts in this study did not allow for determining if bacterial levels were clinically significant (Level 5)

An *in-vitro* study18 established toxicity indexes of 17 commercially available skin and/or wound cleansers for fibroblasts and keratinocytes. Acetic acid 0.25% generated a toxicity index of 10 on a scale of 0-100,000 for both fibroblasts and keratinocytes. This compares to hydrogen peroxide and povidone-iodine with a toxicity index of 1,000 for fibroblasts, and 10,000 and 100,000 respectively for keratinocytes. (Level 5)

The previously mentioned *in-vivo* study10 employing a porcine wound model also examined the effects of five commonly used antiseptic or antimicrobial treatments on wound repair. The topical agents were mafenide acetate 5%, povidone 10% with free iodine 1%, sodium hypochlorite 0.25% (“half strength” Dakin), hydrogen peroxide 3% and acetic acid 0.25%. Four components of wound healing were assessed at four and seven days. Compared to the control (no treatment), at four days wounds treated with acetic acid showed significantly increased fibroblast proliferation (p<0.05) and 77% re-epithelialisation but significantly less neo-dermal thickness (p <0.01). By day seven in the wounds treated with acetic acid re-epithelialisation was complete, neo-dermal thickness was now greater than the control as was capillary ingrowth but not significantly so. None of the tested antiseptics had either a positive or negative effect on collagen production. All wounds treated with acetic acid and controls exceeded the set threshold for infection (105 colonies per gram of tissue) (Level 5)

In the clinical studies 11,12,13,16 reported above (total of 100 cases) that assessed healing as well as anti-microbial effect, in general wounds healed after 10 to 14 days with a range of 2-16 days. In three of these studies11,12,13 there was purulent discharge from the wounds and cultures grew *P. aeruginosa* . In the remaining study16 there was a higher percentage of infection in the control group (35%) than the group treated with acetic acid (15%). No problems with healing were reported in any of these studies. (Levels 3 (x 2), 4 & 4) A study19 of 19 cases of wounds with hyper-granulation tissue treated with 5% acetic acid (vinegar) soaks for one to two weeks resulted in all the wounds healing successfully by secondary intention. (Level 3)

*Method of application*

Four methods of applying acetic were identified in the nine clinical studies included in this summary, however detail on the methods was very limited. Two6, 12 washed the wound (one 6 for 15 minutes twice daily), another11 combined washing and irrigating the wound with a soaked gauze pad, two referred to soaks. 2, 6 while the remaining four studies applied soaked gauze pads left in situ between dressing changes.4,5,13,14 The strength of the acetic acid ranged from 1-5% with a trend towards using lower strengths of 3% and 1% to eliminate adverse effects such as pain. The frequency of dressing changes varied widely from 4 hourly to alternate days, with the most common being daily. The length of treatment again ranged widely from 2-14 days governed in most cases by the results of wound cultures i.e. infection had been eliminated. All these methods had successful outcomes.

*Side effects*

In two of the reported clinical studies11,16 that used a 3% solution of acetic acid, no local allergic or systemic side effects were identified (Levels 5 & 3 respectively). However pain, itching, stinging, discomfort and/or odour have been reported when using higher concentrations.3, 6,13 (Levels 1, 3 & 4 respectively)

*Adverse events*

The unintentional use of pure acetic acid (“glacial acetic acid”) results in severe burns if immediate counteraction is not taken.20 (Level 4)

In a review article published in 1995,21 the authors referred to the risk of acidosis from protracted use of acetic acid over large surface-area wounds, however no evidence was provided to support this potential risk. Fearn, et. al.4 found no acid base disturbances in the sub-group of nine burn patients (n=31) on whom frequent serum electrolyte levels were done during treatment with a daily 1% acetic acid dressing (Level 3). Two more recent clinical studies of the use of acetic acid in burns patients 14,16 found either no systemic effects or did not report any with daily dressings using 1% acetic acid for 4-5 days or 3% for 10-14 days respectively. (Levels 3 & 3)

**METHODOLOGY**

This evidence summary is based on a systematic literature search conducted in Medline, EMBASE, the Cochrane Library, AMED and the WHO Afro library, combining search terms that describe management of skin wounds and acetic acid. Key words:wound care, acetic acid, traditional wound care. Retrieved studies were appraised for relevance and rigour using Joanna Briggs Institute appraisal tools. 20**s**

**REFERENCES**

1. Ryssell H, Radu C, Germann G, Kloeters O, Reidel K, Otte M, et al. Suprathel-antiseptic matrix: In vitro model for local antiseptic treatment? Adv Skin Wound Care. 2011;24(2):64-7.

2. Milner S. Acetic acid to treat *Pseudomonas aeruginosa* in superficial wounds and burns. The Lancet. 1992;340(8810):61.

3. Phillips I, Lobo A, Fernandes R, Gundara N. Acetic acid in the treatment of superficial wounds infected by pseudomonas aeruginosa. The Lancet. 1968;291(7532):11-2.

4. Fearn J, Ahmed S, Hasan N. Efficacy of 1 per cent acetic acid in the control of pseudomonas wound infection Burns. 1976;3:229-31.

5. Gruber R, Vistnes L, Pardoe R. The effect of commonly used antiseptics on wound healing. Plast & Reconstr Surg. 1975;55(4):472-6.

6. Sloss J, Cumberland N, Milner S. Acetic acid used for the elimination of *Pseudomonas aeruginosa* from burn and soft tissue wounds. J R Army Med Corps. 1993;139:49-51.

7. McKenna P, Lehr G, Leist P, Welling R. Antiseptic effectiveness with fibroblast preservation. Ann Plast Surg. 1991;27(3):265-8.

8. Nagoba B, Selkar S, Wadher B, Gandi R. Acetic acid treatment of pseudomonal wound infections - a review. J Inf Public Health. 2013;6:410-5.

9. Ryssell H, Kloeters O, Germann G, Schafer T, Wiedermann G, Oehlbauer M. The microbial effect of acetic-acid - an alternative to common local antiseptics? Burns. 2009;35:695-700.

10. Bennett L, Rosenblum R, Perlov C, Davidson J, Barton R, Nanney L. An in vivo comparison of topical agents on wound repair. Plast & Reconstr Surg. 2001;108(3):675-85.

11. Nagoba B, Wadher B, Kulkarni P, Kolhe S. Acetic acid treatment of pseudomonal wound infections. Eur J Gen Med. 2008;5(2):104-6.

12. Nagoba B, Deshmukh S, Wadher B, Patil S. Acetic acid treatment of pseudomonal postoperative wound infection. J Hosp Infect. 1997;36(3):243-4.

13. Salati S, Rather A. Management of pseudomonal wound infection. Internet J Surg. 2008;20(1):1-7.

14. Al-Ibran E, Khan M. Efficacy of topical application of 1% acetic acid in eradicating pseudomonal infections in burn wounds. J Dow Univ Health Sc. 2010;4(3):90-3.

15. Ryssell H, Germann G, Riedel K, Reichenberger M, Hellmich S, Kloeters O. Suprathel-acetic acid matrix versus Acticoat and Aquacel as an antiseptic dressing: an in-vitro study. Ann Plast Surg. 2010;65(4):391-5.

16. Ryssell H, Gazyakan E, Germann G, Hellmich S, Reidel K, Reichenberger M, et al. Antiseptic therapy with a polylacticacid-acetic acid matrix in burns. Wound Rep Reg. 2010;18:439-44.

17. Lineaweaver W, Howard R, Soucy D, McMorris S, Freeman J, Crain C, et al. Topical antimicrobial toxicity. Arch Surg. 1984;120:267-70.

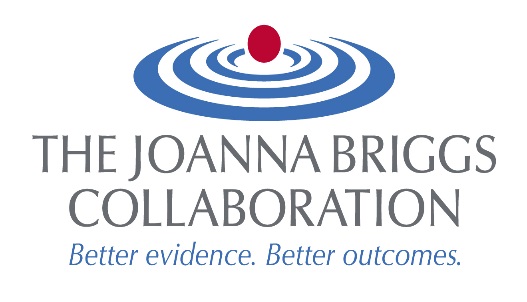
18. Wilson J, Mills J, Prather I, Dimitrijevich S. A toxicity index of skin and wound cleansers used on in vitro fibroblasts and keratinocytes. Adv Skin & Wound Care 2005;18(7):373-8.

19. Prodanovic E, Fosko S. Use of vinegar (acetic acid) to promote wound healing complicated by hypergranulation tissue. J Am Acad Dermatol. 2009;61(3 Supp1):AB203.

20. Grissinger M. End the "ice age": Is glacial acetic acid really needed? P&T. 2009;34(2):62.

21. Scott Ward R, Saffle J. Topical agents in burn and wound care. Physical Therapy 1995;75:526-38.

22. The Joanna Briggs Collabortion. Handbook for Evidence Transfer Centers – Version 4. The Joanna Briggs Institute, Adelaide. 2013.

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