WHAM Evidence summary: Antiseptics: Acetic acid

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CLINICAL QUESTIONS

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

CLINICAL PRACTICE RECOMMENDATIONS

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

In adults 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 (Grade B).

SOURCES OF EVIDENCE

This summary was conducted using methods published by the Joanna Briggs Institute.[1-4] This evidence summary is based on a structured 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 for evidence from 1990 to 2014 in English. Levels of evidence for intervention studies are reported in the table below.

BACKGROUND

Acetic acid is a traditional antiseptic with an ancient history claimed to go back more than 6,000 years.[5] 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.[6] There have been a number of studies conducted on the efficacy of acetic acid since that time.[6-11] 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.[12]

CLINICAL EVIDENCE

Anti-microbial effect

A standardised *in-vitro* study[13] 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 five minutes at the lowest dilution (10^{-2}). In respect to *P. vulgaris,* acetic acid was more effective

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**
None	None	3.c Cohort study with control group[14] 3.e Observational study without a control group[15-17]	4.c Case series[18] 4.d Case study[19]	5.c Bench and animal research[5, 13, 20-23]

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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*[13] (*Level 5*).

In contrast, an *in-vivo* study[20] 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 $>10^5$ colonies per gram of tissue at 4 and 7 days of treatment[20] (*Level 5*).

In a study conducted in India,[15] 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)[15] (*Level 3*). 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.[19] On completion of treatment the wound had healed completely and cultures were negative[19] (*Level 4*).

Two other clinical studies[16, 18] also reported on the effectiveness of acetic acid in treating Pseudomonal wound infections. Salati and Rather (2008)[18] 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[18] (*Level 4*). Al-Ibran and Khan[16] 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[16] (*Level 3*).

Ryssell. et. al. (2011)[5] also investigated the effectiveness of a polylactic acid-acetic acid (3%) matrix to treat burns. This combined the regenerative effects of polylactic acid with the antiseptic action of acetic acid. In the *in-vitro* study[5] the same range of bacteria and antiseptics were tested, with H_2O as the control, as in the study[13] 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[5] (*Level 5*). 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* study.[21] After 60 minutes of incubation the matrix eliminated *P. aeruginosa, A. baumannii* and *K.pneumoniae* while the other two dressings still showed $>10^3$ CFU, although this was not at a clinically significant level of infection[21] (*Level 5*).

These laboratory studies were accompanied by a matched pair study[14] involving 20 patients with IIb^0 or III^0 burns. The polylactic acid-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 10^5 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 polylactic acid-acetic acid matrix (15%).[14] Also there were lower numbers of Gram–negative bacteria (*P. aeruginosa* and *A. baumanii)* found in the burns treated with the acetic acid matrix[14] (*Level 3*).

Wound healing findings from animal and bench research

One of the earlier studies[22] of topical antimicrobial toxicity examined the effects of three antibiotics and four antiseptic agents, including acetic acid, on fibroblasts studied both *in-vitro* and in animals (rats). 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).[22] 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* study[23] 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[23] (*Level 5*).

The previously mentioned *in-vivo* study[20] 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 ($p < 0.01$).[20] 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 (10^5 colonies per gram of tissue)[20] (*Level 5*).

In the clinical studies[14, 15, 18, 19] 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 studies[15, 18, 19] there was purulent discharge from the wounds and cultures grew *P. aeruginosa*. In the remaining study[14] 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 & 4*). A study[17] 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[17] (*Level 3*).

CONSIDERATIONS FOR USE

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. In two studies[11, 19] the wounds were washed (one[11] for 15 minutes twice daily), another[15] combined washing and irrigating the wound with a soaked gauze pad, two referred to soaks,[6, 11] while the remaining four studies applied soaked gauze pads left in situ between dressing changes.[7, 8, 16, 18] 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 to 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 studies[14, 15] that used a 3% solution of acetic acid, no local allergic or systemic side effects were identified (*Levels 5 & 3*). However pain, itching, stinging, discomfort and/or odour have been reported when using higher concentrations[10, 11, 18] (*Levels 1, 3 & 4*).

Adverse events

The unintentional use of pure acetic acid ("glacial acetic acid") results in severe burns if immediate counteraction is not taken.[24]

In a review article,[25] 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 (1976)[7] 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[14, 16] of the use of acetic acid in burns patients 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 to 14 days respectively (*Level 3*).

Considerations when using acetic acid

- The use of a polylactic acid- 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 polylactic acid.
- 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.
- Daily application of acetic acid to the wound should be sufficient.
- 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.

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. More information is available on the WHAM website: https://www.whamwounds.com/ .

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 was published in The Joanna Briggs Collaboration library of evidence summaries in 2015.

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