Diluted Dakin's Solution:

Support for Antisepsis of Chronic Wounds

Integrated Literature Review

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Introduction

Great controversy exists among wound care experts regarding the use of topical antiseptics in wound care.

At a joint meeting of the Wound, Ostomy and Continence Nurse's Society and the Wound Healing Society in Minneapolis in June 1999, a consensus forum was held to discuss topical antisepsis, and it became clear that there was no consensus on this subject. There has been a trend to avoid the use of any topical antiseptics since the publication of the AHCPR guidelines for the treatment of pressure ulcers in 1994 which advised that topical antiseptics not be used for wound cleansing due to their cytotoxic effects on fibroblasts, cells essential to the creation of granulation tissue in wounds (AHCPR Clinical Practice Guideline Number 15, 1994, pg. 50). Dr. George Rodeheaver, Professor and Director of Plastic Surgery Research at the University of Virginia, has advised "not to put anything in a wound that you wouldn't put in your eye" (Rodeheaver, 1989).

It must be noted, however, that the intact, functioning eye has an intact system to control bacterial growth. A wound is an opening in the skin; a normal function of the skin is protecting the body from bacterial invasion. Thus, the protective barrier is removed, and wounds become contaminated and colonized with bacteria. Infection, in clinical practice, has been defined as the product of the entrance, growth, metabolic activities, and resultant pathophysiologic effects of microorganisms in the tissues of the patient (Robson, 1997). An uncompromised host often has the immune capability to overcome any contamination of the wound. If host defense mechanisms are compromised or there is a heavy bioburden of bacterial inoculum in the wound, clinical infection may result. The AHCPR guidelines site several studies that document a bacterial content in a wound of greater than 100,000 organisms per gram of tissue impairs wound healing. Persistently high levels of bacteria due to infection and necrosis keep the wound in an inflammatory state.

The cascade of events at the cellular level that moves the wound toward the proliferative phase of

healing is disrupted, and chronicity results (Robson, 1997). The healing process can proceed when the bacterial bioburden in wounds is reduced. In open wounds healing by secondary intention, the proliferative phase involves granulation, tissue formation, wound contraction, and resurfacing by epithelialization (Doughty, 1994).

The key cells in the proliferative phase of wound healing are fibroblasts, which are responsible for synthesis of connective tissue, endothelial cells, which are required for the development of new capillaries, and kerantinocytes which provide epithelialization.

The dilemma is finding an antiseptic solution that reduces the bacterial load in chronic wounds while being non-cytotoxic to the cells needed for proliferation. Studies have suggested that sodium hypochlorite solution (NaOCI), also known as Dakin's solution, at dilute concentrations, effectively reduces the bacterial burden while maintaining fibroblast viability. The purpose of this literature review is to determine if there is research that supports the use of a diluted Dakin's solution to promote healing of chronic wounds.

Methodology

This review of literature began by searching MEDLINE and CINAHL for research articles using the keywords sodium hypochlorite, Dakin's solution, wound, bacteria, antiseptics, and cytotoxic. The articles initially were limited to those published after 1990. The search was extended back to 1982 to find more primary sources of research. Articles that were anecdotal or did not include an actual research design were excluded. The criteria used for isolating research articles include 1) articles published after 1982; 2) articles that research the medical use of sodium hypochlorite solution, not dental use; 3) various concentrations of sodium hypochlorite solution were researched; and 4) that the bactericidal effects of the various concentrations were quantified.

Elements abstracted from each study review included: author, date, solution concentrations tested, species of pathogens studied, cells studied, *in vitro* versus *in vivo* testing, data analysis, and outcomes. It was then determined if the research did or did not support the

use of diluted NaOCL, or Dakin's solution, in topical wound therapy. Following the criteria established, six articles were retained.

Review of the Literature

Clinical studies have confirmed that Dakin's, or sodium hypochlorite (NaOCl) solution is bactericidal to organisms commonly found in open wounds. Lineaweaver and associates(1985) applied various concentrations of three topical antibiotics and four antiseptics to cultured human fibroblasts to quantitatively assess their cytotoxicity. At full strength, none of the antibiotics and all of the antiseptics were cytotoxic. However, no decrease of fibroblast survival was found with a 0.005% NaOCl solution. A bacterial toxicity assay was conducted by suspending cultures of *Staph aureus* in serial dilutions of topical agents for 15 minutes, then washed, applied to agar plates, and incubated for 24 hours. A 0.005% NaOCl solution was 100% bactericidal. Thus, a sodium hypochlorite (Dakin's) solution diluted to 0.005% is bactericidal while being non-cytotoxic to fibroblasts.

Heggers and colleagues (1991) examined 3 different concentrations of NaOCl for chemical parameters, bactericidal activities, and tissue toxicity. Ten microorganisms commonly found in wounds (*Enterococcus* species, *Streptococcus mitis, Staphylococcus aureus, Staphylococcus epidermidis, E. coli, Klebsiella pneumoniae, Enterobacter cloacae, Serratia marcescens, Proteus mirabilis,* and *Pseudomonas aeruginosa*) were exposed to buffered and non-buffered NaOCl solutions at the standard concentration of 0.25% and dilutions of 0.025%, 0.0125% and 0.007%. After timed exposures of 5, 10, 15, and 30 minutes, the bacterial cultures were inoculated onto agar plates and incubated. Concentrations of 0.25% and 0.025% proved to be bactericidal against all organisms tested within 30 minutes(either buffered or unbuffered). Gram-negative organisms selectively survived the 0.0125% concentration; the gram-positive organisms were susceptible.

In vitro toxicity was assessed in Hegger's study by exposing cultured mouse fibroblasts to buffered NaOCl solutions at concentrations of 0.25%, 0.025%, and 0.0125% for 10, 20, and 30 minute intervals. It was found that fibroblasts remained viable at the 0.025% and 0.0125% dilutions. To assess NaOCl for inhibition of wound healing, an *in vivo* toxicity assay was

conducted using rats (n=104). Three 2.5 cm full-thickness incisions were made along the dorsum of each rat. The incisions were closed with sutures interrupted with bolsters. The bolsters were saturated with buffered concentrations of 0.25% and 0.025% NaOCl solution, and normal saline every 4 hours. On days 3, 7, and 14, the animals were killed and tissue sections from the incisions were tested for tensile strength. There was found to be little or no difference between the test solutions and normal saline controls.

A study by Kozol and associates (1987) examined the effects of NaOCl on the function and viability of neutrophils, fibroblasts, and endothelial cells. Functional studies evaluated the influence of NaOCl on the viability and *in vitro* migration of neutrophils derived from rabbit peritoneal tissue. Serum suspensions of viable neutrophils were placed in the top compartment of filtered chambers; control media or various dilutions of NaOCl were placed in the lower chambers. The chambers were incubated for 1 hour, then the filters were examined. It was found that dilutions of NaOCl from 0.025% to 0.00025% resulted in 90% inhibition of neutrophil migration when compared to controls. The neutrophils remained viable, but failed to migrate. A return of chemotactic function was seen at a lower concentration of 0.000025%. Bovine endothelial cells and fibroblasts derived from rabbit skin were exposed to dilutions of NaOCl from 0.025% to 0.00025% for 30 minutes. Cellular damage was noted in both types of cells.

The bactericidal effects of antiseptics against *Xanthomonas maltophilia* and *Serratia marcescens,* pathogens that commonly cause nosocomial infections, were studied by Yasuda and colleagues(1997). Bacterial suspensions were exposed for periods from 20 seconds to 60 minutes to varying concentrations of five antiseptic solutions. All bacteria were killed after 20 seconds of exposure of NaOCl dilutions ranging from 0.02% to 0.002%.

A study by Cooper, Laxer, and Hansbrough (1991) used cultured human fibroblasts and kerantinocytes to evaluate the cytotoxicity of commonly used topical agents. The cell cultures were exposed to serial dilutions of these agents. The cells were then assessed for viability. They found that a 0.125% solution was cytotoxic to both fibroblasts and keratinocytes, but a 0.0125% solution caused no damage.

McKenna and associates (1991) studied the bactericidal capacity of various concentrations of antiseptics previously determined in Lineaweavers research to be non-cytotoxic to fibroblasts. Organism cultures of common pathogens were obtained from actual human wounds. These organisms were clinical isolates of *Staph aureus, E. coli,* Group D *Enterococci, Pseudomonas aeruginosa,* and *Bacteroides fragilis.* The cultures were exposed to the antiseptics for 15 minutes at room temperature, washed, then re-cultured. A 0.005% NaOCl solution suppressed all bacterial growth and was significantly more effective that the other antiseptics. It was the only antiseptic that inhibited *B. fragilis,* Group D *Enterococcus,* and *E. coli.*

Discussion

The topical therapy of chronic wounds using antiseptics balances between management of bacterial toxicity and inhibition of wound healing. Wound healing cannot be simply correlated with the viability of proliferative cells. Reducing bacterial counts and supporting the immune response of the host without compromising the activities of proliferative cells would constitute optimal antisepsis. Dilute concentrations of Dakin's solution from 0.025% to 0.005% have been demonstrated by these studies to meet all these parameters. In addition, it is extremely inexpensive to produce, and maintains its bactericidal capacity for several days when stored in an opaque, closed container (McKenna, 1991; Rutala, 1998).

With the tremendous human and monetary costs associated with chronic wound care, utilization of an inexpensive, readily available antiseptic that supports wound healing makes ethical and economic sense. In this author's wound care practice as Director of a wound care program for a home health agency, the care of patients with wounds from sixteen counties of north central Florida was supervised. Using a 0.0125% Dakin's solution as either an irrigant or in a daily wet-to-moist gauze dressing protocol, a variety of chronic wounds were healed, some of which had been present for years and had received myriad of other standard therapies. The author has observed consistently excellent clinical results when utilizing the diluted Dakin's solution. The studies included in this integrated review support the results of personal clinical observations. Further research using *in vivo* applications and human subjects for clinical trials is

indicated. By obtaining data concerning patient outcomes in wound healing, the effectiveness of various "safe" concentrations of diluted Dakin's solution could be examined. Subjects could include outpatients or long-term care patients with chronic wounds of a specific duration that had failed to heal after treatment with other standard topical therapies. Quantification of bacteria at the wound base, before and after application of various concentrations of diluted Dakin's solution determined to be bactericidal but non-cytotoxic to the proliferative cells, could be evaluated. Promotion of healing could be evaluated by measuring changes in wound volume and assessment of epithelial migration. Cost analyses could be carried out by calculating and recording the cost per dressing change and total costs to wound closure, and correlating this information with the cost incurred by other forms of topical therapy, if applied per protocol for the same period of time.

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