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Original Research Article

Effects of acetic acid and povidone iodine dressings as modulators of local environment in chronic wounds as synergists and separate agents

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ABSTRACT

Background: Wound care management has long been a primary point of care for surgeons and clinicians alike. The burden of care and time required in the management of wounds has led to development of innovative and expensive materials which alleviate the burden of healing on our physiology and reinforce the healing mechanisms.
Methods: A case series analysis of 240 patients included on accrual was carried out. These patients were randomly assigned to 3 groups. Group A ulcers were dressed with 2% acetic acid soaked sterile pads. Group B received the acetic acid-iodine combination and group C dressed with traditional Povidone-Iodine ointment and solution. These ulcers were evaluated on admission and on intervals of 5 days with a customized scoring system, Dr. Kamal's adaptive wound healing score (KAWHS). A sterile culture swab with coverage of healthy granulation tissue was considered the primary end point of the study.
Results: Resolution of slough was significantly earlier in group A and B as compared to group C. odor subsided earliest in group A, followed by group B and C. Resolution of purulent discharge was achieved earliest in Group B which was significant in comparison to group A and C. Wound healing was observed to be better in acetic acid usage groups.
Conclusions: Acetic acid dressings are effective in treating chronic non-healing wounds with mono and poly-microbial culture.

Keywords: Acetic acid dressings, Chronic wounds, Poly-microbial wounds, Wound healing score, Wound contraction, pH modification

INTRODUCTION

Wound care management has long been a primary point of care for surgeons and clinicians alike. The burden of care and time required in the management of wounds has led to development of innovative and expensive materials which alleviate the burden of healing on our physiology and reinforce the healing mechanisms. The fact of the matter is these innovations are not only expensive, but scarcely available in cities and villages where primary health care physicians are the only source of healthcare for the population. In the era of advancing medical sciences, we have somewhat overlooked the basics of wound healing, where the wound environment plays a major role in the process. Among the modifiable factors is the local pH of the wound, which is pivotal in the colonization of bacteria. Alkaline milieu has been found to be a prerequisite for the growth of most of the pathogens.[1-3] With the healing of the wound, there is a shift in pH towards neutral.[4-6] Modifying the wound pH can be the key in reducing infection. In our study we attempted a comparison of the healing prowess of 2% acetic acid, traditional topical antimicrobial (povidone-iodine) and the combination of both agents.

METHODS

This is a multi-center case series analysis of 240 patients suffering from chronic non-healing ulcers of varying etiologies. The study was carried out in two phases and two different hospitals between the period of February to June of 2016 in Pravara Rural Medical college, Loni and July 2016 to December 2019 in Al-Ameen Medical college, Bijapur.

Chronic non-healing ulcers are defined as, "ulcers that show no tendency to heal after 3 months of appropriate treatment or are still not fully healed at 12 months".[7] The exclusion criteria of the study were as follows: 1) patients with chronic debilitating systemic diseases (TB, Leprosy, and connective tissue disorders) 2) malignancy 3) graft rejections 4) age<20 yrs.

Daily dressings were done for all the patients.

Preparation of 2% acetic acid solution

Total 10 ml glacial acetic acid was filled in a syringe and mixed with 500 ml of sterile saline solution to achieve a concentration of 2% acetic acid.

Preparation of 2% acetic acid solution+povidone iodine solution

Total 2% acetic acid solution was prepared as mentioned above and 10 ml 10% povidone iodine solution was added to the mix to create a 2%Acetic Acid-iodine mixture.

Cleaning of the ulers

Each of these patient's ulcers were presoaked in EUSOL 1 hr before the dressing. EUSOL was used as the lone de-sloughing agent. This was followed by cleaning with saline solution and occasional removal of non-adherent slough as and when required. The ulcers were then dressed with the desired antimicrobial agent/2%acetic acid/ combination.

Patients were included on accrual and randomly assigned into 3 groups. Group A ulcers were dressed with 2% Acetic Acid soaked sterile gauze. Group B received the acetic acid-iodine combination and group C was dressed with traditional povidone-iodine ointment and solution. Acetic acid lowers pH for only one hour after which it returns to pretreatment levels, therefore patients were asked to sprinkle the wound with the respective solutions every hour so as to keep the wound in continuous contact with the agents.[8]

Culture and sampling

Cultures of the wounds were taken at admission and repeated every 5 days. Isolates were noted down at each interval.

The wounds were assessed clinically as follows: 1) presence of slough 2) odor 3) discharge 4) granulation tissue area in cm^2 5) wound size in cm^2.

A sterile culture swab with coverage of healthy granulation tissue was considered the primary end point of the study. Rate of wound contraction in each group was also assessed as an additional parameter.

Assessment of wound healing

Wound healing was assessed on the basis of a customized wound healing score which would not only help us with the assessment but also guide us when the healing process off tracked, stopped or even worsened. Since the parameters being used to monitor were clinically evident and the prevailing wound classifications either dealt with simple grading or needed to be assessed daily, we adopted and customized a score which would require an initial assessment at the time admission and re-assessment at intervals of 5 days. Although it helped us to objectively assess the progress of each wound, its efficacy is still to be evaluated in other types of wounds for which further studies are required.

The variables of slough, odor, discharge and culture isolate are assessed on the day of admission and subsequently at intervals of 5 days each. Wound contraction is assessed from day 5 onwards. Since the score would change with the condition of the wound, we arrived at the following nomenclature for the score-Dr. Kamal's Adaptive wound healing score (KAWHS) (Table 1). The system has a maximum score of 12 and minimum of 5, with 5 indicating a healthy healing wound and 12 indicating a non-healing wound.

Table 1: Dr.Kamal's adaptive wound healing score (KAWHS).

Parameter		Score
Slough	Present	2
	Absent	1
Odor	Present	2
	Absent	1
Discharge	Purulant/seropurulant	2
	Serous/clear	1
Culture isolate	Present	2
	Absent	1
Wound contraction (to be assessed from day 5 onwards)	<25%	4
	25-49%	3
	50-74%	2
	75-100%	1

Statistics

Quantitative parameters were described as standard measures of deviation whereas qualitative analysis was done using one-way ANOVA (Independent measures) for overall significance and independent t-test as post hoc test of significance between the means of the groups A, B and C for a 95% confidence interval (p=<0.05).

RESULTS

The mean age of the patients treated was 48.35 yrs in group A (acetic acid), 54 yrs in group B (acetic acid+ iodine) and 50 yrs in group C (iodine). Male predominance was noted in group A & C with 57.5% and 52.5% respectively, whereas it was 1:1 ratio in group B.

Most common etiology was traumatic (37.5%) in group A, diabetes (40%) in group B and secondary infections (37.5%) in group C.

Pseudomonas was found to be the most common isolate in all the three groups, it accounted for 32.5% of cases in group A, 40% in group B and 30% in group C, it was followed by Klebsiella (group A and B) and Proteus (group C).

Table 1: Variables and data distribution.

Variables	Results		
	A	**B**	**C**
Age	48.35±13.8	54.17±14.5	50.82±15
Most common etiology	Traumatic	Diabetic	Infective
Most common Isolate	Pseudomonas	Pseudomonas	Pseudomonas
Mean wound size in cm^2on admission	37±23.89	48.9±22.84	49.66±21.47
Days for sterile culture	10.675	9.825	21.425

Table 3: Significance values for parameters.

Parameters	P value for duration required for resolution between groups		
	A and B	**B and C**	**C and A**
Slough	0.148	0.00001	0.0006
Odor	0.000015	0.00001	0.00001
Discharge	0.00001	0.00001	0.0918
Wound contraction			
25%	0.457	0.000338	0.00858
50%	0.914	<0.00001	0.000049
75%	0.933	<0.00001	0.00001
Sterile culture	1.2421	<0.00001	<0.00001

All the wounds were measured on admission with the mean area being 37 cm2 in group A, 48.9 cm2 in group B, and 49.66 cm2 in group C (Table 2).

All these wounds were examined and followed for the resolution of slough, odor and discharge over period of the treatment. Mean durations required for resolution of these parameters were noted and tested for significance between the groups. There was a statistically significant difference between groups for slough, odor and discharge as determined by one-way ANOVA. The f-ratio value is 27.49. The p-value is <0.00001. The result is significant at p<0.05.

Duration required for resolution of slough was significantly lower in group A (M=7.9, SD=2.3) &B (M=7.1, SD=2.1) when compared to group C (M=9.5, SD=1.7), t (79)=3.5; 5.47 p=0.0006 & <0.00001 respectively. There was no significant difference between group A and B (Table 3).

The duration of resolution of odor also had a significant difference between the groups, group A (M=4.8, SD=1.6), group B (M=7.05, SD=2.6), group C (M=9.3, SD=1.04) with p=0.000015 for group A & B, .00001 for group B and C, 0.00001 for group C & A. Among the three groups, group A showed the least duration for resolution of odor.

Duration for resolution of wound discharge was significantly lower in group B (M=6.8, SD=1.9) as compared to group A (M=10.4, SD=2.6) and group C (M=9.6, SD=1.34); p=0.00001 for group B and A and p=0.00001 for group B and C. There was no significant difference between A and C (p=0.0918).

Duration required to achieve sterile wound culture was significantly less in group A (10.675 days) and group B (9.825 days) as compared to group C (21.425 days), however no significant difference was noted between group A and B, p=1.2421.

Group A exhibited similar healing trajectory as Group B by achieving a score of 6 in 20 days and a baseline normal score of 5 by day 25. On the other hand, group C achieved a score of 6 by day 25 and a normal score of 5 by day 45.

DISCUSSION

Chronic wounds have been a problem for patients and clinicians alike. A variety of factors contribute towards the formation of a micro-environment that delay/retard collagen synthesis, fibroblast proliferation and epithelization. These factors may be systemic such as the presence of co-morbidities, nutritional status, and hygiene, prolonged use of steroids or local factors which include bacterial load, microbial isolate and area of the wound. Although topical agents have been and will be an integral part of wound management, many agents contribute towards the development of an adverse micro-environment. Repeated and excessive treatment of wounds with antiseptic agents, except for short-time application to attack the causative pathogens and to control the infection, may have negative outcomes or promote a microenvironment similar to those found in chronic wounds.[8]

Silver sulfadiazine has a broad spectrum of antibacterial, antifungal and antiviral activity. It is the most commonly used antiseptic agent in burn wound management but it is toxic to fibroblasts in culture.[9] Also, it requires frequent dressing changes, delays re-epithelization and stains tissue. It may also cause allergic reaction and transient leucopenia.[10] Mafenide acetate (sulfamylon) has a broad antibacterial spectrum and has ability to penetrate eschar, its disadvantages include occasional pain on application and inhibition of epithelization.[11,12] Silver nitrate also has a broad antibacterial spectrum but its application to wound can slow down the process of epithelization.[13]

Betadine (povidone-iodine) is most commonly used antiseptic agent. It covers a broad antibacterial and antifungal spectrum but in most instances, it does not effectively promote good wound healing. Most studies show that it impairs wound healing and reduces wound strength.[13] Cooper and Laer observed that betadine solution tested at multiple dilutions was found to be most toxic of all agents tested on fibroblasts and has deleterious effect on wound epithelization when used in non-diluted concentrations.[14,15]

Dakin's solution containing hypochlorite (dilute bleach) has a broad antibacterial activity but is toxic to fibroblasts and it has been found that it also retards collagen synthesis and delays epithelization, and also inhibits migration of neutrophils in a wound bed, thus undermining the body's natural defense system.[15] The wound treated with Dakin's solution were significantly slower to epithelize and neo-vascularize.[16-18] They are toxic to tissues because they oxidize tissue enzymes.[19] Antiseptic agents such as hydrogen peroxide, iodine and alcohol and others are also cytotoxic and retard wound healing process.[20,21]

Acetic acid is easily available, inexpensive and non-toxic as compared to other topical agents or systemic antibiotics. Very high concentrations may cause burning sensation and skin irritation, and are generally not required. Some studies have suggested cytotoxic effects of acetic acid in vitro, but clinically no such effects have been found.[20] Acetic acid lowers the pH of the wound, consequently affecting the healing process of the wound by several mechanisms. Since most pathogenic bacteria require a pH value higher than 6, their growth is inhibited by application of acetic acid.[22-24] It has been found that lowering of pH in the wound leads to reduction in bacterial protease activity.[25,26] Low pH in wound surroundings promotes wound healing and oxygen radical production for killing of bacteria by improving cell oxygenation by Bohr effect.[27] It also leads to increase in macrophage fibroblast activity and reduces toxicity of bacterial end products.[28] All these actions collectively lead to rapid decontamination with improved granulation.

In our study we used a concentration of 2% Acetic acid which was used individually in group A and in combination with 10% Povidone iodine solution in group B. None of the patients experienced skin irritation or burning. 10% Povidone Iodine solution was used in group C as the sole topical antiseptic.

Effects on slough, odor and discharge

Resolution of slough was significantly earlier in group A and B as compared to group C. Odor subsided earliest in group A, followed by group B and C. Resolution of purulent discharge was achieved earliest in group B which was significant in comparison to group A and C (no significant difference noted between these two groups).

Effects on poly-microbial wound environment

The most common organism isolated in chronic wounds is Pseudomonas, although poly-microbial infections are encountered. In the present study we encountered similar trends where pseudomonas was the dominant microbe in most wounds and in some cases it was present along with another microbe. 2% acetic acid and the acid-iodine combo were able to eradicate these microbes significantly earlier than the lone iodine solution. Agarwal.et.al were able to achieve and demonstrate poly-microbial efficacy of acetic acid in their study.[29]

Povidone-iodine is a water-soluble iodophor (or iodine-releasing agent) that consists of a complex between iodine and a solubilizing polymer carrier, polyvinyl-pyrrolidone (PVP).[30] In aqueous solution, a dynamic equilibrium occurs between free iodine (I2), the active bactericidal agent, and the PVP-I-complex. In combination with the bacteriostatic properties of acetic acid which includes membrane disruption, interruption of metabolic reactions and accumulation of toxic anions, the PVP-I complex is able to eliminate microbes in a more efficient manner. This would otherwise be time consuming when Povidone-Iodine is used as a single agent, as is observed with the mean duration to achieve a sterile culture being lesser in group A (10.675 days) and least in group B (9.825 days). This duration more than doubled in group C (21.425 days).

Wound contraction is a sign of healthy wound healing and the rate of contraction is clinically evaluated on every dressing. The groups A and B showed better and faster wound contraction than group C. There was also a better even distribution of pink granulation tissue in A and B, whereas group C showed patchy un-even distribution of granulation.

Although we observed the efficacy of acetic acid dressings in chronic wounds, the study has its limitations. We could not study the efficacy of acetic acid dressings in fungal infections (as done by Agarwal et al), graft rejections and burn wounds. We also were unable to compare the efficacy of acetic acid dressings with other newer dressings such as the silver and hydrocolloid dressings.

CONCLUSION

Total 2% acetic acid when used individually or in combination with Povidone-Iodine is significantly effective in chronic wounds with mono and poly-microbial cultures than Povidone-Iodine up to as a single antiseptic. Dr. Kamal's adaptive wound healing score (KAWHS) provided a simple, hassle free monitoring system.

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