Efficiency of Cadexomer Iodine in Healing of Chronic Leg Ulcer in View of Size and Volume

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ABSTRACT

BACKGROUND

An ulcer is a break in the skin or mucous membrane with loss of surface tissue, disintegration and necrosis of epithelial tissue, and often infection. Chronic ulcers are ulcers present for more than 6 weeks and do not show the tendency of normal healing and require intervention for the healing process. There are several studies regarding wound treatment with topical applications and dressings that evaluate change in the bacterial bioburden and healing of the wound. In this study, we wanted to emphasize the in-vivo effect of cadexomer iodine antibacterial dressing on chronic non-healing ulcers.

METHODS

In this study, we have taken 20 patients with chronic non-healing ulcers of various types and used cadexomer iodine dressing for 6 weeks. We have compared the surface area and volume of the ulcer in the 4th and 6th weeks.

RESULTS

Over the study period, there was a median reduction of 10.66 ± 7.00 cm^2 of the wound surface area. There were no patients who completely healed their ulcer over the 6 week study period. This was accompanied by a median reduction of volume of the ulcer 19.82 ± 27.50.

CONCLUSIONS

There is a decrease in the surface area and volume of the chronic leg ulcer which helps in the preparation of the wound bed. The use of cadexomer iodine is a cost-effective method for treating chronic wounds in rural India.

KEY WORDS

Biofilm, Venous Ulcer, Diabetes, Dressing.

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BACKGROUND

An ulcer is a break in the skin or mucous membrane with loss of surface tissue, disintegration and necrosis of epithelial tissue, and often infection. [1] Chronic ulcers are ulcers present for more than 6 weeks and do not show the tendency of normal healing and require intervention for the healing process. The chronic ulcer has common and rare aetiology. Common causes are venous insufficiency, arterial disorders, diabetes and vasculitis. [2,3] The prevalence of acute and chronic wounds was 10.55 and 4.48 per 1000 population respectively according to Indian based study. Wound dressing selection plays a key role in managing wounds by clinically assessing and ruling out the agent causing the chronicity of the wound. Management of chronic wound dressing is to achieve a moist wound environment, preventing infection and minimizing skin irritation. [4] There is growing recognition that biofilm is the major cause for the chronicity of the wound and the recent issue of biofilm over chronic wounds has altered the therapeutic modalities for breaking down the biofilm.[5] Treatment modalities of chronic ulcer are complex, it requires wound characteristics and patient selections. There are several challenges such as appropriate dressing, patient adherence, painful therapies etc.[6] in treating chronic ulcers. The use of antiseptics is preferred to antibiotics because of the risk of the development of bacterial resistance in the treatment of wounds. Topical treatment with iodine has proven to be effective against a wide range of bacterial and fungal infections and to our knowledge, bacterial resistance against iodine has never been reported.[7]

The skin has a quick and efficient wound healing process in absence of complicating factors and maintains barrier function. Healing is relatively slow in aged people but there are many associated conditions such as diabetes, vascular diseases, immobility leading to the development of the chronicity of the ulcer. As the duration increases there will be a change in the microenvironment of the wound, so that accumulated change reaches beyond level leading to the non-healing nature of the wound. These microenvironment changes include failure to re-epithelialize, prolonged inflammation, defective extracellular matrix, defective capillary functioning finally leading to the decrease in tissue oxygenation and arrest in the inflammatory stage resulting in the chronic ulcer.[8]

Iodine is a natural dark violet, a non-metallic element that mainly helps in human metabolism. Davaine first demonstrated the antimicrobial properties of iodine in 1882. Since the mid-19th century, iodine-based preparations have had an important role in the prevention of surgical site infections. To overcome the side effects of elemental iodine, iodophors were developed. Iodophors are preparations that bind iodine to a solubilizing agent or carrier. The water-soluble complex allows the slow release of a low concentration of free iodine when the carrier comes into contact with wound exudates. Bonding iodine with other molecules results in the slow release of iodine that helps in preventing the effects of high concentrations of iodine. The controlled release of iodine helps in preventing the elemental side effects of free iodine. Povidone and Cadexomer iodine are types of iodophors used in ulcer dressings.[9]

Cadexomer is a hydrophilic starch polymer bead, containing 0.9 % w/w iodine. Pharmacodynamic study reveals that when in contact with wound exudates, cadexomer iodine releases free iodine (an antiseptic), which reduces the bacterial count.[10] Cadexomer iodine is being preferred over povidone-iodine as there is controlled release of iodine and prevents the systemic and local side effects compared to the povidone-iodine. In this study, the purpose was to emphasize the effect of cadexomer iodine in decreasing the surface area and volume of the chronic ulcer.
Wound closure is faster and there is significant re-epithelialization with wounds treated with cadexomer iodine compared to the normal saline dressings. Histology of the wounds treated with cadexomer iodine shows thicker epidermis when compared to other wounds dressings and there were significant differences in the number of cell layers in cadexomer iodine treated wounds. Chondroitin sulfate normally presents in the basement membrane of intact skin detected in the cadexomer iodine treated wounds as early as 12 days after starting the treatment. Wound contraction seems to be higher in wounds treated with cadexomer iodine than the normal saline dressings. Iodine released from the ointment was sufficiently low such that angiogenesis, granulation tissue formation and wound contracture were not affected and tissue toxicity was avoided.[7] In this study, the purpose was to emphasize the effect of cadexomer iodine in decreasing the surface area and volume of the chronic ulcer.

METHODS

A prospective interventional study for 6 weeks was conducted in the rural hospital, a tertiary care teaching hospital situated in Central India. Twenty patients with a chronic wound belonging to age between 18 and 65 years of both genders in outpatient department of General Surgery, (as per incidence of patients at our institute i.e. 10 patients per month) were enrolled for the study. Patients having immunosuppression, hepato-renal dysfunction and thyroid dysfunction were excluded. Wound size was calculated by placing an acetate sheet over the wound and tracing the wound border with a permanent pen. The area of the wound was calculated by counting the complete and half or more than half squares within the wound border taking it as 1 cm^2[10] Patients with chronic ulcers were taken for dressing on an OPD basis with a minimum size of 3 cm to a maximum size of 11 cm. Saline wash was given to the ulcer and 0.9 % cadexomer iodine was applied with 3 mm thickness over the ulcer. The ulcer was covered with gauze pieces, pads and a proper bandage was applied. The patient was advised to review in OPD after 48 hours. The dressing was repeated every 3rd day for 6 weeks of duration. Wound size and volume was assessed on the 4th week and 6th weeks. This procedure was explained to the patient with proper informed consent and the project was approved by the ethics committee (IEC no: DMIMS (DU)/IEC/2019/7893). Statistical analysis was done by using descriptive and inferential statistics using student's paired t-test and software used in the analysis was SPSS 26.0 version and $P < 0.05$ was considered as the level of significance. (As samples were paired and equal in number

for comparing the area with baseline most appropriate test was student paired t-test and mean reduction over the size of six weeks was compared using student paired t-test)

RESULTS

A total of 20 patients were enrolled in the study. Among them, 14 (70 %) were males and 6 (30 %) were females. The age of patients ranged from 45 to 65 years with a mean age of 55.60 ± 6.44 (55 - 65 years). 10 patients (50 %) belonged to age between 55-64 years. 10 patients (50 %) were having duration of ulcer more than 6 weeks. Out of 20 patients, 8 patients had diabetes, 4 patients with hypertension as co-morbidities. 4 patients had a traumatic ulcer and 6 patients had varicose veins. We have compared the surface area on the 2nd, 4th, and 6th weeks from baseline.

Assessment of Ulcer Surface Area

The mean ulcer area at baseline was 28.2 ± 17.26 cm^2. There was no significant reduction of ulcer area in the first 2 weeks. There was a mean ulcer area reduction of 2.30 ± 2.55 cm^2 observed overall in patients from 0 to 4th week and 10.66 ± 7.00 cm^2 area reduction from 0 to 6th week corresponding to a 37 % reduction in surface area from baseline to final assessment.

Assessment of Ulcer Volume

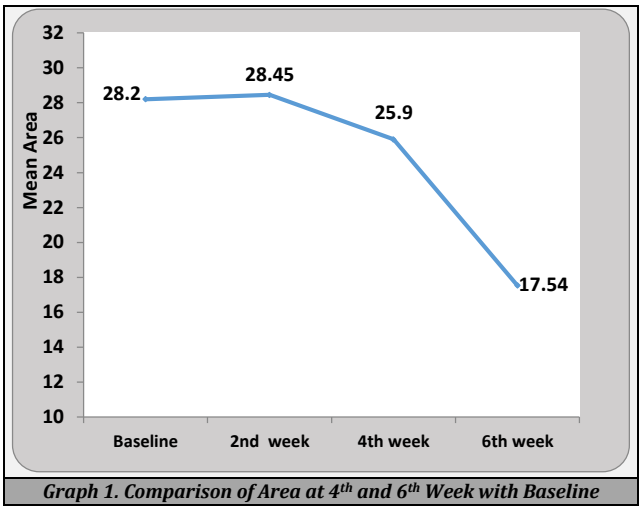
The mean ulcer volume at baseline was 49.5 ± 47.98 cc. There was no significant reduction of ulcer area in the first 2 weeks but there was a mean ulcer volume reduction of 19.82 ±2 7.50 observed overall in patients from 0 to 4th week and 41.42 ± 41.46 cc volume reduction from 0 to 6th week corresponding to an 83 % reduction in volume from baseline to final assessment. There was no significant reduction of surface area and volume of ulcer from the baseline to 2nd week but there was a decrease in the surface area and volume on 4th and 6th week.

		Mean	N	Std. Deviation	Std. Error Mean	Mean Difference	t-value
area	Baseline	28.20	20	17.26	3.86		
	2nd week	28.45	20	17.04	3.81	0.25±0.55 (0.88%)	2.03 P=0.056, NS
	4th week	25.90	20	17.54	3.92	2.30±2.55 (8.15%)	4.02 P=0.001, S
	6th week	17.54	20	12.61	2.82	10.66±7.00 (37.80%)	6.81 P=0.0001, S

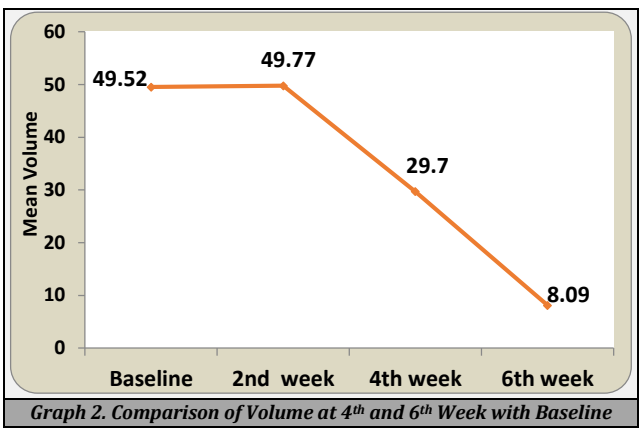
Table 1. Comparison of Area at 2nd 4th and 6th Week with Baseline

		Mean	N	Std. Deviation	Std. Error Mean	Mean Difference	t-value
Volume	Baseline	49.52	20	47.98	10.73		
	2nd week	49.77	20	47.83	10.69	0.25±0.63 (0.50%)	1.75 P=0.096, NS
	4th week	29.70	20	28.30	6.32	19.82±27.50 (40.02%)	3.22 P=0.004, S
	6th week	8.09	20	7.29	1.63	41.42±41.46 (83.66%)	4.46 P=0.0001, S

Table 2. Comparison of Volume at 4th and 6th Week with Baseline



Graph 1. Comparison of Area at 4th and 6th Week with Baseline



Graph 2. Comparison of Volume at 4th and 6th Week with Baseline

DISCUSSION

A chronic ulcer is a major devastating problem in old age people with comorbidities like diabetes, peripheral vascular disease, infections and trauma which are associated with severe pain and social discomfort.[11] There are several dressings starting from the sterile gauze to the advanced and adjuvant dressings[4] with cost variability from low to high cost.

Wound dressings are mainly used to protect the wound from contamination and term can be used as platforms to deliver the bioactive agents to wound sites. Topical bioactive agents such as creams, solutions and ointments are not effective as they rapidly absorb the fluid resulting in wound soakage and becoming mobile. Hence solid dressings came into the existence and were preferred in exudative wounds and prolonged residence at the wound site.

Traditional dressings such as gauze and cotton have no active role in the wound healing process; hence biological active agents came into existence. These biological agents play an active role in debridement, antimicrobial effect and tissue regeneration. In chronic wound patients who usually undergo prolonged treatment and frequent changes in dressings, a system that delivers the drug in a controlled fashion can improve patient's compliance and therapeutic outcomes. [12]

Evidence-Based Dressing Selection

Negative pressure wound therapy has proven to decrease wound size and time to healing and decreases the frequency of dressing changes to improve patient comfort.

Moisture-modulating dressings are maintaining a moist environment to prevent desiccation or maceration of the wound bed. Alginates, hydrocolloids, and hydrogels moisten dry ischemic wounds; foams protect the wound and prevent dehydration. Enzymatic products like protease-modulating matrices have been shown to decrease healing time compared with wet-to-dry dressings.

Skin substitutes provide tissue coverage and faster healing.

Antimicrobial dressings have no evidence that supports these treatments over standard coverings. Silver- and honey-impregnated dressings may not improve outcomes. [4]

Antibiotic resistance is the major problem for the treatment of chronic and also a major public health issue and this results in the higher use of the topical agents and evolution of the wound care dressings over time. The use of topical dressings also results in a decrease in the wound bioburden. Over the last 10 years, there is an increase in the use of silver applications due to its anti-inflammatory and antimicrobial properties. The use of iodine reduces the bacterial bioburden but it is toxic to the human cells but cadexomer iodine releases a low concentration of iodine which has no toxicity and has higher efficacy compared to the other wound dressings. Activated carbon is also used in place of concentrated metronidazole gel for fowl offensive wounds. Local application of honey also accelerates wound healing.[13]

Cadexomer iodine consists of spherical beads of modified biodegradable starch that forms covalent bonds with iodine, which is insoluble in water. Starch absorbs the fluid from the ulcer and the molecule increases in size and slowly releases the iodine ions into the ulcer, which provides antiseptic action. The starch gel acts to extract microorganisms and debris from the wound, and the iodine produces an environment on the dressing, which prevents their culture.[14]Cadexomer iodine is a painless dressing and helps in maintaining prolonged antiseptic action due to slow release of the iodine[10,14] Biofilm in chronic ulcers is the major issue resulting in the non-healing of the ulcer and can be faced by using cadexomer iodine as it reduces the microbial load leading to the breakdown of the biofilm.[15] Application and removal of the cadexomer iodine are easy and it doesn't stain the clothes, bed, and skin and thus helps in maintaining hygiene and nursing care.[16] Literature is available on the therapeutic benefits of cadexomer iodine in the treatment of chronic wounds, particularly in varicose ulcers. However, limited studies exist on its role in the treatment of diabetes and pressure ulcers. Its cost-effectiveness in the treatment of cavity foot ulcers of patients with diabetes also has been documented. [17]

Chronic wounds of the lower extremities are increasing in prevalence. Chronic wounds are associated with increased mortality and substantial morbidity due to infection, pain, limitation of daily activities, and psychosocial consequences. Diagnosis starts with determining whether the wound is one of the four most common chronic wounds: venous leg ulcers, diabetic foot ulcers, pressure ulcers and arterial ulcers. Despite many recent advances in wound care, the challenge of managing chronic wounds is complicated by the lack of consistently accepted diagnostic methods and wound-care standards.

Knowing the cause of a chronic wound starts with determining whether the wound is one of the four common chronic wounds, and wound location is often quite helpful. The most common chronic leg wound is the venous leg ulcer (VLU) followed by the diabetic leg ulcer but the most common chronic leg ulcers are associated with diabetes.[7] In my study, 19 of 20 were leg ulcers out of which 14 patients were having diabetes and varicosities.

In this study, the effect of cadexomer iodine in reducing the area and volume of the ulcer was emphasized. In the 1st 2 weeks of dressings, there was no significant effect on the growth of granulation tissue and a decrease in surface area was seen in the study conducted by miller cn et al.[12] small ulcers have a rapid reduction in the area than large ulcers. In our study, there was a reduction in the area of ulcer in the 1st 4 weeks but a significant reduction in the area occurred in the last 2 weeks of the dressing. Similar results were seen in the study conducted by Radhakrishnan et al.[15]

CONCLUSIONS

Cadexomer iodine dressing is cost-effective, useful in rural areas. There is a significant decrease in the surface area and volume of the ulcer with the use of cadexomer iodine. Although healing rates are important, they are not an essential part of debridement, where the focus is on wound bed preparation. The aim is to remove necrotic/fibrinous tissue, to control oedema, to achieve a well-vascularized wound-bed, to decrease the bacterial burden and minimize wound exudates.

Limitations

There is no literature regarding the decrease in the volume of ulcers with the use of cadexomer iodine.

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