A Comparative Study of Topical Sucralfate and Povidone Iodine Dressing in Diabetic Foot Ulcers in a Tertiary Care Hospital in Tirupati

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ABSTRACT

BACKGROUND

Diabetic patients have reduced ability to metabolize glucose resulting in elevated blood sugar levels which further burdens the wound healing process. This leads to non-healing chronic ulcers. The sufferers of chronic diabetic foot ulcers are increasing globally due to lack of preventive and control measures. Sucralfate has been demonstrated in molecular studies to enhance the granulation tissue proliferation and thus promoting ulcer healing in the skin. Various clinical studies have also showed the efficacy of sucralfate in complete healing of the wound and in reducing the size of the wound. The purpose of this study was to compare the efficacy of topical sucralfate with that of povidone iodine dressing, in the healing of diabetic ulcers.

METHODS

This is a randomized comparative study. Among 100 patients, 50 patients received treatment in the form of povidone iodine dressings and 50 took treatment with sucralfate dressing. The patient underwent a detailed clinical examination. Relevant investigations were also done. The initial wound area was recorded after thorough debridement by measuring length x width. Both the groups underwent dressings once daily. The patients were followed up daily for a period of 3 weeks in both the groups.

RESULTS

In this study, the mean ± SD area of reduction of the ulcer was observed to be higher in sucralfate group 54.17 ± 10.08 than the povidone iodine group 16.07 ± 4.19. There was a statistically significant difference between the groups for the mean of area reduction ($P < 0.0001$, significant).

CONCLUSIONS

The ulcers in subjects treated with sucralfate dressing (S group) contracted more than the ulcers in the patients treated with povidone iodine (P group) (54.17 % Vs 16.07 %; $P = < 0.0001$, significant) which points out that sucralfate dressing is an effective modality in helping the reduction of wound area in patients with diabetic foot ulcers.

KEYWORDS

Diabetic, Sucralfate, Area of Reduction

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BACKGROUND

Diabetes is a multifaceted metabolic disease that affects more than 340 million individuals and about 20 % of them develop diabetic wounds worldwide.[1] Diabetic patients have reduced ability to metabolize glucose resulting in elevated blood sugar levels which further complicates the wound healing process. This can result in non-healing chronic wounds. The incidence of delayed healing process in diabetic patient is increasing globally due to lack of preventive and control measures. A significant fraction of yearly world-wide health budgets is consumed on diabetes mellitus and diabetic wounds. World health organization (WHO) report speculate that diabetes will be the 7th foremost reason for death in 2030.[2] In 2014, 9 % of adults had diabetes and was the reason for death of 1.5 million patients in 2012.[3] Majority of the diabetes deaths occur in the developing and under developed countries. Majority of all the limb amputations are because of diabetic wounds and it was reported that in every 30 s, one leg is amputated due to diabetic wounds in worldwide.[4]

Wound healing is a complex process. The final result of it should be restoration of continuity of the skin and also its function. The major concerns related with normal wound healing is alteration in normal physiological functions like deprived blood circulation, obesity, diseases like diabetes and stressed environmental conditions. Presence of diabetes mellitus is one important factor hampering with normal wound healing. Spreading infection and sepsis can hinder the rapid and complete healing of wounds to a great extent. Acute wounds which are less contaminated usually heal with ease without any problem. Chronic wounds include tissue injuries which do not heal in an organized set of stages and is prolonged than normal. Normally, healing process starts with haemostasis which involves platelet plug formation and clotting of the blood. It helps by preventing the blood loss and blocks the entry of microbes to wounded area. Next phase is the inflammatory phase which is overlapped with haemostasis phase in varying extents. In this phase, pro-inflammatory cells, neutrophils and macrophages destroys and cleans up microbes and dead tissues with the help of along with growth factors and other inflammatory mediators and cells.

Proliferative phase commences in the late stages of inflammatory phase in which granulation tissue is laid consisting of new tissue, new blood vessels (angiogenesis) and matrix to the wounded area. In the final remodelling phase, the tensile strength of the extracellular matrix is increased by changing the alignment and type of collagen and blood supply to the damaged area is reduced. Diabetic is one of the major issues in wound healing, especially for ulcers involving the lower extremities. Diabetes delays healing process by impairing each phase of wound healing i.e., haemostasis, inflammation, proliferation, and remodelling phase, which increases the morbidity and mortality of the patient and can severely affect the quality of life. Diabetic ulcers are associated with a persistent inflammatory phase associated with a delay in the formation of mature granulation tissue and reduction in wound tensile strength. This may be due to a number of factors like the vascular damage resulting in ischemia, decreased ability to fight infection, altered biomechanics of the foot etc. Generally, wounds are categorized into two types on the basis of origin - external and internal. External origin wounds are caused by external elements, for example like lacerations, abrasions, burns and contusions. These external wounds may increasingly go unnoticed by the patient because of lack of sensations due to peripheral neuropathy. Internal origin wounds like skin ulcers of spontaneous onset and calluses causes damage of skin and surrounding tissues which may further get infected.

Current standard approach utilizes series of methods to clean and eliminate the infected tissue, by chemical and mechanical means and maintain adequate moisture and blood supply. The earlier thought that ulcers should be kept dry, is no longer considered true. We now know that ulcers re-epithelialize much faster or develop granulation tissue faster when treated with dressings which allow moist wound healing.[5] It is understood that occluding ulcers does not lead to infection.[6] A number of new techniques are being introduced in the recent times for the management of chronic ulcers. Many techniques have evolved over the centuries to treat diabetic leg ulcers. Still no dressing is considered as an ideal one. Recently, a wide range of innovative dressings have been introduced into practice. Now, non-conventional dressings like paraffin impregnated gauze, collagen, benzoyl peroxide, gentian violet, topical phenytoin, oxygen therapy, mercurochrome, aloe vera, vinegar, honey and sugar are being increasingly used by surgeons all over the world.

Many studies have now proven that topical sucralfate promotes enhanced healing of trophic ulcers, venous stasis ulcers, traumatic wounds, burns, trophic ulcers and was seen to be superior in the management of diabetic ulcers.[7] Sucralfate was initially introduced as an oral gastrointestinal medication indicated for the treatment of active duodenal ulcers, gastroesophageal reflux disease (GERD) and stress ulcers. Recently it has demonstrated the potential effect in the healing of skin ulcers. Sucralfate stimulates proliferation of fibroblasts and keratinocytes of the skin.[8] It also enhances interleukin-1- stimulated interleukin-6 release from fibroblasts, prostaglandin E2 synthesis in basal keratinocytes.[9] Thus, it helps in the rapid proliferation of granulation tissue in the ulcer bed. It also has shown to promote rapid epithelialization of 2nd degree burns.[9] A number of animal studies have shown that the wound repair process is promoted by sucralfate. Many molecular studies have also shown the effect of sucralfate on granulation tissue proliferation and thereby enhancing ulcer healing process in the skin. Various human cellular studies have proven well the fact that topically applied sucralfate is an effective therapy for diabetic ulcers which are not improving on conventional methods of treatment. Many studies have already shown the efficacy of sucralfate in healing of the wound completely, and in reducing the wound size.

Objectives

To compare the efficacy of topical sucralfate with that of povidone iodine dressing, in the healing of diabetic ulcers.

METHODS

This randomized comparative study was conducted in Department of General Surgery, S.V.R.R.G.G. Hospital, Tirupati, with sample size of 100 patients – 50 in study group and 50 in control group. The duration of the study was one year from April 2019 to March 2020.

Inclusion Criteria

- Patients between age 30 and 75 years
- Non healing diabetic ulcer of more than 2-week duration.
- Size of the ulcer < 15cm x 15cm
- Patient giving written informed consent for topical sucralfate therapy.

Exclusion Criteria

- Patient septicaemic or unstable
- Bone involvement or osteomyelitis
- Ulcers due to malignancies
- Diabetic ketoacidosis
- Exposed bones or tendon
- Charcot joint

100 patients were selected and they were divided into two groups each of 50 members using computerized randomization chart into P group and S group. P group patients received treatment in the form of povidone iodine dressings and S group received treatment with sucralfate dressing. Off-loading of pressure from the affected area was done. Photos of the ulcers were taken before and after the dressings. Bacterial culture and sensitivity of the ulcers before and after the dressings were also taken from the ulcer bed. Antibiotics were started empirically and changed later according to the culture sensitivity. The patients underwent a detailed clinical examination. Relevant investigations were also done. The initial wound area was recorded after thorough debridement by measuring length x width. Both the groups underwent dressings every day. The patients in both the groups were examined daily for 3 weeks. The area of the target ulcer after the treatment was measured using a transparent graph sheet and later measuring its area.

Statistical Analysis

The results were calculated using student 't' test with the help of Microsoft Excel and Statistical Package for Social Sciences (SPSS software).

RESULTS

The mean age in the P group (povidone group) was found to be 59.82 with SD 11.3, whereas in the S group (sucralfate group) it was 61.84 with SD 9.4. However, there is no statistically significant difference between the groups for the mean of age (P = 0.328, not significant). In the P group, 30 (60.0 %) patients were males and 20 (40.0 %) patients were females. In the S group, 25 (50.0 %) patients were males and 25 (50.0 %) patients were females. However, there is no association between the sex and group (P = 0.315, not significant). Overall, the incidence of diabetic ulcers was more in males (55 %) compared to females (45 %). In the P group, 35 (70.0 %) patients were spontaneous and 15 (30.0 %) patients were traumatic. In the S group, 32 (64.0 %) patients were spontaneous and 18 (36.0 %) patients were traumatic. However, there is no association between the onset and group (P = 0.523, not significant). In the P group, 23 (46.0 %) patients had ulcer on the dorsum of foot, 4 (8.0 %) patients had on lateral malleolus and medial malleolus, and 19 (38.0 %) patients had ulcer on plantar surface.

Variable(s)	Group	Mean	Std. Deviation	t-Value	P Value
Initial area	P Group	47.2364	21.42529	-1.522	0.131 (Not Sig.)
	S Group	56.2953	36.23528		
Final area	P Group	39.6302	17.91235	3.313	0.001 (Sig.)
	S Group	26.7758	20.77790		
Area of reduction	P Group	16.0668	4.18929	-24.687	<0.0001 (VHS)
	S Group	54.1675	10.07718		

Table 1. Area of Reduction

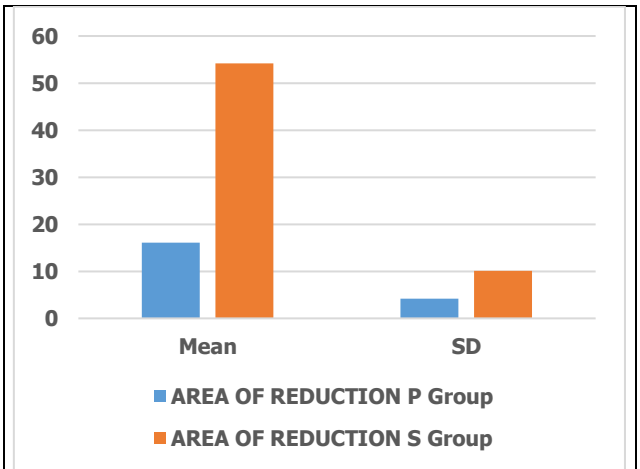

Figure 1. Mean Area of Reduction

	P group	S Group
Culture positive	39	7
Culture negative	11	43

Table 2. Culture Sensitivity

Chi-square value =41.224, P < 0.0001 (Very High Sig.)

In the S group, 20 (40.0 %) patients had ulcer on dorsum of foot, 4 (8.0 %) patients had ulcer on lateral malleolus and medial malleolus, and 22 (44.0%) patients had ulcer on planter aspect of foot. However, there is no statistically significant association between the site and group (P = 0.934, not significant.). The mean ± SD in initial area was higher in S group (56.29 ± 36.24) than the P group (47.23 ± 21.43). However, there is no statistically significant difference between the groups for the mean of initial area (P = 0.131, not significant). The mean ± SD final area was higher in P group (39.63 ± 17.91) than the S group (26.78 ± 20.78). It is observed that, there is a statistically significant difference between the groups for the mean of final area (P = 0.001, significant). The mean ± SD area of reduction of the ulcer was higher in S group (54.17 ± 10.08) than the P group (16.07 ± 4.19). However, there is a

statistically significant difference between the groups for the mean of area reduction (P < 0.0001, significant). In the P group, after dressing for 3 weeks only 11 out of 50 patients had culture negative, as compared with 43 out of 50 patients who had culture negative in the S group after 3 weeks. There was a statistically significant association between the culture sensitivity after the intervention and the group (P < 0.0001 - very high significant).

In the P group, for 8 (16.0 %) patients, no skin grafting was required, and 42 (84.0 %) patients required skin grafting eventually. In the S group, for 31 (62.0 %) patients, no skin grafting was required and only 19 (38.0 %) patients had skin grafting done eventually. There was a statistically significant association between the skin grafting required and group (P < 0.0001, very high significant).

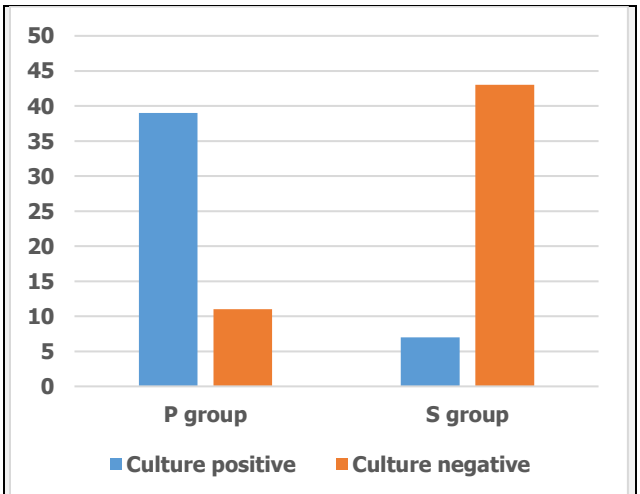

Figure 2. Bacterial Growth after Treatment

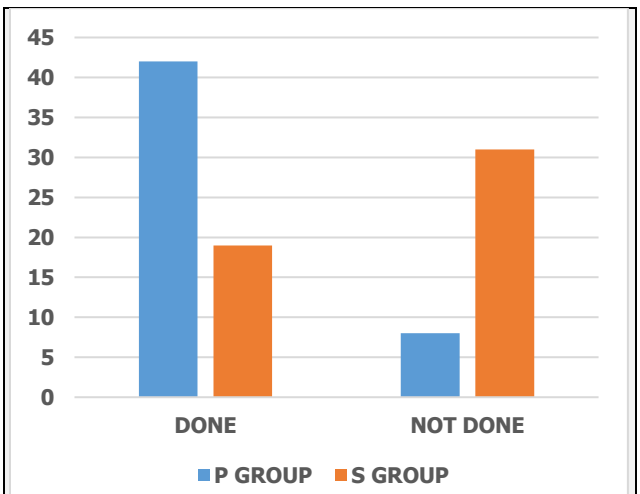

Figure 3. Requirement of Grafting

Grafting	Done	Not Done
P GROUP	42	8
S GROUP	19	31

Table 3. Requirement of Skin Grafting

DISCUSSION

Diabetic ulcers are chronic wounds, stuck in inflammation phase and shows cessation of epidermal growth. They are more prone for infection and ischemia due to several factors such as elevated blood sugar levels and microangiopathy respectively. The present study was conducted at S.V.R.R.G.G Hospital, Tirupati, to compare the effect of topical sucralfate with that of povidone iodine which is a conventional mode of topical therapy on diabetic ulcer healing dynamics.

In this study it was seen that the incidence of diabetic ulcers was more in males (55 %) as compared to females (45 %). The second national data source, NHDS documented higher hospital rates in males suffering from diabetic ulcers. In a similar study conducted by Nagalakshmi et al.[10] similar findings were obtained, with slightly higher incidence in males, with males 57 % as compared to females who were 43 %.

The mean age in the P group was 59.82 years with SD 11.3, whereas in the S group it was 61.84 years with SD 9.4. In the study conducted by Nagalakshmi G et al. the mean age belonged to the elderly group and was 62.28 in the control group and 58.88 in the study group. In another study conducted by Reddy et al.[11] comparing sucralfate and honey dressing, the mean age was found to be 57.28 years for the sucralfate group and 57.04 years for the honey dressing group. Overall, 67 % of the subjects had ulcer of spontaneous onset and the 33 % had ulcer of traumatic onset. In the other study conducted by Nagalakshmi et al. too, majority of the subjects had ulcers of spontaneous onset.

In this study, among the P group subjects, 46 % of the ulcers were located on the dorsum of the foot, 38 % on the plantar aspect, 8 % each in or around the medial and lateral malleolus of the leg. Whereas, among the S group, 40 % of the ulcers were on the dorsum of the foot, 44 % on the plantar aspect, 8 each in or around the medial malleoli and lateral malleoli. Thus overall, there was slightly higher incidence (43 %) of ulcers over the dorsal aspect of the foot in this study. A study conducted by Edmonds et al. in 1986, (Edmonds) showed that more foot ulcers were located on plantar and fore foot areas.[12] This study showed that most of the diabetic foot ulcers are invariably shoe related and associated with gait abnormalities. They can be prevented by appropriately sized footwear. However, in the study conducted by Nagalakshmi et al. the incidence of ulcers over the plantar aspect of the foot was not as high as postulated by Edmonds et al. This difference in incidence in different locations could be due to different inclusion and exclusion criteria used in these various studies.

In this study, the culture and sensitivity of the ulcers before the initiation of sucralfate dressings was positive for many microbes. In the S group, 21 patients were positive for *Staphylococcus aureus*, 8 patients for *Pseudomonas aeruginosa*, 5 patients for *Proteus mirabilis*, 4 patients for *Klebsiella pneumoniae*, 2 patient showed *E. coli*. 10 patients did not show any growth. In the P group, 19 of them were positive for *Staphylococcus aureus*. 6 of them for *Proteus mirabilis*. 10 patients were positive for *Pseudomonas aeruginosa*, 4 patients for *Klebsiella pneumoniae* and 3 of them for *E. coli*. 8 of the patients had negative culture.

After the patients were treated with sucralfate dressings, bacterial culture sensitivity obtained on the 21st day showed

negative culture in 43 patients in the S group, whereas 39 patients in the P group still had a positive culture. Similar results were obtained in the study by Nagalakshmi et al. for they had got negative culture for 46 patients in the study group. This may be due to the antimicrobial activity of sucralfate.

But for the P group, still 49 patients showed culture positivity as compared to 39 in the S group. This might be due to different type of dressing used in the P group. The later study used normal saline dressing which has no antimicrobial effect, whereas povidone iodine has antimicrobial effect of its own. In this study, only 19 patients among the S group had to undergo skin grafting, as the rest of the patients had almost complete epithelisation of the ulcer at the end of three weeks. However, 42 patients in the P group had to undergo skin grafting for the complete healing of the ulcer. In another study conducted by Reddy et al. comparing sucralfate with honey dressing in diabetic ulcers, 60 % of the patients in the sucralfate group underwent split skin graft (SSG) and 64 % patients in the honey dressing group underwent SSG.

In this study, it was noticed that participants in the S group had higher mean percentage area of reduction of 54.17 % (S.D: 10.07) as compared with the P group receiving only conventional dressing (povidone iodine dressing) in whom the percentage of mean area of reduction was 16.07 % (S.D: 4.19).These differences were found to be significant statistically on independent sample T test ($P < 0.0001$) showing that sucralfate has a positive effect on wound healing in diabetic ulcers.

Better results were obtained in the study conducted by Reddy et al. with mean percentage area of reduction of 59.53 % for the sucralfate group and 55.005 % for the honey dressing group. This might be attributed to the lesser sample size in this study. But in the study conducted by Nagalakshmi et al. the percentage mean area of reduction was found to be slightly lesser, 40.87 %. Thus, it can be confidentially stated that topical sucralfate is one excellent therapeutic agent in healing of diabetic ulcers which is efficacious, cheap and easily available. Thus, sucralfate dressing in the treatment of diabetic foot ulcers was noted to be more efficacious, safe, enhances wound healing, and therefore can be recommended as an alternative modality for the treatment of diabetic ulcers.

Limitations of This Study

The main limitation in our study was the sample size. A sample of 100 individuals is enough for statistical analysis, but for further substantiation of observations and for revelation of variations which weren't noticed in the present study, a randomised controlled comparative study with a much larger population is more appropriate. Factors other than cost of the dressings were not taken into account in this study. Many other factors can influence the patient burden like social conditions. These were not taken into account.

CONCLUSIONS

The ulcers in subjects treated with sucralfate dressing (S group) contracted more than the ulcers in the patients treated with povidone iodine (P group) (54.17 % Vs 16.07 %; $P < 0.0001$, significant) which points out that sucralfate dressing is an effective modality in helping the reduction of wound area in patients with diabetic foot ulcers and it can be used alone or along with conventional dressings for faster and better healing of diabetic ulcers.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
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