



A comparative study of effectiveness of topical cadexomer iodine versus topical sucralfate in the management of diabetic foot ulcer

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Abstract

Various agents have been used in the management of Diabetic Foot Ulcer. The use of Cadexomer iodine and Sucralfate have been proved effective. Although various studies have been done using both agents separately, the comparative studies between these two agents are limited. Hence, we are studying these two agents to observe if they are efficacious and cost effective, especially in a patient population from a poor socio-economic status.

Objective: To compare the effectiveness of topical Cadexomer iodine and topical Sucralfate in management of diabetic foot ulcer in terms of healing (clearance of infection, decrease in slough, appearance of granulation tissue, decrease in size, readiness for grafting).

Methodology: A Comparative Prospective study was conducted in Department of General Surgery at a tertiary care center among patients with diabetic foot ulcers with Grade I-III (Meggitt-Wagner Grade). 70 patients were divided into 2 groups. 1 Group was treated with Cadexomer iodine and other group was treated with Sucralfate. Institutional ethical clearance was obtained prior to start of study. Patients were explained the

procedure and consent was obtained from all the patients involved prior to the start of the study.

Results: The Mean age group in Sucralfate group and Cadexomer iodine group was 57.11 ± 11.36 years and 56.09 ± 12.16 years respectively. Majority of patients were males and mode of onset was spontaneous. Mean reduction in ulcer size in Sucralfate group and Cadexomer iodine group was 24.99 ± 5.38 sqcm and 31.79 ± 5.51 sqcm respectively. Cadexomer iodine group showed significant reduction in slough at the end of 1st week compared to Sucralfate.

Conclusion: Based on the results we conclude that Cadexomer iodine seems to be better agent in terms of reduction in size of ulcer and clearance of necrotic tissue in the treatment of Diabetic foot ulcer.

Keywords: Cadexomer iodine, Sucralfate, Diabetic Foot Ulcer

Introduction

Diabetes Mellitus is defined by World Health Organization as a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both with disturbances of carbohydrate, fat and protein metabolism.

Diabetic foot is a complication of diabetes. Due to the peripheral nerve dysfunction, patients have reduced ability to feel pain leading to minor injuries going unnoticed for a long period causing infection at the site. Diabetic foot ulcer (DFU) may be caused due to trauma, infections or any underlying neurovascular cause. Lifetime incidence of foot ulcers is estimated to be up to 34% in type 2 diabetes patients¹. In diabetes, peripheral nerve dysfunction along with peripheral artery disease causes poor blood circulation to the extremities. According to International Diabetes Federation by 2045, approximately 700 million people are estimated to have diabetes².

The risk for ulcer recurrence is high with recurrence rates of 40% in the first year and 65% in the first 3 years after healing.³ Majority of the foot ulcers will heal (60-80%) while 10-15% of them remain active and 5-24% of them will lead to limb amputations within a period of 6-18 months of first evaluation and there is an increased risk with duration of diabetes and age. Hence, Diabetic foot ulcer needs strict management which includes strict control of blood glucose, prevention through education and regular dressings. Conventional treatment like wound debridement, vacuum-assisted closure, electrical stimulation, oxygen therapy etc., cannot provide a satisfactory healing since there are no available necessary growth factors that enhance healing and are also not cost effective.

Diabetic Foot Syndrome is sequelae of diabetes leading to amputations, restricted mobility and even death. The term refers to two types of disease: lower extremities ulcers including the associated states of risk and diabetes-related Charcot foot. Latter is a syndrome with joint and bone abnormalities due to underlying neuropathy, trauma and disturbances in bone metabolism.

Several agents are being used to manage diabetic foot ulcers. Cadexomer iodine and Sucralfate have been proved effective. Various studies were done using both agents individually but the studies comparing these two agents remain limited. Hence, we are studying these two agents to observe if they are efficacious and cost effective, especially in a patient population from a poor socio-economic status.

Objective

To compare the effectiveness of topical Cadexomer iodine and topical Sucralfate in management of diabetic foot ulcer in terms of healing (clearance of infection, decrease in slough, appearance of granulation tissue, decrease in size, readiness for grafting).

Materials and Methods

The present study was a cohort study conducted in Tertiary care center in Department of General Surgery, R.L. Jalappa hospital Tamaka, Kolar from October 2019 to March 2021 with a sample size of 70.

Inclusion Criteria

All the patients with Diabetic Foot Ulcer of Wagner's grade 1, 2 and 3.

Exclusion Criteria

1. Patients with Diabetic Foot Ulcer having peripheral vascular disorder and varicose veins.
2. Patients with immune-compromised status, trophic ulcers.
3. In pregnant or lactating women.

Methodology

The study was estimated to include DFU patients satisfying inclusion criteria who were admitted in surgical wards of RLJH and RC. A complete detailed history was obtained and documented. All patients underwent clinical examination with relevant investigations after obtaining an informed consent about the need for study and the methodology and which group

they were going to be placed under. Patients initially underwent wound debridement were split into 2 groups using even odd method to include similar type of cases in both groups, where in group A-Cadexomer iodine and in group B-Sucralfate was used. In group A, dressing was changed three times/week or when there was color change to yellow/grey and in group B, dressing was changed daily. The ulcer was closely observed for reduction in discharge from the ulcer, clearance of infection, decrease in slough, appearance of granulation tissue, decrease in size, contraction of wound and readiness for grafting. Microbiological parameters were assessed by culture and sensitivity from discharge or tissue culture from the ulcer. The initial area and final area of ulcer size (when the ulcer is ready for split skin grafting i.e clinically appearance of adequate granulation tissue with culture and sensitivity or tissue culture rules out significant bacterial growth), was measured and values recorded in chart for statistical analysis. The percentage of ulcer size reduction was calculated weekly using the formula.

$$\text{Reduction in size} = \frac{\text{Initial size} - \text{final size}}{\text{Initial size}} \times 100$$

Measurement of ulcer⁴

Graphical method-Wound area was determined by tracing the outline of the wound onto a graph paper, and then calculated manually by counting the number of squares within the wound which gives area in terms of square CMS.

Statistical Analysis

Collected data was coded and entered into an excel data base. All the quantitative measures like age, wound size, wound area etc. was presented by (Mean ± SD) and confidence interval, qualitative measures by proportions and Confidence Interval. The significance of differences in both were compared by Student t test/Mann Whitney

U test. Chi-square test, Fisher's exact test was used to compare difference in proportions. P value < 0.05 was considered as statistically significant.

Statistical methods

Ulcer size, Granulation Tissue (%) and Necrotic Tissue (%) were considered as primary outcome variables. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots. All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution. For normally distributed Quantitative parameters the mean values were compared between study groups using independent sample t-test (2 groups). Categorical outcomes were compared between study groups using Chi square test /Fisher's Exact test (If the overall sample size was < 20 or if the expected number in any one of the cells is < 5, Fisher's exact test was used.) P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis⁵.

Results

A total of 70 subjects were included in the final analysis.

Table 1: Age distribution of patients.

	Range	Count	%
Age(years)	<40	4	4.65
	40-49	15	17.44
	50-59	22	25.581
	60-69	13	15.116

	70 or >70	16	18.60
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The observations showed that most of the patients were in the age group of 50-59 years i. e 22 (31.42%). The youngest patient was of 38 year and eldest being 77years. The next common age group was 70 or >70years with 16(22.85%) patients followed by 40-49 years group with 15(17.44%).

Table 2: Comparison of gender between groups (N=70)

Gender	Groups		Chi square	P value
	Sucralfate (N=35)	Cadexomer iodine (N=35)		
Male	28 (80%)	30 (85.71%)	0.402	0.526
Female	7 (20%)	5 (14.29%)		

Of the 70 subjects under study, males were the most affected with 58(82.85%) male patients and 12(17.14%) female patients. In Sucralfate group, 28 (80%) were males and 7 (20%) were females and in Cadexomer iodine group, 30 (85.71%) were males and 5 (14.29%) were females. There was no statistically significant difference in Gender between Groups (P value 0.526)

Table 3: Comparison of Onset between groups (N=70)

Onset	Groups		Chi square	P value
	Sucralfate (N=35)	Cadexomeriodine (N=35)		
Spontaneous	21 (60%)	19 (54.29%)	0.233	0.629
Traumatic	14 (40%)	16 (45.71%)		

Out of 70 patients under study, In 40 patients, mode of onset of ulcer was spontaneous in nature with no underlying cause. In Sucralfate group, 21 participants had onset of spontaneous in nature and 14 patients had traumatic cause. In Cadexomer iodine group, in 19 patients, onset was spontaneous in nature and 16 participants had traumatic onset. There was no statistically significant difference in Onset between Groups (P value 0.629)

Table 4: Comparison of Site between groups (N=70)

Site	Groups		Chi square	P value
	Sucralfate (N=35)	Cadexomer iodine (N=35)		
Left Foot-Plantar	5 (14.29%)	8 (22.86%)	0.981	0.806
Left Foot -Dorsum	8 (22.86%)	7 (20%)		
Right Foot-Plantar	12 (34.29%)	12 (34.29%)		
Right Foot -Dorsum	10 (28.57%)	8 (22.86%)		

In Sucralfate group, 5 (14.29%) participants had ulcer on plantar aspect and 8 (22.86%) on dorsal aspect of left foot, 12 (34.29%) participants had ulcer on plantar aspect and 10 (28.57%) patients on the dorsal aspect of right foot. In Cadexomer iodine group, 8 (22.86%) participants had ulcer on plantar side and 7 (20%) on dorsal aspect of left foot, 12 (34.29%) participants on plantar region and 8 (22.86%) on dorsal part of right foot. There was no statistically significant difference in Site between Groups (P value 0.806)

Table 5: Comparison of mean of Ulcer size at admission between groups (N=70)

Ulcer size(sqcm)	Groups (Mean± SD)		P value
	Sucralfate (N=35)	Cadexomer iodine (N=35)	
At Admission	26.54 ± 10.44	27.26 ± 10.43	0.775
1 st Week	25.43 ± 9.68	26 ± 9.88	0.808
2 nd Week	22.4 ± 9.32	22.63 ± 9.29	0.918
3 rd Week	20.2 ± 8.87	18.77 ± 8.35	0.490
% Reduction	24.99 ± 5.38	31.79 ± 5.51	<0.001

The Mean Ulcer size (sqcm) at Admission in Sucralfate group and Cadexomer iodine group was 26.54 ± 10.44 and 27.26 ± 10.43 respectively. The Mean Ulcer size at end of 1st Week in Sucralfate group and Cadexomer iodine group was 25.43 ± 9.68sqcm and 26 ± 9.88 sqcm

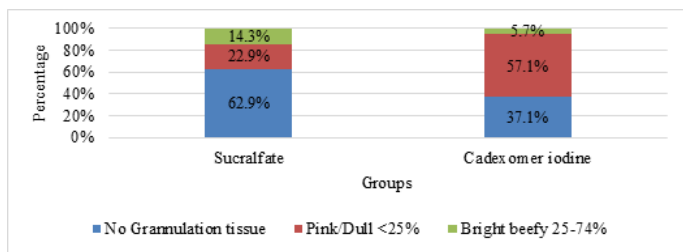
respectively. The Mean Ulcer size (mm) at end of 2nd Week in Sucralfate group and Cadexomer iodine group was 22.4 ± 9.32sqcm and 22.63 ± 9.29sqcm respectively. The Mean Ulcer size at end of 3rd Week in Sucralfate group and Cadexomer iodine group was 20.2 ± 8.87sqcm and 18.77 ± 8.35sqcm respectively. The mean ulcer size is not significant at admission, 1st Week, 2nd Week and 3rd Week difference between two groups (P-value > 0.05). The size reduction (sqcm) in the Sucralfate group was 25.43(4.18%), 22.4(15.59%) and 20.2(23.88%) at 1st, 2nd and 3rd weeks respectively. In Cadexomer iodine group, the reduction in size(sqcm) of ulcer was

27.26(4.62%) in 1st week, 22.63(16.98%) in 2nd week and 18.77(31.14%) in 3rd week. There was no significant difference in mean ulcer size from baseline to 2nd week between two groups. There was significant difference in mean Ulcer size at 3rd week between two groups with increased reduction seen in Cadexomer iodine group. The overall Mean reduction in size in Sucralfate group and Cadexomer iodine group was 24.99 ± 5.38 sqcm and 31.79 ± 5.51sqcm. The Mean Reduction in size is significant (P-value <0.001) with increased reduction seen in Cadexomer iodine group.

Table 6: Comparison of Granulation Tissue (%) between groups (N=70)

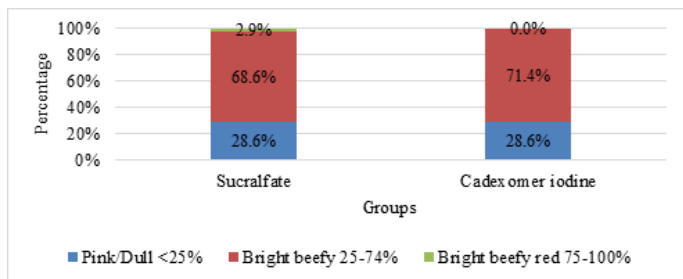
Granulation Tissue (%)	Groups		Chi square	P value
	Sucralfate (N=35)	Cadexomer iodine (N=35)		
At Admission				
No Granulation Tissue	22 (62.86%)	13 (37.14%)	8.743	0.013
Pink/Dull (<25%)	8 (22.86%)	20 (57.14%)		
Bright Beefy (25-74%)	5 (14.29%)	2 (5.71%)		
Bright Beefy Red (75-100%)	0(0%)	0(0%)		
1 st Week				
No Granulation Tissue	0(0%)	0(0%)	1.020	0.600
Pink/Dull (<25%)	10 (28.57%)	10 (28.57%)		
Bright Beefy (25-74%)	24 (68.57%)	25 (71.43%)		
Bright Beefy Red (75-100%)	1 (2.86%)	0 (0%)		
2 nd Week				
No Granulation Tissue	0(0%)	0(0%)	2.29	0.318
Pink/Dull (<25%)	2 (5.71%)	0 (0%)		
Bright Beefy (25-74%)	29 (82.86%)	32 (91.43%)		
Bright Beefy Red (75-100%)	4 (11.43%)	3 (8.57%)		
3 rd Week				
No Granulation Tissue	0(0%)	0(0%)	1.120	0.290
Pink/Dull (<25%)	0(0%)	0(0%)		
Bright Beefy (25-74%)	8 (22.86%)	12 (34.29%)		
Bright Beefy Red (75-100%)	27 (77.14%)	23 (65.71%)		

Graph 1: Staked bar chart of comparison of granulation at admission between both groups.



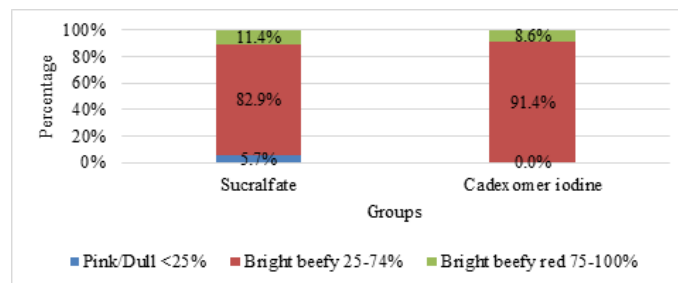
In Sucralfate group, most of the subjects 22 (62.86%) had no granulation tissue, 8 (22.86%) had pink/dull granulation tissue followed by bright beefy granulation in 5 (14.29%) patients at admission. In Cadexomer iodine group, 13 (37.14%) subjects had no granulation tissue, 20 (57.14%) had pink/dull granulation tissue followed by bright beefy granulation in 2 (5.71%) subjects at admission. There was significant difference in appearance of granulation tissue between two groups at admission with (P-value 0.013).

Graph 2: Staked bar chart of comparison of at 1st Week between groups (N=70)



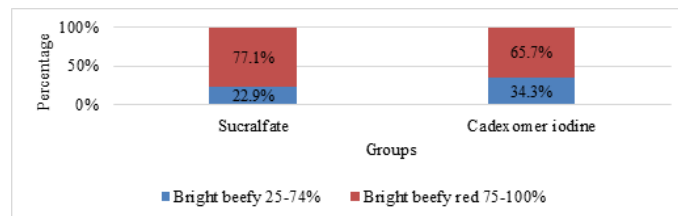
In Sucralfate group, most of the subjects 24 (68.57%) had bright beefy granulation (25-74%) tissue, followed by pink/dull (<25%) granulation tissue in 10 (28.57%) patients and Bright Beefy Red (75-100%) granulation tissue in 1 (2.86%) subject. In Cadexomer iodine group, most of the subjects 32 (91.43%) had bright beefy (25-74%) granulation tissue, followed by pink/dull (<25%) granulation tissue in 3 (8.57%) patients. There was no significant difference in appearance of granulation tissue between two groups at 1st Week with (P-value 0.600)

Graph 3: Staked bar chart of comparison of at 2nd Week between groups (N=70)



In Sucralfate group, most of the subjects 29 (82.86%) had bright beefy (25-74%) granulation tissue, followed by Bright Beefy Red (75-100%) granulation tissue in 4 (11.43%) subjects and Pink/Dull (<25%) granulation tissue in 2 (5.71%) patients. In Cadexomer iodine group, most of the subjects 32 (91.43%) had bright beefy (25-74%) granulation tissue, followed by bright beefy red (75-100%) granulation tissue in 3 (8.57%) patients. There was no significant difference in appearance of granulation tissue between two groups at 2nd Week with (P-value 0.318)

Graph 4: Staked bar chart of comparison of at 3rd Week between groups (N=70)

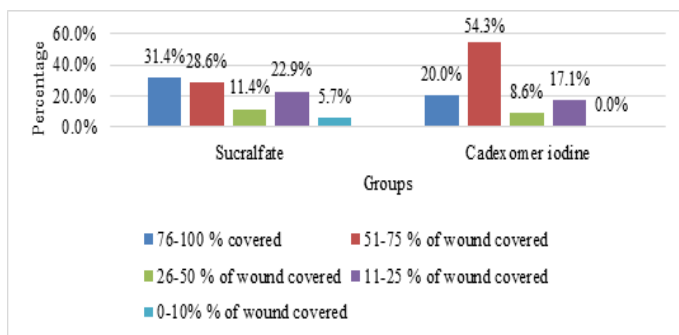


In Sucralfate group, most of the subjects 27 (77.14%) had bright beefy red (75-100%) granulation tissue, followed by bright beefy (25-74%) granulation tissue in 8 (22.86%) subjects. In Cadexomer iodine group, most of the subjects 23 (65.71%) had bright beefy red 75-100% tissue, followed by bright beefy (25-74%) granulation tissue in 12 (34.29%) subjects. There was no significant difference in appearance of granulation tissue between two groups at 3rd Week with (P-value 0.290)

Table 7: Comparison of Necrotic Tissue (%) between groups (N=70)

Necrotic Tissue (%)	Groups		Chi square	P value
	Sucralfate (N=35)	Cadexomeriodine (N=35)		
At Admission				
76-100 % Covered	11 (31.43%)	7 (20%)	6.111	0.191
51-75 % Of Wound Covered	10 (28.57%)	19 (54.29%)		
26-50 % Of Wound Covered	4 (11.43%)	3 (8.57%)		
11-25 % Of Wound Covered	8 (22.86%)	6 (17.14%)		
0-10% % Of Wound Covered	2 (5.71%)	0 (0%)		
1st Week				
26-50 % Of Wound Covered	15 (42.86%)	5 (14.29%)	11.007	0.012
11-25 % Of Wound Covered	7 (20%)	18 (51.43%)		
0-10% % Of Wound Covered	13 (37.14%)	11 (31.43%)		
No Necrotic Tissue	0 (0%)	1 (2.86%)		
2nd Week				
11-25 % Of Wound Covered	5 (14.29%)	5 (14.29%)	5.711	0.058
0-10% % Of Wound Covered	23 (65.71%)	14 (40%)		
No Necrotic Tissue	7 (20%)	16 (45.71%)		
3rd Week				
11-25 % Of Wound Covered	2 (5.71%)	0 (0%)	2.47	0.291
0-10% % Of Wound Covered	2 (5.71%)	1 (2.86%)		
No Necrotic Tissue	31 (88.57%)	34 (97.14%)		

Graph 5: Cluster bar chart of comparison of slough at admission between groups (N=70)

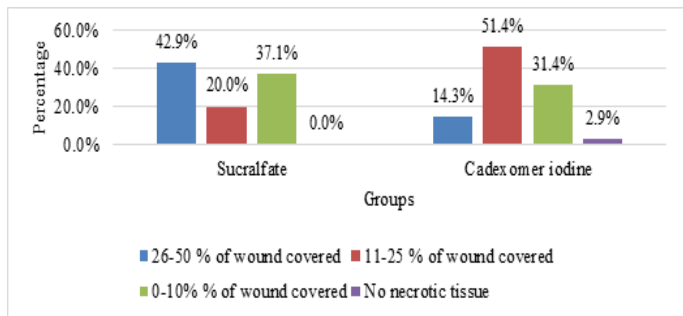


The Sucralfate group had most of the subjects with 76-100% of necrotic tissue i. e in 11 (31.43%) patients followed by 10 (28.57%) patients with 51-75% slough, 8 (22.86%) patients with 11-25% slough, 4 (11.43%)

patients with 26-50% slough and 2 (5.71%) patients with 0-10% of wound covered with necrotic tissue.

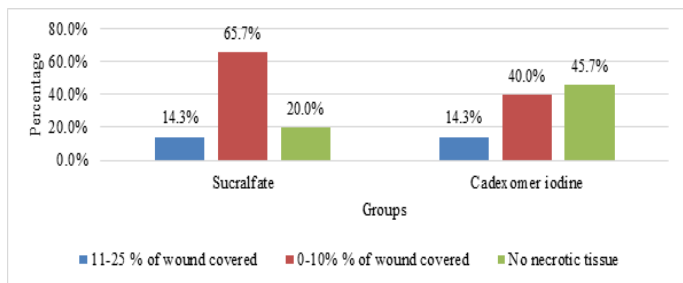
The Cadexomer iodine group had most of the subjects with 51-75% of necrotic tissue i. e in 19 (54.29%) patients followed by 7 (20%) patients with 76-100% slough, 6 (17.14%) patients with 11-25% slough and 3 (8.57%) patients with 26-50% slough. There was no significant difference in Necrotic Tissue (%) at admission between two groups. (P value 0.191)

Graph 6: Cluster bar chart of comparison of slough at 1st week between groups (N=70)



The Sucralfate group had most of the subjects with 26-50% of necrotic tissue i. e in 15 patients (42.86%) followed by 13 patients (37.14%) with 0-10% slough and 7 (20%) patients with 11-25% of ulcer covered by necrotic tissue. The Cadexomer iodine group had most of the subjects with 11-25% of necrotic tissue i. e in 18 patients (51.43%) followed by 11 patients (31.43%) with 0-10% slough, 5 patients (14.29%) with 26-50% slough and 1 patient (2.86%) not had necrotic tissue. There was significant difference in Necrotic Tissue (%) at 1st Week between two groups with significant reduction in slough in Cadexomer iodine group. (P value 0.012)

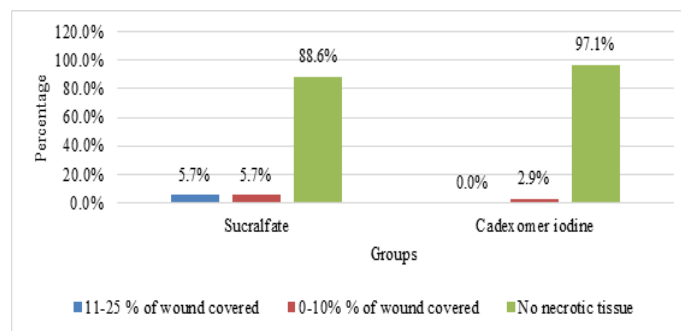
Graph 7: Cluster bar chart of comparison of slough at 2nd week between groups (N=70)



The Sucralfate group had most of the subjects with 0-10% of necrotic tissue i. e in 23 patients (65.71%) followed by 7 patients (20%) had no necrotic tissue and 5 (14.29%) patients had 11-25% slough. The Cadexomer iodine group had most of the subjects with no necrotic tissue i. e in 16 (45.71%) patients followed by 14 (40%) patients with 0-10% slough and 5 patients (14.29%) had 11-25% slough.

There was no significant difference in Necrotic Tissue (%) at 2nd week between two groups. (P value 0.058)

Graph 8: Cluster bar chart of comparison of slough at 3rd week between groups (N=70)



The Sucralfate group had 2 patients (5.71%) each with 0-10% and 11-25% slough and 31 (88.57%) patients had no necrotic tissue.

The Cadexomer iodine group had 1 patient (2.86%) with 0-10% slough and 34 (97.14%) patients had no necrotic tissue at 3 weeks. There was no significant difference in Necrotic Tissue (%) at 3rd week between two groups. (P value 0.291)

Table 8: Comparison of mean of HbA1c (%) between two groups (N=70)

Parameter	Groups (Mean± SD)		P value
	Sucralfate (N=35)	Cadexomeriodine (N=35)	
HbA1c (%)	9.76 ± 2.07	9.31 ± 1.91	0.349

The Mean HbA1c (%) in Sucralfate group and Cadexomer iodine group were 9.76 ± 2.07 and 9.31 ± 1.91 respectively. The mean HbA1c (%) showed no significant difference between two groups (P-value 0.349)

Discussion

Foot ulcers are diverse in terms of causes like traumatic, due to extrinsic factors such as pressure or shear, post-surgical intervention or underlying conditions like Diabetes or vascular disease. They have a huge impact on

the entire health care system irrespective of the cause and hence is being called as a “Silent epidemic”⁶.

Diabetic foot ulcer have a subtle effect on quality of life which may be evident as pain, distress, social isolation, anxiety, extended hospital stay, morbidity or mortality⁷. They need strict management which includes strict glycemic control, prevention through education, regular dressings and rehabilitation.

Cadexomer iodine was developed in the early 1980s. It acts by releasing iodine that has broad spectrum germicidal function, stimulation of granulation tissue and overall ulcer healing. Sucralfate mainly acts on the proliferative phase of wound healing. It binds to the fibroblast growth factors (FGF) and epithelial growth factors (EGF) and accelerates neo-angiogenesis⁸.

In present study conducted in R. L. Jalappa Hospital, Kolar with sample size of 70, 35 patients underwent Cadexomer iodine dressings and 35 patients were dressed with Sucralfate. Parameters which were compared included Age, Sex, Initial and final ulcer size, reduction in ulcer area, necrotic tissue/slough, granulation tissue.

Age distribution

DFUs were more commonly seen in the age >50 years with 51 patients (72.85%) falling into that range. Decade wise distribution revealed that age group of 50-59 years had most i.e 22 (31.42%) patients followed by 70 or >70 years with 16(22.85%) patients followed by 40-49 years group with 15(17.44%). In elderly, there is physiologic impairments in wound healing and hence ulcers heal at a slower rate due to various factors like Nutrition, Cell senescence, decreased angiogenesis and less synthesis of critical growth factors. Elderly have a higher rate of death associated with specific morbidities such as sepsis and ARDS directly attributed to infection and hence requires early intervention and comprehensive management which includes safe topical therapies,

growth factors and cellular therapy. It is vital to preserve limb function as much as possible and to reduce the handicap by limiting amputations as old people are self-dependent and may be abandoned by family members. Recent studies and study by Costa RH et al in 2017 reported similar trend of DFUs⁹.

Gender distribution

DFUs were more common in male subjects compared to females with 58(82.85%) males contrary to 12(17.14%) female patients. Males being often the source of income for families especially in a rural community are prone to trivial trauma and due to unawareness; poor screening for DM and negligence increases the disease affliction. Social stigmas, misdirection by kin, native treatment in terms of topical applications which are basically irritants aggravate the disease and increases risk of morbidity. Estrogen protects women from vascular comorbidity and causes potential differences in immune competence. Behavioral differences like smoking habits, risk-taking lifestyle and carelessness to health also come into play. Educational programs should be implemented aimed at the empowerment of people with DM and the individualization of treatment.

A study by Spanos K et al on the risk factors in diabetes ulcer revealed similar trend of high male predilection¹⁰.

Mode of onset

DFUs most commonly occurred spontaneously in 40(57.14%) patients in our study. Poor glycemic control is an important factor which serves as media for growth of bacteria and other microorganisms leading to cutaneous infections and blebs which spontaneously rupture to form an ulcer. Trauma also contributes to majority of ulcers (30 patients) mostly due peripheral neuropathy which usually goes unnoticed till infection sets in. Similar studies depict spontaneous ulcerations are common. Due to autonomic dysfunction, there is reduced

hydration to the skin making it less elastic and vulnerable.

Tissue glycosylation and collagen abnormalities lead to stiffness of plantar fascia and Achilles tendon causing loss of flexibility and elasticity increasing risk of trauma.

Site of ulcer:

DFUs in our study showed no significant variation in site of ulcer with 37 patients (52.85%) affected over plantar aspect and 33 patients (47.15%) affected over dorsal aspect even though plantar side being more prone to trauma, dryness, callosities, fissures and cracks. They affect areas of the foot which encounters repetitive trauma and pressure sensations. Frequent trauma of the callus results in subcutaneous haemorrhage and eventually it erodes and becomes an ulcer. Plantar side being weight-bearing area such as the plantar metatarsal head, heel, tips of hammer toes and other prominent areas is usually affected.

Reduction in ulcer size

On a weekly basis from the time of admission, percentage ulcer size reduction was calculated using the formula,

$$\text{Reduction in size} = \frac{\text{Initial size} - \text{final size}}{\text{Initial size}} \times 100$$

The mean ulcer size reduction was calculated in both groups and compared. The size reduction (sqcm) in the Sucralfate group was 25.43(4.18%), 22.4(15.59%) and 20.2(23.88%) at 1st, 2nd and 3rd week respectively. In Cadexomer iodine group, the reduction in size(sqcm) of ulcer was 27.26(4.62%) in 1st week, 22.63(16.98%) in 2nd week and 18.77(31.14%) in 3rd week. There was no significant difference in mean ulcer size from baseline to 2nd week between two groups. There was significant difference in mean Ulcer size at 3rd week between two groups with increased reduction seen in Cadexomer iodine group. The overall mean % reduction in ulcer size

is significant (P-value <0.001) with increased reduction seen in Cadexomer iodine group 31.79 ± 5.51sqcm in contrast to 24.99 ± 5.38 sqcm reduction in Sucralfate group.

Table 9: Comparison based on reduction in ulcer size

	Group		P value
	Cadexomer iodine	Sucralfate	
	Mean sqcm	Mean sqcm	
Initial area	26.54	27.26	0.775
1 st week	25.43	26	0.808
2 nd week	22.4	22.63	0.918
3 rd week	20.2	18.77	0.490
Mean reduction	24.99	31.79	<0.001

Cadexomer iodine in which iodine is incorporated into modified starch matrix is highly fluid absorbing, antimicrobial and debrides dead and necrotic tissue. It is very effective in exudative wounds. Sucralfate stimulates the synthesis epidermal growth factor which in turn stimulates healing and affects prostaglandin synthesis. A study by Apelqvist J has shown similar reduction in ulcer size with use of topical Cadexomer iodine¹¹. Another study by Szabo S et al showed significant role of Various growth factors in the ulcer healing with use of topical sucralfate¹².

Granulation tissue

The best measure for ulcer healing is granulation tissue. At the time of admission Cadexomer iodine group had baseline granulation tissue between 25-50% and Sucralfate group had baseline granulation <25%. In Cadexomer iodine group, progression of granulation tissue appearance was 25-74% at 1st and 2nd week and 75-100% at 3rd week. In Sucralfate group, appearance of granulation tissue was 25-74% at the end of 1st and 2nd week and 75-100% at the end of 3rd week.

Table 10: Comparison based on Progression of granulation tissue

Time (weeks)	Group (Granulation %)		P value
	Cadexomer iodine	Sucralfate	
1 st week	25-74%	25-74%	0.600
2 nd week	25-74%	25-74%	0.318
3 rd week	75-100%	75-100%	0.290

There was no significant difference in appearance of Granulation tissue between two groups at 1st, 2nd and 3rd Week. Sucralfate group slightly had more patients with 75-100% of granulation tissue i. e, 27 (77.14%) compared to 23 (65.71%) patients in Cadexomer iodine group. The early appearance of granulation tissue helps in early readiness for grafting and decreases the frequency of dressing and debridement. There have been no studies till date to compare efficacy between Cadexomer iodine and Sucralfate but individual studies on both groups have shown to both have beneficial effect in appearance of granulation tissue and wound healing.

Necrotic tissue clearance

Necrotic tissue hampers wound healing as bacterial load remains in sloughed out and dead tissue. At admission most of the patients fell into the group with 51-75% slough with 10 (28.57%) patients in Sucralfate group compared to 19 (54.29%) patients in Cadexomer iodine group. In 1st week, most of the patients in Cadexomer iodine group had 11-25% slough i.e,18 (51.43%) patients whereas most of the patients in sucralfate group had 26-50% which shows significant reduction in slough in Cadexomer iodine group (p value- 0.012). In 2nd week, 23 (65.71%) patients had 0-10% of wound covered in slough whereas 16 (45.71%) patients had no necrotic tissue in Cadexomer iodine group which was significant reduction in slough. In 3rd week, 34 (97.14%) patients in Cadexomer iodine group had no necrotic tissue compared to 31 patients of Sucralfate group.

Table 11: Comparison based on reduction in slough

Time(weeks)	Group (Slough %)		P value
	Cadexomer iodine	Sucralfate	
1 st week	11-25%	26-50%	0.012
2 nd week	0-10%	0%	0.058
3 rd week	0%	0%	0.291

Various studies on Cadexomer iodine has shown that it significantly reduces Necrotic tissue and has proven to be super effective in exudating wounds in reducing the discharge in study by Raju R et al¹³. Similar results were observed in our study with significant reduction in frequency of dressings on a weekly basis.

Diabetic control

We monitored the glyceemic control with measurement of HbA1c levels. There was no significant variation in HbA1c levels between two groups which helped prevent confounding. The Mean HbA1c (%) in Sucralfate group and Cadexomer iodine group were 9.76 ± 2.07 and 9.31 ± 1.91 respectively. HbA1c is an accurate and easy-to-administer test and can be an effective biomarker in establishing the diagnosis of diabetes. Study by Manjunath HR et al showed that every 1% increase in HbA1c levels, the rate of ulcer-area healing decreased by 0.028 cm²/day signifying the importance of HbA1c¹⁴. HbA1c has been termed a biomarker i.e, “characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses to a therapeutic intervention”. Specifically in Diabetic foot ulcers, HbA1c plays an important role as foot ulcers are usually long standing disease¹⁴.

In our study, we observed that the patients who were treated with Cadexomer iodine agent had better outcome in terms of reduction in size of ulcer and clearance of necrotic tissue with overall enhancement in the ulcer

healing process. Both the groups had similar effect on formation of granulation tissue.

Conclusion

From our comparative study on topical application of Cadexomer iodine and Sucralfate agents in the treatment of diabetic foot ulcer, we can conclude that:

- Elderly age group was the most common to be affected with diabetic foot ulcers.
- Cadexomer iodine is better compared to Sucralfate in terms of reduction in ulcer size and clearance of necrotic tissue.
- Both Cadexomer iodine and Sucralfate had similar effect on formation of granulation tissue.
- HbA1c is an important determinant of ulcer healing which acts like a Biomarker.

We conclude from the present study that Cadexomer iodine has better outcome in Diabetic foot ulcer healing in terms of reduction in ulcer size and clearance of necrotic tissue and in turn augments the ulcer healing process.

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