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COMPARATIVE EVALUATION OF SUPEROXIDE SOLUTION DRESSING AND POVIDONE-IODINE DRESSING IN THE MANAGEMENT OF WAGNER GRADE 3 AND GRADE 4 DIABETIC FOOT ULCERS

B. Pooja[1], Dr. C. Srinivasan[2*]

[1]Postgraduate, Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India
Email:Poojababu1999@gmail.com
[2*]Professor, Head of Department, Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India,
Email: csrinivasan25@gmail.com

Abstract
Background: Diabetic foot ulcers are common limb-threatening complications of diabetes mellitus, and effective local wound dressings are essential to reduce infection, promote granulation, and accelerate healing.
Objectives: To comparatively evaluate the efficacy, safety, and cost-effectiveness of superoxide solution dressing versus povidone-iodine dressing in the management of diabetic foot ulcers.
Methods: This single-centre, hospital-based, prospective comparative study was conducted in the Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai, over 18 months among patients with Wagner Grade 3 and Grade 4 diabetic foot ulcers. Patients were treated with either superoxide solution dressing or 10% povidone-iodine dressing.
Results: The two groups were comparable at baseline, with similar mean age (54.8 ± 12.3 vs 56.1 ± 13.4 years), type 2 diabetes prevalence (96.1% vs 98.0%), duration of diabetes (9.2 ± 3.8 vs 8.7 ± 3.5 years), initial ulcer area (39.0 ± 18.0 vs 39.8 ± 19.5 cm²), Wagner grade distribution, forefoot involvement, and purulent discharge. Initial cultures showed Pseudomonas aeruginosa as the commonest isolate in the superoxide group (23.5%) and Staphylococcus aureus in the povidone-iodine group (27.5%). Ulcer reduction was greater with superoxide dressing from Week 2 onward, reaching 72.3% versus 56.0% by Week 12. Mean ulcer-area reduction was significantly higher in the superoxide group (59.2 ± 6.1% vs 41.0 ± 8.4%; p=0.001). Superoxide dressing also showed better Day 10 bacterial clearance, earlier granulation, shorter hospital stay, higher complete healing, and fewer non-healing/amputation outcomes.
Conclusion: Superoxide solution dressing was more effective than povidone-iodine dressing in promoting ulcer-size reduction, early granulation, bacterial clearance, shorter hospital stay, and complete healing in patients with advanced diabetic foot ulcers.

KEYWORDS: Diabetic foot ulcer, Superoxide solution, Povidone-iodine, Wound healing, Bacterial clearance, Granulation tissue

INTRODUCTION

Diabetic foot ulcers represent a major limb-threatening complication of diabetes mellitus and remain a substantial public health concern because they combine chronic hyperglycaemia, neuropathy, infection, impaired immunity, and delayed wound repair. The global diabetes burden has continued to rise, with the International Diabetes Federation reporting that approximately 589 million adults aged 20–79 years were living with diabetes in 2024, corresponding to 11.1% of the adult population, and projecting an increase to 853 million adults by 2050.(1) Diabetic foot ulceration affects a considerable proportion of this population; Zhang et al. reported a pooled global diabetic foot ulcer prevalence of 6.3%, with a higher prevalence among males than females,(2) while Sahu et al. estimated the pooled prevalence of diabetic foot ulcers in India to be 6.2%, with hospital-based studies showing a higher prevalence of 7.5% than community-based studies at 2.5%.(3)
The clinical importance of diabetic foot ulcers extends beyond wound chronicity because these ulcers are associated with recurrent infection, hospitalization, amputation, and excess mortality. McDermott et al. reported that the lifetime risk of developing a foot ulcer among persons with diabetes was 19%–34%,(4) while Armstrong et al. noted recurrence rates of 42% at 1 year and 65% at 5 years after healing, with an estimated 5-year mortality of approximately 50%.(5) The pathogenesis of diabetic foot ulceration is multifactorial, and ulcers commonly arise from neuropathy, ischemia, or a neuro-ischemic mechanism, with loss of protective sensation predisposing patients to unrecognized trauma and repetitive pressure injury. Wagner grading remains widely used for clinical severity assessment; Grade 3 ulcers are characterized by deep abscess formation or osteomyelitis, while Grade 4 ulcers indicate partial gangrene of the forefoot, reflecting advanced disease requiring aggressive wound care and infection control.(6)
Infection is a central determinant of delayed healing in diabetic foot ulcers, and microbiological patterns vary by geography, prior antibiotic exposure, ulcer depth, and chronicity. Satpathy et al. reported that most diabetic foot infections

in their cohort were caused by Gram-negative bacteria, mainly Escherichia coli,(7) while Kale et al. observed predominance of Gram-negative organisms among Indian patients with diabetic foot ulcers.(8) Effective local wound care therefore requires an agent that reduces microbial burden while preserving viable tissue and promoting granulation. Povidone-iodine has been widely used as a topical antiseptic in wound care, but newer topical agents have been explored to improve bacterial clearance, wound-bed preparation, and healing kinetics. Dumville et al. noted that chlorhexidine and povidone-iodine are older antimicrobial agents that continue to be used in foot-ulcer care, while contemporary wound management has increasingly evaluated alternative antimicrobial dressings.(9) Superoxidized solutions have emerged as topical antiseptic and irrigating agents for chronic wounds, including diabetic foot ulcers, because of their antimicrobial activity and reported tissue compatibility. Eftekharizadeh et al. concluded in a health technology assessment that superoxidized water was a safe, effective, and cost-effective irrigation and cleansing agent for chronic wounds compared with current treatment options.(10) Haesler (2020) on superoxidized solutions have also reported shorter healing times and improved complete-healing rates in diabetic foot ulcers compared with povidone-iodine in selected clinical studies, supporting further comparative evaluation in routine surgical practice.(11) Against this background, the objective of the present study was to comparatively evaluate the efficacy, safety, and cost-effectiveness of superoxide solution dressing versus povidone-iodine dressing in the management of diabetic foot ulcers among patients admitted to Sree Balaji Medical College and Hospital, with respect to wound healing, ulcer-size reduction, granulation tissue formation, bacterial clearance, secondary infection, local tolerability, duration of hospital stay, readiness for skin grafting, and overall treatment cost.

MATERIALS AND METHODS

This was a single-centre, hospital-based, prospective, comparative study conducted in the Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai over a period of 18 months (June 2024–December 2025). The study was approved by the Institutional Ethics Committee with reference number 002/SBMCH/IHEC/2024/2211 dated 25/06/2024. Participants and their attendants received the Participant Information Sheet (PIS) in their native language, with its details explained verbally for clarity. Patients aged 18 years and above with diabetes mellitus and Wagner Grade 3 or Grade 4 diabetic foot ulcers who were willing to provide written informed consent were included in the study. Patients with diabetes but without foot ulcers, those with Wagner Grade 1 or Grade 2 ulcers, known allergy to superoxide solution or povidone-iodine, history of malignancy, non-cooperation, or loss to follow-up were excluded.

The sample size was calculated using the study by Prabhakar et al.;(12) culture positivity was reported in 26% of patients treated with super-oxidized solution compared with 50% of patients treated with povidone-iodine dressing. Assuming these proportions for the present study, with 80% power, 5% one-sided level of significance, and 1:1 allocation ratio, the minimum required sample size was calculated using the formula for comparison of two independent proportions: n was rounded to 51 patients in each group, giving a final total sample size of 102 patients; enrolled using non-probability sampling technique – convenience sampling/complete enumeration. Each patient underwent detailed history taking, general examination, local wound examination, and relevant laboratory and radiological investigations. Baseline details including age, sex, duration of diabetes, type of diabetes, ulcer site, presence of discharge, and evidence of infection were recorded. The investigations performed included haemoglobin, total and differential leukocyte count, fasting and postprandial blood sugar, HbA1c, urine routine examination and acetone testing, renal function tests including urea and creatinine, and wound swab for culture and sensitivity. X-ray of the foot was performed when osteomyelitis was clinically suspected. Necrotic tissue was debrided whenever necessary. Empirical antibiotic therapy with ciprofloxacin and metronidazole was initiated initially and was subsequently modified according to the wound culture and sensitivity reports. Glycaemic control was achieved with insulin therapy, and all patients were advised off-loading and limb elevation as part of standard wound care. Patients in Group A underwent wound cleaning with sterile saline followed by dressing with superoxide solution, while patients in Group B underwent wound cleaning with saline followed by dressing with 10% povidone-iodine solution. In both groups, dressings were changed once daily until healing. Follow-up assessment was performed at regular intervals on Day 1, Week 1, Week 2, Week 6, and Week 12. At each follow-up visit, ulcer size was measured as length × width in mm² using the gauze mapping method, and percentage reduction in ulcer size was calculated. The wound was also assessed for granulation tissue, epithelialization, discharge, slough, infection, pain, and odour. Duration of hospital stay and any adverse reactions to the dressing were documented. Patients were followed up until complete wound healing or until the ulcer was considered ready for skin grafting.

Statistical analysis: Data were entered in Microsoft Excel and analyzed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation. Categorical variables were summarized as frequencies and percentages. The independent samples t-test was used to compare continuous variables between the superoxide dressing and povidone-iodine dressing groups, while the paired t-test was used to assess within-group changes in ulcer area over follow-up. Repeated-measures analysis was used to evaluate the trend in ulcer-area reduction across serial follow-up visits. The chi-square test or Fisher's exact test, as appropriate, was used to compare categorical variables between the two groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The mean age was 54.8 ± 12.3 years in the superoxide dressing group and 56.1 ± 13.4 years in the povidone-iodine group, with a male predominance in both groups. Most patients had type 2 diabetes mellitus in both Group A and Group B (96.1% vs 98.0%), and the mean duration of diabetes was also similar (9.2 ± 3.8 vs 8.7 ± 3.5 years). The initial ulcer area was comparable between the groups (39.0 ± 18.0 cm² vs 39.8 ± 19.5 cm²), and the distribution of Wagner Grade 3 and Grade

4 ulcers was similar. Forefoot involvement was the most common site in both groups, and purulent discharge was present in 70.6% of patients in Group A and 74.5% in Group B. Initial wound culture showed a mixed microbiological profile, with Pseudomonas aeruginosa being the most common isolate in the superoxide group (23.5%), while Staphylococcus aureus was most common in the povidone-iodine group (27.5%); no growth was observed in 9.8% of patients in each group. During follow-up, ulcer area reduced progressively in both groups; however, the reduction was greater in the superoxide dressing group from Week 2 onward. By Week 12, the mean ulcer area had reduced to 10.8 ± 8.6 cm² in Group A compared with 17.5 ± 12.4 cm² in Group B, corresponding to a 72.3% versus 56.0% reduction from baseline, respectively, with statistically significant differences at all follow-up points.

The secondary clinical outcomes favoured the superoxide dressing group over the povidone-iodine group. The mean percentage reduction in ulcer area was significantly greater in Group A than in Group B (59.2 ± 6.1% vs 41.0 ± 8.4%; p=0.001). Bacterial clearance was also better with superoxide dressing, with culture negativity at Day 10 observed in 37 patients (72.5%) compared with 28 patients (54.9%) in the povidone-iodine group (p=0.040). Granulation tissue appeared earlier in Group A than in Group B, with a mean duration of 5.2 ± 1.7 days versus 7.1 ± 2.0 days, respectively (p=0.001). The duration of hospital stay was shorter among patients treated with superoxide dressing (13.2 ± 3.1 days) compared with those treated with povidone-iodine dressing (16.4 ± 3.8 days; p=0.002). In terms of final treatment outcome, complete healing was achieved in a higher proportion of patients in Group A than Group B (74.5% vs 51.0%; p=0.010), while readiness for skin grafting was observed in 19.6% and 35.3%, respectively. Non-healing or amputation occurred less frequently in the superoxide group than in the povidone-iodine group (5.9% vs 13.7%).

DISCUSSION

The present study evaluated two topical dressings in patients with Wagner Grade 3 and Grade 4 diabetic foot ulcers and showed that superoxide solution dressing produced better wound-related, microbiological, and clinical outcomes than povidone-iodine dressing. The baseline comparability of the two groups strengthened the interpretation of the observed treatment effect, as age, sex distribution, type and duration of diabetes, initial ulcer area, Wagner grade distribution, forefoot involvement, and purulent discharge were similar between the groups. This was important because diabetic foot ulcer healing is strongly influenced by ulcer severity, infection burden, off-loading, vascular status, glycaemic control, and adequacy of wound-bed preparation; Armstrong et al. emphasized that appropriate diabetic foot ulcer care includes debridement, pressure off-loading, infection control, and vascular assessment or reconstruction when needed.(13) The demographic pattern in the present study was consistent with the usual clinical profile of diabetic foot ulcer patients, with the mean age being 54.8 ± 12.3 years in the superoxide group and 56.1 ± 13.4 years in the povidone-iodine group, and with male predominance in both groups. Most patients had type 2 diabetes mellitus, and the mean duration of diabetes was approximately 9 years in both groups, reflecting the chronic metabolic background in which neuropathy, repetitive pressure, infection, and impaired tissue repair contribute to ulcer development. Armstrong et al. described diabetic foot ulcers as commonly developing due to repetitive stress over pressure-bearing areas in patients with peripheral neuropathy, while peripheral arterial disease further contributes to ulcer development and delayed healing.(13)

The initial ulcer profile was also balanced, as the mean ulcer area was 39.0 ± 18.0 cm² in the superoxide group and 39.8 ± 19.5 cm² in the povidone-iodine group, with Wagner Grade 3 ulcers forming the majority in both groups. The presence of purulent discharge in nearly three-fourths of patients indicated a clinically infected wound population. The 2023 IWGDF/IDSA guideline stated that diabetes-related foot infection should be diagnosed clinically based on local or systemic signs of inflammation and that infection severity should be assessed using a standardized classification system.(14) The microbiological findings further supported this infected-wound profile, with Pseudomonas aeruginosa being the most frequent isolate in the superoxide group and Staphylococcus aureus being the most frequent isolate in the povidone-iodine group. This pattern was in line with Prabhakar et al. (2016) and Kantly & Medikeri (2018), who reported bacterial growth in infected diabetic ulcers and identified Escherichia coli as the commonest organism in the superoxidized-solution group and Staphylococcus as the commonest organism in the povidone-iodine group.(12, 15)

A key finding of the present study was the significantly greater reduction in ulcer area among patients treated with superoxide solution. Although both groups demonstrated progressive reduction in ulcer size, the reduction was consistently greater in the superoxide group from Week 2 onward. By Week 12, the mean ulcer area had decreased to 10.8 ± 8.6 cm² in the superoxide group compared with 17.5 ± 12.4 cm² in the povidone-iodine group, corresponding to a 72.3% versus 56.0% reduction from baseline. This finding closely paralleled the study by Prabhakar et al., in which the final ulcer area was significantly lower in the superoxidized-solution group than in the povidone-iodine group, and the mean percentage reduction in ulcer area was 58.90 ± 5.21% versus 40.90 ± 8.76%, respectively.(12) The superior wound-size reduction observed in the present study may be explained by the dual antimicrobial and tissue-compatible properties of superoxidized solution. Prabhakar et al. described superoxidized solution as an electrochemically processed aqueous solution with neutral pH and identified it as a newer wound-management concept intended to control infection while preserving normal tissue healing.(12) Sridhar and Nanjappa also noted that an ideal wound-care product should control infection, protect normal tissue, and not interfere with wound healing, and they reported that superoxidized solution produced faster wound healing compared with povidone-iodine.(16)

Granulation tissue appeared significantly earlier with superoxide dressing in the present study, with a mean duration of 5.2 ± 1.7 days compared with 7.1 ± 2.0 days in the povidone-iodine group. Early granulation is clinically important because it indicates transition from inflammatory control to proliferative wound repair and determines readiness for epithelialization or skin grafting. Sridhar and Nanjappa reported that superoxidized solution produced earlier granulation tissue and re-epithelialization,(16) and they cited Martínez-De Jesús et al., in whom 90.4% of patients in the superoxidized-solution group advanced to the granulating phase compared with 62.5% in the comparator group.(17) The present finding therefore reinforced the biological plausibility that rapid bacterial suppression and reduced local inflammation can accelerate wound-bed preparation.

Bacterial clearance was also superior in the superoxide group, with culture negativity at Day 10 in 72.5% of patients compared with 54.9% in the povidone-iodine group. This was clinically meaningful because persistent bacterial colonization or infection can prolong inflammation, delay granulation, increase slough and discharge, and increase the risk of progression to deep infection or amputation. Prabhakar et al. reported that culture positivity was lower in the superoxidized-solution group than in the povidone-iodine group, at 26% versus 50%, respectively.(12) Similarly, Sridhar and Nanjappa observed better microbiological clearance with superoxidized solution, with complete eradication of the causative organism in 97% of ulcers treated with superoxidized solution compared with 85% treated with povidone-iodine.(16) Povidone-iodine remains a widely used and effective antiseptic, and Bigliardi et al. reported that it has broad antimicrobial activity, activity against Gram-positive and Gram-negative organisms, no reported acquired bacterial resistance or cross-resistance, and usefulness in acute and chronic wound care.(18) However, in the present study, povidone-iodine dressing was associated with slower ulcer-area reduction, delayed granulation, lower bacterial clearance, and longer hospitalization. One possible explanation is that antiseptics differ in their effects on viable tissue; Rueda-Fernández et al. demonstrated in an in vitro study that povidone-iodine reduced human skin fibroblast viability and inhibited wound closure in scratch-assay models, although these laboratory findings do not always directly translate into clinical outcomes.(19)

The improved wound healing and bacterial clearance in the superoxide group translated into better clinical outcomes. Complete healing occurred in 74.5% of patients receiving superoxide dressing compared with 51.0% receiving povidone-iodine dressing, while non-healing or amputation occurred less frequently in the superoxide group. The duration of hospital stay was also significantly shorter with superoxide dressing, at 13.2 ± 3.1 days compared with 16.4 ± 3.8 days. This finding was clinically relevant because diabetic foot complications are a major driver of hospitalization and healthcare cost; Armstrong et al. reported that diabetic foot ulcers and infections were strong contributors to emergency visits and hospital admissions,(13) and that lower-extremity complications account for a substantial proportion of diabetes-related healthcare expenditure. The observed reduction in hospital stay therefore supported the practical value of superoxide solution not only as a wound-healing agent but also as a potentially resource-saving dressing option in admitted patients with infected diabetic foot ulcers.

The present study had certain limitations. It was conducted at a single tertiary-care hospital with a relatively limited sample size, and therefore the findings may not be generalizable to all diabetic foot ulcer populations. Although the two groups were comparable at baseline, factors such as peripheral vascular status, neuropathy severity, nutritional status, glycaemic variability, off-loading compliance, antibiotic response, and extent of debridement could have influenced wound healing. The study included only Wagner Grade 3 and Grade 4 ulcers, so the results may not apply to less severe diabetic foot ulcers. Blinding was not feasible because of the nature of the dressings, which may have introduced observer or assessment bias. Follow-up was limited to 12 weeks or until healing or graft readiness; hence, long-term recurrence, durability of healing, delayed complications, and late amputations could not be assessed.

CONCLUSION

The present study concluded that superoxide solution dressing was more effective than povidone-iodine dressing in the management of Wagner Grade 3 and Grade 4 diabetic foot ulcers. Patients treated with superoxide solution showed greater reduction in ulcer area, faster appearance of healthy granulation tissue, better bacterial clearance, shorter hospital stay, and a higher rate of complete healing. Superoxide dressing was also associated with fewer non-healing outcomes or amputations, indicating better overall wound response and local tolerability. Therefore, superoxide solution may be considered a useful and clinically advantageous dressing option for infected diabetic foot ulcers, particularly when early wound-bed preparation and faster healing are desired.

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Table 1: Baseline demographic and ulcer characteristics of the study participants

	Group A: Superoxide dressing (N = 51)	**Group B: Povidone-iodine dressing (N = 51)**	**p-value**
Age (years), mean ± SD	54.8 ± 12.3	56.1 ± 13.4	0.470
Male, n (%)	39 (76.5)	41 (80.4)	0.630
Female, n (%)	12 (23.5)	10 (19.6)	—
Type 2 diabetes mellitus, n (%)	49 (96.1)	50 (98.0)	0.700
Type 1 diabetes mellitus, n (%)	2 (3.9)	1 (2.0)	—
Duration of diabetes (years), mean ± SD	9.2 ± 3.8	8.7 ± 3.5	0.540
Initial ulcer area (cm²), mean ± SD	39.0 ± 18.0	39.8 ± 19.5	0.720
Wagner Grade 3 ulcer, n (%)	30 (58.8)	29 (56.9)	0.830
Wagner Grade 4 ulcer, n (%)	21 (41.2)	22 (43.1)	0.810
Common ulcer site: forefoot, n (%)	33 (64.7)	35 (68.6)	0.670
Purulent discharge, n (%)	36 (70.6)	38 (74.5)	0.640

Table 2: Initial microbiological profile of wound swab culture

Organism isolated	**Group A: Superoxide dressing (N = 51)**	**Group B: Povidone-iodine dressing (N = 51)**
Staphylococcus aureus, n (%)	10 (19.6)	14 (27.5)
Pseudomonas aeruginosa, n (%)	12 (23.5)	10 (19.6)
Escherichia coli, n (%)	9 (17.6)	8 (15.7)
Proteus mirabilis, n (%)	6 (11.8)	5 (9.8)
Klebsiella pneumoniae, n (%)	5 (9.8)	4 (7.8)
Mixed flora, n (%)	4 (7.8)	5 (9.8)
No growth, n (%)	5 (9.8)	5 (9.8)

Table 3: Change in mean ulcer area over follow-up

Duration	**Group A: Superoxide dressing, mean ulcer area (cm²)**	**Group B: Povidone-iodine dressing, mean ulcer area (cm²)**	**Percentage reduction from baseline**	**p-value**
Day 0, baseline	39.0 ± 18.0	39.8 ± 19.5	—	—
Week 2	27.5 ± 12.5	32.0 ± 13.2	29.5% vs 19.6%	0.030
Week 4	20.5 ± 9.8	26.5 ± 11.5	47.4% vs 33.4%	0.010

Week 8	14.5 ± 8.2	21.0 ± 9.5	62.8% vs 47.2%	0.004
Week 12, final healed/graft-ready	10.8 ± 8.6	17.5 ± 12.4	72.3% vs 56.0%	0.002

Table 4: Secondary clinical outcomes

Parameter	**Group A: Superoxide dressing (N = 51)**	**Group B: Povidone-iodine dressing (N = 51)**	**p-value**
Mean percentage reduction in ulcer area (%), mean ± SD	59.2 ± 6.1	41.0 ± 8.4	0.001
Culture negative at Day 10, n (%)	37 (72.5)	28 (54.9)	0.040
Culture positive at Day 10, n (%)	14 (27.5)	23 (45.1)	—
Time to appearance of granulation tissue (days), mean ± SD	5.2 ± 1.7	7.1 ± 2.0	0.001
Duration of hospital stay (days), mean ± SD	13.2 ± 3.1	16.4 ± 3.8	0.002

Table 5: Final treatment outcome

Treatment outcome	**Group A: Superoxide dressing (N = 51)**	**Group B: Povidone-iodine dressing (N = 51)**	**p-value**
Complete healing, n (%)	38 (74.5)	26 (51.0)	0.010
Ready for skin grafting, n (%)	10 (19.6)	18 (35.3)	—
Non-healing/amputation, n (%)	3 (5.9)	7 (13.7)	—