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# A Comparative Study of Efficacy of Superoxidized Solution against Povidone Iodine in the Treatment of Diabetic Ulcers

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**Abstract:** ***Background: Super-oxidised solution is one of the relatively newer, efficacious, and potent topical wound dressing solutions. Aim: Present study was conducted to compare the efficacy and safety of povidone iodine and superoxidised solution with respect to wound healing & complication. Methods: This was a block-randomised, comparative study. One hundred fifty patients with ulcers were randomised into the two treatment groups. One group treated with povidone iodine and other group with superoxide solution. Patients were observed for six weeks with regular assessments. Wound healing was objectively assessed by measurement of wound area, scoring of wound exudation and tissue type, and using the Pressure Ulcer Scale of Healing Tool (validated for multiple wound etiologies). Results: One hundred patients, fifty in each group completed the study. There was insignificant statistical difference in age, sex ratio, leucocyte count, edema & arterial doppler study of the limbs in both the groups. Difference in change in wound tissue type in the two groups was significant (p-value <0.05).The wounds dressed with superoxidised solution showed earlier appearance of healthy granulation tissue, earlier disinfection of wounds and lesser number of complications. Conclusion: Superoxidised solution is efficacious than povidone iodine in treatment of diabetic ulcers.***

**Keywords:** Ulcer, diabetes, superoxide solution.

## 1. Introduction

Diabetes mellitus is a condition primarily defined bythe level of hyperglycaemia giving rise to risk of microvasculardamage (retinopathy, nephropathy and neuropathy). It is associatedwith reduced life expectancy, significant morbidity due to specificdiabetes related microvascular complications, increased risk of macrovascular complications (ischaemic heart disease, stroke and peripheral vascular disease), and diminished quality of life.

Recent estimates indicate there were 171 million people in the worldwith diabetes in the year 2000 and this is projected to increase to366 million by 2030(1).

Diabetic foot infection is a common cause for the hospital admissions of the diabetic patients in India (2). This could be attributed to several sociocultural practices such as barefoot walking; inadequate facilities for diabetic care low education and poor socio-economic conditions (2).

The role of iodine in wound care is primarily as an antimicrobial agent. Povidone iodine has been used and tested in wound healing for many decades (3). In povidone iodine, iodine forms a complex with the synthetic carrier polymer povidone, which itself has no microbicidal activity (3). In an aqueous medium, free iodine is released into solution from the povidone iodine complex and an equilibrium is established, with more free iodine being released from the povidone iodine reservoir as iodine-consuming germicidal activity proceeds (4). The active moiety is iodine, oxidising pathogen nucleotides and fatty/amino acids and thus deactivates proteins as well as DNA/RNA (4)

Superoxidized aqueous solution(SOS) is non toxic, neutral pH water that contains reactive oxygen species (ROS) generated by the electrolysis of sodium chloride and water.SOS contains ROS and free radicals similar to those produced and released during the respiratory burst inside the mitochondria to produce energy (adenosine triphosphate, ATP), CO2 and water. Microbial killing requires the ability of leucocytes to generate ROS, as well as the action of various microbicidal enzymes and peptides contained in leucocyte secretory granules. Superoxide anion and granule microbicidal enzymes are the mechanisms phagocytic leucocytes use to kill their targets.

The primary objective of present study is to evaluate the efficacy of povidone iodine in comparison to that of SOS in wound healing assessed by a scoring system for wound exudation and wound tissue type. The secondary objectives are to evaluate the efficacy of povidone iodine in comparison to that of SOS in the number of complication and the rate of disinfection of the wound.

## 2. Materials and Methodology

This study was a comparative study. Patients were enrolled in blocks of two, to ensure uniformity and wound size score by the pressure ulcer scale of healing (PUSH) Tool. Using computerised randomization, patients in each block were randomly assigned to two treatment groups: A (POV) treated with povidone iodine and B (SOS) treated with superoxidized solution. Thus the allocation ratio remained 1:1. This study was conducted after approval from the Institutional Ethics Committee.

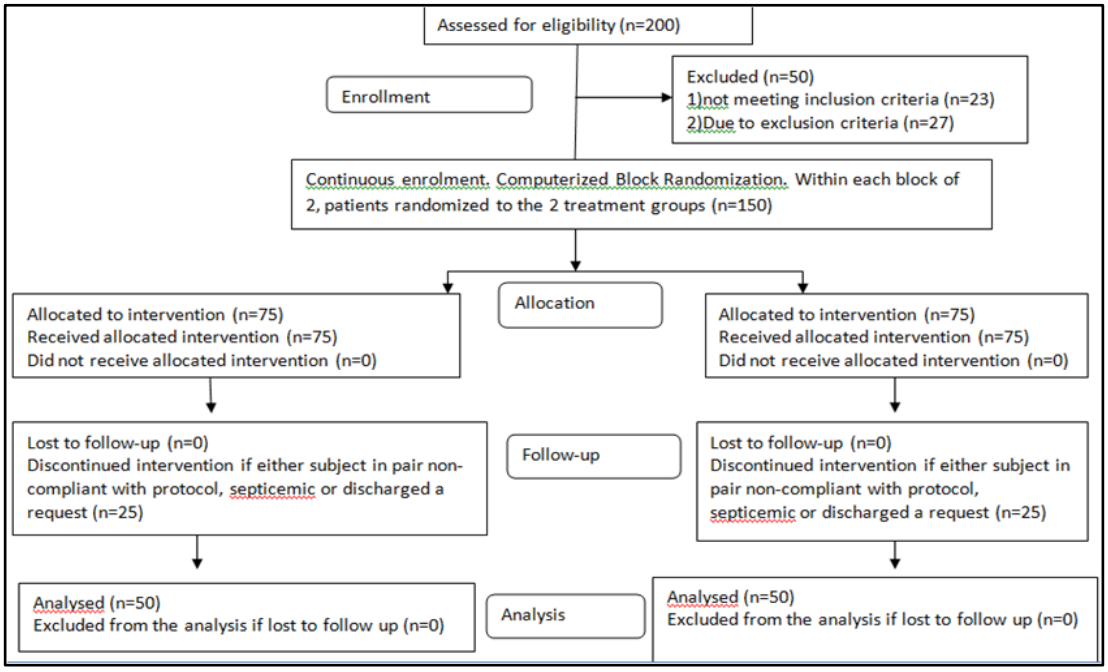



**Figure 1:** CONSORT 2010 flow diagram (5)

The study sample included patients with diabetic ulcers, above 18 years, both male and female, type 1 and 2 diabetes patients and Grade 1,2 and 3 ulcers according to Wagner Meggit Classification(6) and Grade 1 and 2 according to TEXAS Classification (7).

The patients with Grade 4 according to Wagner Meggit Classification and Grade 3 according to TEXAS Classification, wound swab negative ulcers, not willing to give consent,vascular occlusion, osteomyelitis in affected foot were excluded from the study.

This study was conducted in a tertiary care hospital in India. The subjects were in-patients from the wards of the department. Patients were enrolled and assessed between July 2017 to October 2019.

A set of 200 patients were screened on a continuous basis, out of which 150 patients met all criteria. Thus 75 blocks were enrolled. Within each block, the patients were randomly assigned to the treatment groups by computer-generated random assignment. A set of 25 patients were non-compliant with the wound-dressing protocol or wished to be discharged for home care. In such cases, the entire block (total= 25 blocks, n= 50) was discarded from the study analysis, maintaining an allocation ratio of 1:1. Thus 50 blocks (n= 100) completed the study.

Group A (povidone iodine) was treated with a solution of povidone iodine. Group B (SOS) was treated with superoxidized solution.

After adequate debridement, the patients were assessed at the end of 1st,3rd and 6th week. On each assessment day, the following procedure was followed:

1) Step 1: Initial examination of the wound was done. The investigators assessed the wounds as per the protocol, including measurement of wound area, scoring of wound exudation and tissue type, and usage of the PUSH Tool.
2) Step 2: The wound was cleaned thoroughly and any necrotic tissue was debrided/ removed with forceps.
3) Step 3:Dressing was done with gauze after applying the test/comparator agent to the wound surface, so as to form a thin moist film of agent on the entire surface of the wound.

Wound recovery was assessed by decrease in wound size (approximate area), which was the primary efficacy variable, as well as improvement in scores of wound exudation and wound tissue type as per the PUSH Tool. Total recovery was measured by the total scores obtained using the PUSH Tool. The scores of both treatment groups were compared with each other for analysis of the comparative efficacies of the treatment agents. For wound area, the longest distances in length (centimetres) and width (centimetres) were measured and multiplied to give an approximate area of wound (square centimetres). In addition, this area was scored as per the PUSH Tool (ranging from 0 to 10).

**Table 1:** PUSH Tool (8)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| LENGTH X WIDTH (in cm²) | 0<br>0 | 1<br>< 0.3 | 2<br>0.3 – 0.6 | 3<br>0.7 – 1.0 | 4<br>1.1 – 2.0 | 5<br>2.1 – 3.0 | Sub-score |
| | | 6<br>3.1 – 4.0 | 7<br>4.1 – 8.0 | 8<br>8.1 – 12.0 | 9<br>12.1 – 24.0 | 10<br>> 24.0 | |
| EXUDATE AMOUNT | 0<br>None | 1<br>Light | 2<br>Moderate | 3<br>Heavy | | | Sub-score |
| TISSUE TYPE | 0<br>Closed | 1<br>Epithelial Tissue | 2<br>Granulation Tissue | 3<br>Slough | 4<br>Necrotic Tissue | | Sub-score |
| | | | | | | | TOTAL SCORE |

Wound culture sensitivity, complete blood check-up, renal and liver function tests, serum protein values, and blood sugar values were recorded at the end of 1st,3rd and 6th week.

Additionally, any abnormal findings from physical examination or laboratory tests considered as adverse events/side effects were documented by the investigator and followed up for 3 months with respect to healing.

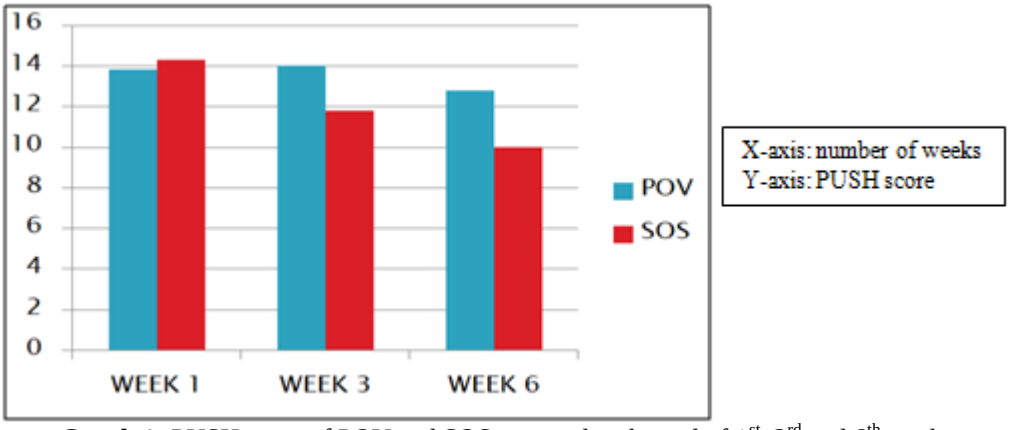
## 3. Results

Recruitment was as shown in the CONSORT 2010 Participant Flow Diagram. The overall mean age of patients in Group A – 52.00+/- 9.821 and Group B – 51.60+/- 16.342,p value for which is >0.05

Out of 50 patients in group A 36 were male patients and 14 were female patients and out of 50 patients in group B 35 were male patients and 15 were female patients.(p-value >0.05).

p-value for Hb(p=0.191), wbc(p=0.734), platelets(p=0.173), diffuse subcutaneous edema on Doppler(p>0.05) were all statistically insignificant.

Ulcer healing in both the groups assessed by comparing PUSH scores in both the groups at the end of week 1,3 and 6 and the results are as given in Graph 1



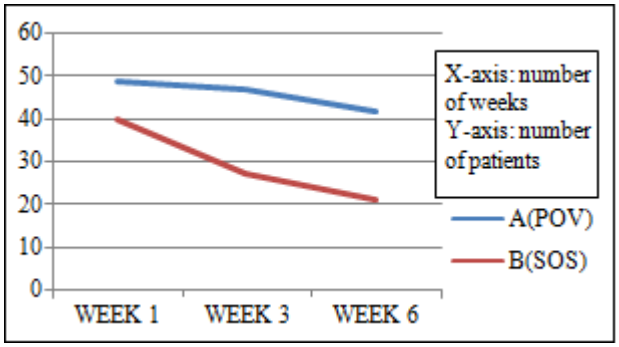

**Graph 1:** PUSH score of POV and SOS assessed at the end of 1st, 3rd and 6th week

The number of complications viz; amputation and redebridement were less in Group B as compared to Group Aand statistically significant (table 1)

**Table 1:** Complications of POV and SOS dressed wounds

| | Group | | p-value using Pearson Chi-square test |
|---|---|---|---|
| | A(POV) | B(SOS) | |
| Below knee amputation | 5 | 0 | <0.05 |
| Forefoot amputation | 0 | 2 | |
| Redebridement | 9 | 1 | |

The wound swabs taken from the ulcers of both the groups were compared at the end of 1st , 3rd and 6th week and number of wound swabs which isolated organisms at the end were less in SOS group as compared to POV group (Graph 2).




**Graph 2:** Comparison of patients with organism isolated on wound swabs from Group A and Group B

Superoxidized Solution

**Figure 2:** (a) Week 1 (b) Week 3 (c) Week 6

Povidone Iodine

**Figure 3:** (a) week 1 (b) week 3 (c) week 6

## 4. Discussion

Diabetic foot amputations are the most frequent complications in developing countries. Patients with foot complications spend a higher percentage of their income (32.3%) for treatment when compared with those without foot infections (9). Considering the immense burden superimposed by foot complications, aggressive management becomes imperative.

These wounds have been managed by local dressings with various agents like Povidone Iodine, Edinburgh University Solution Of Lime(EUSOL),Acetic acid, hydrogen peroxide, Silver sulfadiazine, local antibiotic ointments or powders etc since long time. Super Oxidized Solution is a newer concept in wound management. Researchers from many parts of the world have investigated Super Oxidized Solution as disinfectant for instruments.The literature also describes the use of this Solution on humans for various indications like ulcers, mediastinal irrigation, peritoneal lavage, hand washing etc.(10)

Hence, conducting present study becomes important owing to the massive burden of diabetic ulcers in our country. The present study included 100 diabetic ulcer patients admitted at a tertiary care hospital satisfying the inclusion criteria and randomized into two groups. Group A was dressed with povidone iodine and Group B was dressed with superoxidised solution. The patients were examined at regular intervals to evaluate the efficacy of both these agents.

The two groups were found to be comparable with respect to age and sex of the patients.

The patients were also compared on the basis of their blood sugar levels: fasting and post-prandial, complete blood count: hemoglobin, total leukocyte count and platelets and the difference was found to be statistically insignificant.

The peripheral circulation of the limbs was evaluated by a Doppler ultrasonography and both the groups were found to be comparable.

To measure wound healing, present study employed the PUSH Tool (Version 3.0) (11,12). This tool was primarily created for pressure ulcers, but it has been validated for ulcers with other etiologies as well (13). In a study by Pillen

et al. (14), ten different instruments proposed to measure wound healing were evaluated. None were found to satisfy all criteria required for instrument validation, defined by content and criterion validity,intra- and inter-rater reliability and sensitivity to change. Among various available tools for wound assessment, the predictive validity of the PUSH Tool has been demonstrated consistently in multiple studies (2).

A study conducted by ÜlküYapucuGünes (8) evaluating the validity and reliability of the PUSH score demonstrated that the PUSH tool 3.0 provided a method for quantitatively describing current wound status. If sequential assessment scores are tracked across time, it establishes a basis for identifying changes in wound status.

Another study conducted by Parikh et al evaluated the efficacy of PUSH tool in evaluating wound healing demonstrated the superiority of SOS in wound healing assessed by using PUSH tool (5)

Similarly, in the present study PUSH score of the ulcers were calculated after initial adequate debridement at the end of $1^{st}$,$3^{rd}$ and $6^{th}$ week. The PUSH score between the two groups were compared at the end of $1^{st}$,$3^{rd}$ and $6^{th}$ week and every time the difference was found to be statistically significant. This reveals the efficacy of superoxidised solution over povidone iodine in the rate of ulcer healing.

Gardner et al (15) found that only the PUSH scores of length x width of the ulcer decreased significantly among the healed ulcers. The PUSH tool differentially weights the three PUSH items. Size is weighted about 3.33 times more heavily than exudates amount and 2.5 times more heavily than tissue type. Thus, when using the PUSH tool, changes in wound size may affect the estimated status of the wound more than changes in exudate amount or tissue type (16). Because tissue type and exudate amount did not change appreciably from week to week, the wound size parameter of the tool contributed to changes in the PUSH score in these studies.

This was observed in the present study also when the PUSH score was compared within each group at the end of the above mentioned weeks. It was observed that the difference of PUSH score of group A at the end of the 3rd and $6^{th}$ week was more than the difference in PUSH score of group B at the same time interval. This observation was due to the change in the ulcer size from a large foot ulcer to a small amputation stump resulting from a complication due to non-healing wounds in patients dressed with povidone iodine showing an apparent fall in the PUSH score without actually speeding up the healing process.

In a study conducted by Dr. Luca Dalla Paola (17) on 218 patients suffering from chronic diabetic foot ulcers 110 patients were treated with SOS and 108 patients with povidone iodine. It was observed that the number of patients managed by conservative approach was more in SOS group than the POV group. Conservative operation included dressing, debridement, skin graft, ulcerectomy, ulcerectomy with exostectomy, and panmetatarsal head resection. Minor amputation included single and multiple toe amputation, single and multiple ray amputation, transmetatarsal amputation (TMA), Lisfranc and Chopart amputation (midfoot), and partial calcanectomy. Major amputations were those conducted below the knee (BKA) and above the knee (AKA).

Similarly in the present study, from the 50 patients in Group A, 5 patients had to undergo a below knee amputation and 9 patients had to undergo redebridement. In Group B, only 2 patients underwent forefoot amputation and 1 patient had to undergo redebridement. This shows that the rate of complication is more in the group dressed with POV.

In a study conducted by kapur et al. (18)diabetic foot ulcer and chronic leg ulcers patients treated with SOS showed early granulation and rapid epithelisation when compared to POV group as evidenced by 70% decrease in the size of the wound at day 21 in the group treated with SOS against 50% decrease in wound size in the group treated with POV.

Astudy conducted by Pandey et al. (19) studied 100 patients with diabetic ulcers by treating 50 patients with SOS and the rest 50 with POV. The study demonstrated early epithelialisation process and speedy granulation tissue formation, less time to lesion healing as evidenced by 80% decrease in the size of the wound at day 29 in group treated with SOS but only 65% decrease in the size in the group treated with POV. The study also demonstrated earlier asepsis in SOS group than the POV treated group of patients. It took 10+/-5 days for SOS group for disinfection of wound but 25+/-5 days for disinfection of POV group.

Another study by Abhyankar S, et al. (20) during 2009 in Mumbai on Efficacy and safety of Super-oxidized solution in the treatment of chronic wounds hasconcluded that the super oxidized solution is novel technology innovation in therapy of chronic wounds. But however both SOS and povidone iodine treated groups showed similar results with regards to decrease in edema, erythema and granulation.

Similar observation was made in the current study. The PUSH score between the two groups were compared at the end of $1^{st}$,$3^{rd}$ and $6^{th}$ week and the difference was found to be statistically significant at the end of every week.Wound swabs were taken from the ulcer at similar intervals mentioned above and the time taken by each group for disinfection of the ulcer was compared. At the end of 6 weeks, 29 patients in the SOS group showed no growth of any organism while only 8 patients in the POV group showed disinfection of the wound. This shows that SOS is efficacious than POV in terms of wound healing, appearance of granulation tissue and disinfection of the wound.

## 5. Conclusion

Superoxidized solution is efficacious than povidone iodine in the treatment of diabetic ulcers. However, more randomized controlled studies should be conducted to establish its advantage.

## References

[1] Wild S, Roglic G, Green A, Sicree R, King H. Global Prevalence of Diabetes: Estimates for the year 2000

and projections for 2030. Diabetes Care. 2004; 27: 1047-53.
[2] Maitra A, Abbas AK Endocrine system. Robbins and CotranPathologic basis of disease (7thedtn). Saunders, Philadelphia.2005;1156-226.
[3] W. Fleischer, K. Reimer, Povidone-iodine in antisepsis estate of the art, Dermatology1997;195: 3-9
[4] S.J. van Meurs, D. Gawlitta, K.A. Heemstra, R.W. Poolman, H.C. Vogely, M.C. Kruyt, Selection of an optimal antiseptic solution for intraoperative irrigation: an in vitro study, J. Bone Jt. Surg. Am. 2014; 96: 285e291.
[5] Parikh R, Bakhshi G, Naik M, Gaikwad B, Jadhav K, Tayade M. The efficacy and safety of tetrachlorodecaoxide in comparison with super-oxidised solution in wound healing. Arch Plast Surg. 2016;43:395–401.
[6] Wagner, F. W. The dysvascular foot: a system for diagnosis and treatment. Foot Ankle. 1981; 2:64-122.
[7] Armstrong D, Lavery LA, Harkless LB. Validation of a diabetic wound classification system: The contribution of depth, infection and ischemia to risk of amputation. Diabetes Care. 1998;21:855-9.
[8] Choi, E.P.H.,Chin, W.Y.,Wan, E.Y.F., & Lam, C.L.K. Evaluation of the internal and external responsiveness of the Pressure Ulcer Scale for Healing(PUSH) tool for assessing acute and chronic wounds. Journal of Advanced Nursing. 2016;72:1134-43
[9] Guidance for Industry, Diabetes Mellitus: Developing Drugs and Therapeutic Biologics for Treatment and Prevention, U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER). 2008: 3
[10] Chittoria, Ravi &Yootla, Mutheeswaraiah&Sampatrao, Leela & Raman, S. The role of super oxidized solution in the management of diabetic foot ulcer: our experience. Nepal Medical College journal : NMCJ. 2007;9:125-8.
[11] Stotts NA, Rodeheaver GT, Thomas DR, et al. An instrument to measure healing in pressure ulcers: development and validation of the pressure ulcer scale for healing (PUSH). J GerontolABiol Sci Med Sci 2001;56:M795-9.
[12] European Pressure Ulcer Advisory Panel; National Pressure Ulcer Advisory Panel. Pressure ulcer prevention and treatment: clinical practice guideline. Washington, DC: National Pressure Ulcer Advisory Panel; 2009;1124-36
[13] Hon J, Lagden K, McLaren AM, et al. A prospective, multicenter study to validate use of the PUSH in patients with diabetic, venous, and pressure ulcers. Ostomy Wound Manage 2010;56:26-36.
[14] Pillen H, Miller M, Thomas J, et al. Assessment of wound healing: validity, reliability and sensitivity of available instruments. Wound Pract Res 2009;17:208-17
[15] Gardner SE, Frantz RA, Bergquist S, Shin CD. A prospective study of the Pressure Ulcer Scale for Healing (PUSH). J Gerontol Med Science. 2005;60:93–7
[16] McNees P. Skin and wound assessment and care in oncology. Sem Oncol Nurs. 2006;22:130–43.
[17] Dalla Paola L, Brocco E, Senesi A, et al. Use of Deracyn, a new antiseptic agent for the local treatment of diabetic foot ulcers. J Wound Heal. 2005;2:201.
[18] VanitaKapur, Anil Kumar Marwaha et al. Evaluation of Effect and Comparison of Superoxidised Solution (Oxum) V/S Povidone Iodine (Betadine) Indian J Surg. 2011;73:48–53.
[19] P.K . Pandey et al ., International journal of Biological Medical Research Outcomes of Superoxide solution dressings in surgical wounds: a randomised case control trial. 2011;2: 965-68
[20] Abhyankar S, Veena V, Karnad S, Kulkarni K P, Juneja M, Nanda B, et al. Efficacy and safety of oxum in treatment of chronic wounds. Journal of Indian Medical Association, 2009; 107: 904-6.