



EVALUATION OF CLINICAL RESPONSE AND BACTERICIDAL EFFICACY AFTER APPLICATION OF SUPEROXIDIZED SOLUTION AND POVIDONE IODINE IN THE HEALING OF PRESSURE ULCERS

Prof. Dr. Raja Ray	MD, PhD. Professor and Head, Dept. of Microbiology, IPGMER/SSKM Hospital, Kolkata, West Bengal
Dr. Bipasa Chakraborty*	MD, Assistant Professor, Dept. of Microbiology, RGKMCH. *Corresponding Author
Dr. Lalbiaktluangi	MD, Medical Officer, Central Govt Health Scheme Wellness Center, Aizawl, Mizoram

ABSTRACT **Background:** Pressure ulcers are one of the major causes of morbidity among chronic bedridden patients and long haul patients with chronic ailments in intensive care units. They usually become infected with bacteria. Proper wound toilet and dressing are two most critical methods for minimizing bacterial bioburden. Superoxidized solution has been used for healing of different types of wounds and is both safe and effective, that moistens, lubricates, debrides and reduces microbial load in various wounds. So this study was done with the objective to determine and compare the clinical and bactericidal efficacy of superoxidized solution and povidone-iodine, another effective gold standard in management of pressure ulcers.

Methods: This prospective randomized interventional study was done with 50 patients with pressure ulcers admitted in Neuromedicine, Orthopaedics, and Intensive Care Unit of a tertiary care level hospital West Bengal. They were randomly divided into two groups of 25 each. Dressing and topical management was done using superoxidized solution in one group and povidone-iodine solution in the other. Evaluation of clinical therapeutic response for both the solutions were based on healing of pressure ulcers using different parameters like reduction in mean ulcer area, erythema, oedema, pain and appearance of granulation tissue and bactericidal efficacy was determined by following bacteriological culture report of wound swabs on day 1, 5, 9, 12, 18, 21 and 28 days after their application. Data analyses were done using Graph Pad Prism software version 5.00 and $P \leq 0.05$ were considered as statistically significant.

Results: In this study the average ulcer area, peri-wound oedema, erythema was significantly reduced with early appearance of granulation tissues among superoxidized solution treated group when compared to povidone-iodine group. Regular dressing with superoxidized solution also showed significantly lower bacterial bioburden than povidone-iodine group.

Conclusion: Superoxidized solution significantly reduced the bacterial load and common signs of inflammation with early granulation tissue formation. Thus superoxidized water was found to be better than povidone-iodine in early wound healing of pressure ulcers.

KEYWORDS : superoxidized water, povidone-iodine, pressure ulcers

Introduction:

Pressure ulcers or bed sores are debilitating and if not managed properly, it may lead to severe wound infection, tissue destruction, disfigurement and disabling scars. They are very difficult to treat and are one of the major causes of morbidity among chronic bedridden patients and in intensive care units. Such ulcers often get infected with endogenous and exogenous bacteria which can be either or both aerobic and anaerobic and can complicate wound healing. And in fact can contribute to sepsis in terminally ill patients.¹ Proper wound cleaning and dressing are two most important methods for minimizing the amount of bacterial bioburden which is most essential for proper healing of the ulcer. The cause of infection of these pressure ulcers are multi-factorial and nature of involved organisms are commonly polymicrobial. The associated underlying morbidity and inappropriate treatment are often responsible for ulcer development.¹ Other host related factors like age, malnutrition, anaemia, hypoproteinemia, obesity, uncontrolled diabetes, malignancy all leads to poor wound healing.² If not treated properly, it may even result in serious complications like osteomyelitis, cellulitis, bacteremia and sepsis.¹ So pressure ulcer treatment requires a multimodal approach with proper wound care, prompt management by wound debridement, cleaning and dressing with appropriate antiseptic solution with broad spectrum microbicidal efficacy.

Povidone iodine is widely used antiseptic solution used for dressing of pressure ulcers. Though it has excellent spectrum of microbicidal actions but it can sometimes be corrosive to skin and can cause itching, rash and local swelling causing delayed wound healing.^{3, 4} Superoxidized solution is less toxic than both povidone iodine and hydrogen peroxide solution and is safe and efficient at the same time.^{2, 5}

Super oxidized solutions are electrochemically processed aqueous solutions with neutral pH. It has rich reactive oxygen species which makes it an ideal solution with excellent bactericidal, virucidal, fungicidal and sporicidal actions on one hand and is stable with longer half life (>12 months), non-inflammatory and non-corrosive on the other hand that needs no further dilution during application on wounds.^{2, 6}

Superoxidized solution has been used for healing of different types of

wounds like diabetic foot ulcers, lower limb ulcers, traumatic and venous stasis ulcers and was found to be both safe and effective, that moistens, lubricates, debrides and most importantly reduces the microbial load in various types of wounds.^{7, 8} So this study was done to find out whether superoxidized solutions can act as a good alternative to commonly used povidone iodine solutions for healing of pressure ulcer. The objective of our study was to determine and compare the clinical and bactericidal efficacy of superoxidized solution and povidone iodine in the management of pressure ulcers.

Methods:

This prospective randomised interventional study was done in department of Microbiology, IPGMER/SSKM Hospital, Kolkata, for one year from August 2014 to July 2015 after taking proper institutional ethical clearance. 50 chronic bedridden patients of adult age group, admitted in Neuromedicine, Orthopaedics and Intensive Care Unit, who developed pressure ulcers of grade 1, 2, 3 and 4 were selected and randomly divided into two comparable groups of 25 each. One group received superoxidized solution (SOS group) and other group received povidone-iodine solution (PI group) as antiseptic solution during dressing of their pressure ulcer wounds. Patients with any other types of ulcers like diabetic foot ulcer, venous stasis ulcers, burn wounds etc were excluded from this study. Clinical response of SOS and povidone-iodine solutions for every patient was done at bedside, in their respective wards during their dressing time in the morning. Evaluation was done based on measurement and assessment of healing of pressure ulcers using different parameters like reduction in ulcer area, oedema, erythema, pain and appearance of granulation tissues on day 1, 5, 9, 12, 18, 21 and 28 days after their application.² Clinical samples like wound swabs and pus were collected from the pressure ulcer site on these same days. Bactericidal efficacies were determined by doing bacteriological culture of wound swabs and pus.⁷ Two wound swabs were collected from each patient from depth of the pressure ulcer wound after superficial wound debridement with normal saline. Before wound swabs were taken the surrounding ulcer margins were cleaned and eschars were removed. One swab was inoculated in blood agar plate and MacConkeys agar plate for aerobic culture. Another swab was immediately inoculated at bedside of the patient, in pre-reduced Brucella blood agar plate, placed inside a

polycarbonate jar, with a candle ignited to absorb oxygen and 5 gm of grease free, grade zero steel wool dipped in 50 ml of freshly prepared acidified 10% copper sulphate solution which was moulded and placed above the inoculated plates for absorption of excess free oxygen. Also CO₂ generator system containing sodium bicarbonate and magnesium carbonate in a test tube was put inside the jar to help growth of medically important anaerobes and the jar was closed with an air-tight lid for anaerobic culture by this modified candle jar method as elaborated in previous publication by Lalbiaktluangi *et al.* ⁹ After proper incubation at 37 °C, if any growth was detected in these plates, they were further processed for identification by conventional methods of identification. ¹⁰ Also antibiotic susceptibility testing for each isolate was done by Kirby-Bauer disc diffusion method and interpretation was done following CLSI guidelines 2014. ¹¹ Any growth detected was recorded and followed up to see if there was any resolution of infection, following regular application of SOS or povidone iodine solution, indicated by no growth of any organisms on subsequent cultures.

Clinical efficacy was evaluated as per following criteria ⁷ – a) Cure-resolution of all signs and symptoms within 28 days of treatment, b) Improvement- resolution of ≥ 2 signs within 28 days, c) Failure-persistence or progression of signs and symptoms after 28 days, d) Indeterminate- not fulfilling above 3 criteria.

Bactericidal efficacy of superoxidized solution and povidone-iodine were evaluated by following the culture reports of those pressure ulcers with positive report on day-1, as per following criteria ⁷ – a) eradication- no growth of causative organism following application of SOS or iodine solution, b) persistence of infection- growth of causative organism even after their application, c) relapse- reappearance of the causative organism after cure, d) superinfection- growth of new organism over the existing pathogen.

Data interpretation and statistical analyses of clinical and bactericidal efficacy between superoxidized solution and povidone iodine were done using Excel spreadsheet (Microsoft Corporation), descriptive biostatistics and Graph Pad Prism software version 5.00 (Graph Pad software, San Diego, CA, USA) and $P \leq 0.05$ were considered as statistically significant.

Results:

In our study, out of 50 patients, 35 were male and 15 were female patients. Mean age of the patients in SOS group(n=25) was 63.24±10.47 years and that of PI group(n=25) was 64.76±9.33 years. 92% patients in SOS group had co-morbidities like diabetes mellitus and hypertension whereas in PI group 88% patients had co-morbidities. All patients were having single pressure ulcer in their buttock. Grade-1 ulcer was present in 6 patients (3 each in SOS group and PI group), grade-2 ulcer in 36 patients (18 in each group), grade-3 ulcer in 8 patients (4 in each group) and there was no grade-4 ulcer patients. (Figure-1)

The mean ulcer area on day-1, in SOS group was 19.73±8.595 cm² compared to 19.28±7.792 cm² in PI group. After topical application of SOS and povidone iodine regularly, there was reduction of ulcer size in both the groups as shown in Figure-2 and Figure-3. The final mean ulcer area on 28th day in SOS group was 0.24±0.8307 cm², which is significantly lower than in PI group, 0.80±1.915 cm² ($P < 0.0001$). Similarly peri-wound edema and erythema were also significantly reduced more in SOS group than in PI group ($P < 0.0001$). (Figure-4). Pain relief was measured by visual analogue scale (score 0 to 10) and percentage of complete relief of pain was found to be significantly more in SOS group ($P = 0.0289$). (Figure-5). Appearance of granulation tissue, a very important sign of healing of wound was also assessed and found to appear early in SOS group than in PI group ($P = 0.0001$). (Figure-6).

Bacterial culture report showed growth in 45 patients (23 patients in SOS group and 22 patients in PI group), out of which 21 ulcers had polymicrobial infections. Most common microorganism isolated was Klebsiella pneumonia. (Table-1) Six anaerobes were also isolated by anaerobic culture method. (Table-1) Significant reduction in growth of bacteria from subsequent culture from pressure ulcer site was noticed more in SOS group than in PI group ($P < 0.0001$). (Figure-7) Analysis of antibiotic susceptibility testing (AST) of each isolate done by Kirby Bauer disc diffusion method showed 69.70% were multidrug resistant (MDR) phenotypes in SOS group and 70% MDR in PI group. AST for

Bacteroides fragilis showed 50% resistance to metronidazole and 75% resistance for penicillins and Peptostreptococcus anaerobius was even more resistant showing 100% resistance to penicillins. Hence all the isolates were highly resistant phenotypes.

Figure-1: Stage-3 pressure ulcer at day-1

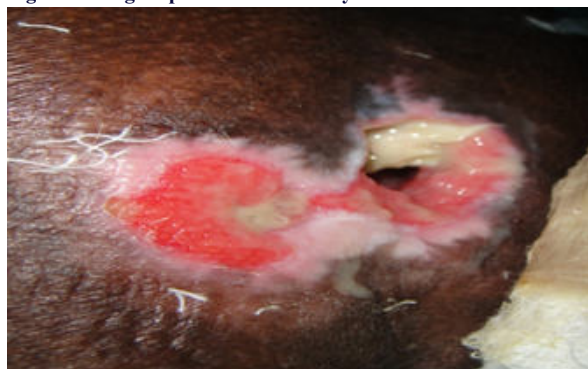


Figure-2: Pressure ulcer healed at day 28 after treatment with Superoxidized solution (SOS)

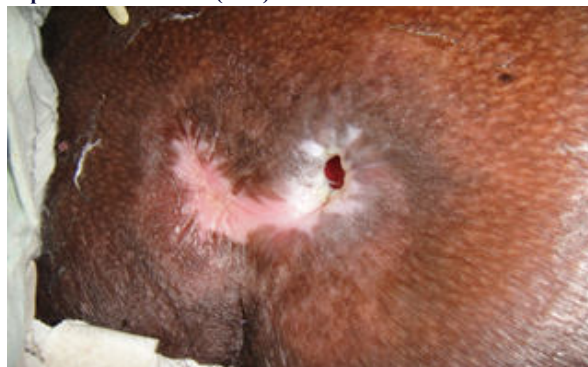


Figure-3: Reduction in mean ulcer size after treatment with SOS and povidone iodine solutions

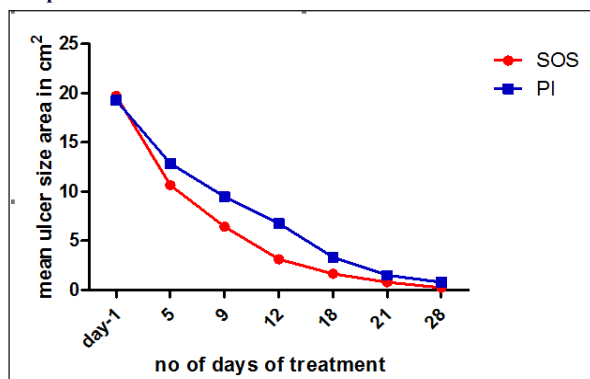


Figure-4: Reduction in peri-wound edema and erythema after treatment with SOS and povidone iodine solutions

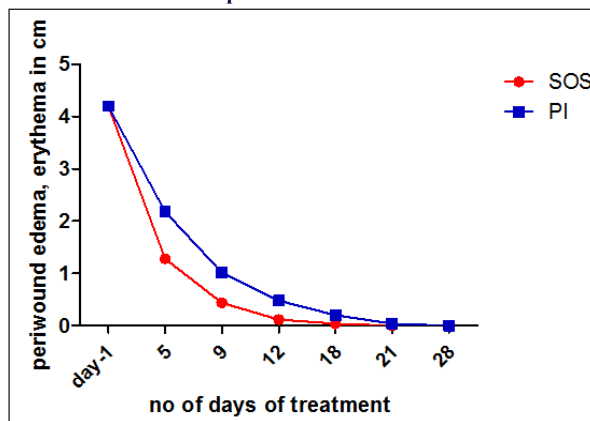


Figure-5: Relief of pain in %, among the study participants after treatment with SOS and povidone iodine solutions

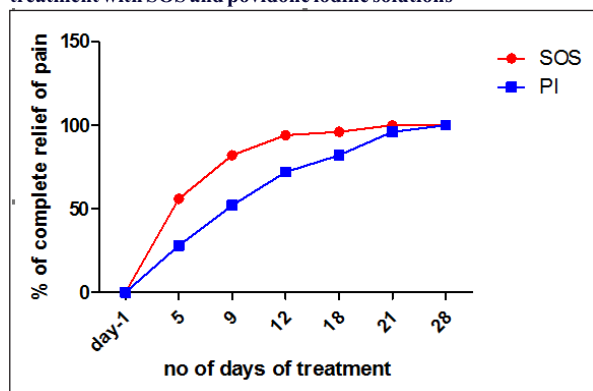


Figure-6: Appearance of granulation tissues in %, after treatment with SOS and povidone iodine solutions

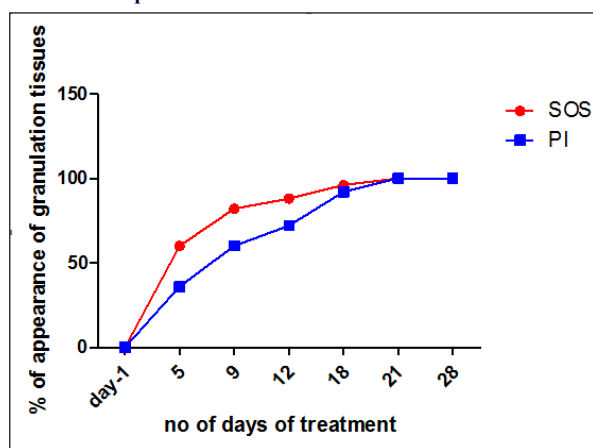
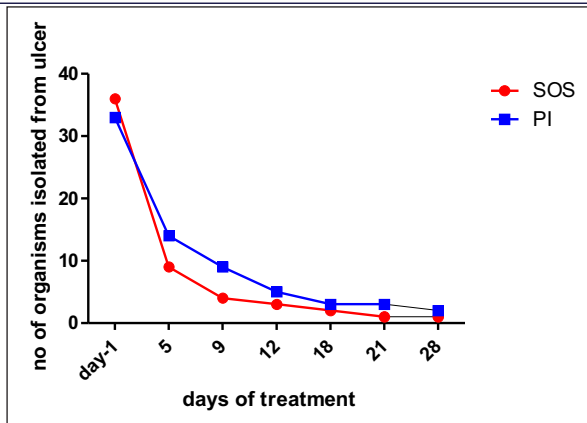


Table-1: Bacteria isolated from culture on day-1

Organisms isolated from culture of swabs taken from pressure ulcer site on day-1	SOS group	PI group
<i>Klebsiella pneumoniae</i>	2	2
<i>Citrobacter freundii</i>	2	2
<i>Proteus mirabilis</i>	2	0
<i>Acinetobacter baumannii</i>	1	0
<i>Providencia rettgeri</i>	0	1
<i>Staphylococcus aureus</i>	0	1
<i>Enterococcus faecalis</i>	2	2
<i>Staphylococcus epidermidis</i>	2	0
<i>Bacteroides fragilis</i>	2	0
<i>Peptostreptococcus anaerobius</i>	0	1
<i>Klebsiella pneumoniae</i> + <i>Pseudomonas aeruginosa</i>	2	1
<i>Klebsiella pneumoniae</i> + <i>Escherichia coli</i>	2	2
<i>Klebsiella pneumoniae</i> + <i>Staphylococcus aureus</i>	2	0
<i>Klebsiella pneumoniae</i> + <i>Proteus mirabilis</i>	1	1
<i>Acinetobacter baumannii</i> + <i>Escherichia coli</i>	1	1
<i>Pseudomonas aeruginosa</i> + <i>Bacteroides fragilis</i>	1	1
<i>Escherichia coli</i> + <i>Proteus mirabilis</i>	0	1
<i>Pseudomonas aeruginosa</i> + <i>Peptostreptococcus anaerobius</i>	0	1
<i>Klebsiella pneumoniae</i> + <i>Citrobacter freundii</i>	1	1
<i>Klebsiella pneumoniae</i> + <i>Citrobacter freundii</i> + <i>Staphylococcus aureus</i>	0	1
<i>Klebsiella pneumoniae</i> + <i>Citrobacter freundii</i> + <i>Enterococcus faecalis</i>	0	1
<i>Klebsiella pneumoniae</i> + <i>Proteus mirabilis</i> + <i>Staphylococcus aureus</i>	1	0
Total bacteria isolated	36	33

Figure-7: Reduction of number of isolated organisms from ulcer site with treatment of SOS and povidone Iodine



Discussion:

In our study, there was no relapse case and all the pressure ulcers improved with regular debridement and dressing with SOS or PI solution. Eradication of bacteria was seen in 96% ulcers in SOS group and 92% ulcers in PI group. Superinfection was noticed only in one case in PI group with *Pseudomonas aeruginosa* on 12th day but that too was eradicated by 18th day. Overall 92% ulcers in SOS group and 80% ulcers in PI group got completely cured by 28th day. In remaining few cases, there was marked improvement but no failure cases. So, the overall performance was better in superoxidized solution in terms of both clinical efficacy and bactericidal efficacy. Similar result was also found in studies by Sridhar S *et al* in the management of lower limb ulcers, where SOS performed better than PI solution.⁷ In another study by Kapur V *et al*, on different types of wounds, also proved SOS to be superior than PI solution.² There has always been a search for an ideal antiseptic that can rapidly kill bacteria and are have bactericidal property for a prolonged period with no or minimal ill effects on host tissues. Superoxidized solutions may represent as a good alternative to the currently available antiseptics like povidone iodine for antiseptics of skin and wounds.

Average day of appearance of granulation tissues in SOS group was 7.68 days whereas in PI group was 10.68 days after their regular application. So SOS reduces morbidity and hospital stay with its early wound healing effect than PI solution. Similar study by Prabhakar K B S *et al* on infected diabetic ulcers, showed SOS accelerated the healing process leading to faster recovery.⁷

To conclude, superoxidized solution is safe and effective alternative in management of pressure ulcers or bed sores, with better clinical and bactericidal efficacy and faster recovery than povidone iodine solution.

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