

# Comparative Evaluation of Intra-Operative Peritoneal Lavage with Super Oxidized Solution and Normal Saline in Peritonitis Cases; Randomized Controlled Trial

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## ABSTRACT

**Aim:** To investigate the efficacy of super-oxidized solution (SOS) over normal saline in peritonitis cases. Our objectives are to present the potential clinical impact of intraperitoneal lavage with solutions for early recovery of the patient by reducing the infection rate.

**Material and methods:** A double-blind random clinical trial was performed in 240 cases diagnosed as peritonitis at MM Institute of Medical Sciences and Research, Mullana, Ambala, India, from December 2013 to November 2015. Subjects were categorized into 2 groups, i.e. 120 cases in the group I and 120 cases in the group II. Both the groups underwent peritoneal lavage; the group I underwent normal saline lavage and group II received SOS. The effectiveness of both the solutions was compared.

**Results:** In both the groups majority of the patients (50.0%) were in the 21 – 40 years of age. The mean age in our study was 45.28 years, median was 45 and the standard deviation was 14.07. The bacterial load was higher in the group II as compared to the group I after the lavage with SOS solution. The superficial wound infection rate was higher in the group II (48 cases) compared to the group I (32). These data was significant with *p* value (0.040). Wound pain was found in 59 cases in group II as compared to 42 in group I. This difference was found to be statistically significant with *p* value 0.036. Post-operatively the morbidity and mortality was less in the group I as compared to group II.

**Conclusion:** SOS significantly reduced the wound pain and infection hence resulting in early recovery. SOS is a high level disinfectant, non-flammable and no special training is required to handle it.

**Keywords:** Peritonitis; peritoneal lavage; solutions; normal saline; infection

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## INTRODUCTION

The peritoneum is the serosal membrane of body composed of two main segments: the parietal peritoneum and the visceral peritoneum. Peritonitis is an inflammatory response which occurs as a result of infection, ischaemia and perforating injuries of gastrointestinal tract and genitourinary system (1). In women, localized peritonitis most often occurs in the pelvis from an infected fallopian tube or a ruptured ovarian cyst (2). Most commonly intraabdominal infections present clinically as peritonitis or an intra-abdominal abscess. Complicated intraabdominal infections are treated with some type of source control, such as an operative procedure or percutaneous drainage (3).

Use of Super Oxidized Solution (SOS) in infected wounds, ulcers, diabetic wounds, abscesses, burns reduced the morbidity and the hospital stay. OXUM (Microcyn Superoxidized solution) has been found to be an effective, non-toxic and safe wound care product for humans. The corrective mode is based on removing necrotic tissue (debriding), irrigating the wound, creating a moist environment and is the precondition for the maintenance mode. The maintenance mode is based on keeping the wound environment moist, while protecting against bacteria and other pathogenic micro-organisms, enabling the human body to perform the wound healing process (4). It is a custom to carry out intraoperative peritoneal lavage (IOPL) with normal saline after laparotomy but there is no clear cut consensus of its effect on surgical site infection, morbidity and mortality. We conducted a study and evaluated role of SOS over normal saline in peritonitis cases. Our aim was to assess the efficacy of two solutions to improve the recovery in peritonitis cases. □

## MATERIAL AND METHOD

Our study was designed to evaluate the early recovery, wound infection, in patients with peritonitis, on those who had received peritoneal lavage with Super Oxidised Solution (SOS) versus normal saline solution therapy. The study was conducted at MM Institute of Medical Sciences and Research Hospital, Mullana, Ambala, India between December 2013 and November

2015. The study was approved by the institute ethical committee board members alongwith project number. The cases of peritonitis in our study were those that met the inclusion criteria and were willing to participate in the study. A total of 290 cases underwent exploratory laparotomy for peritonitis out of which 50 were excluded. The patients of age more than 15 year were included in this study (Table 1). In both groups, patients were distributed according to age and the tabulated data shows that most of the patients were in the age group of 2nd to 4th decade of life. 21-30 years comprised 43 patients and 11 to 20 years were 24 in number. So it can be inferred that peritonitis is a disease of young and middle aged people.

Age group (in yrs)	No. of patients in group I(oxum)	No. of patients in group II
15-20	24 (20%)	26 (20%)
21-30	43 (36%)	24(20%)
31-40	19 (16%)	35 (28%)
41-50	19 (16%)	10(8.0%)
51-60	5 (4.0%)	10(8.0%)
>60	10 (8.0%)	14 (12.0%)
TOTAL	120 (100%)	120 (100%)

TABLE 1. Distribution of patients according to age in both groups

The gender involvement in group I: about 77(64%) were males and 43(36%) were females whereas in group II, 96 (80%) were males and 24 (20%) were females (Table 2). The heavy preponderance of males could be due to more use of intoxicating substances like alcohol, smoking, consumption of NSAIDS for prolonged periods, irregular meals, more outdoor life and eating spicy foods. Five patients had diabetes mellitus in group I and 10 patients had same disease in group II. These increased comorbidities in males may also be associated with increased incident of perforation in males (Table 3). Table 4 indicates that 100 % of patients in study group and control groups had pain abdomen, so pain abdomen is the most common presenting complaint. Most of the patients presented with pain abdomen, abdominal distention, vomiting and altered bowel habit. 5 patients in group I and 14 in group II presented in emergency ward with features of shock and were resuscitated prior to laparotomy.

Gender	No. of patients in group I	No. of patients in group II
Male	77 (64%)	96 (80%)
Female	43 (36%)	24 (20%)
Total	120 (100%)	120 (100%)

**TABLE 2.** Distribution of patients according to gender in both the groups

Co-morbidities	No. of patients in group I	%	No. of patients in group II	%
Diabetes mellitus	5	4.0	10	8.0
Hypertensive	0	0.0	0	0
Drug addict	0	0.0	0	0.0
Alcoholic	0	0.0	0	0.0
Smoker	20	16.0	15	12.0

**TABLE 3.** Distribution of patients according to associated co-morbidities in both groups

Chief complaints	No. of patients in group I	No. of patients in group II
Pain abdomen	120 (100%)	120(100%)
Abdominal distention	110 (92.0%)	105 (88.0%)
Vomiting	110 (92.0%)	96 (80.0%)
Altered bowel habit	91(76.0%)	86 (72.0%)
Fever	38 (32.0%)	57 (48.0%)
Shock	5(4.0%)	14 (12.0%)

**TABLE 4.** Distribution of patients according to chief complaints in both groups

The diagnoses of peritonitis e.g.: gastric, duodenal, ileal perforation, appendicitis, abdominal pathology causing peritonitis was included in the study. The exclusion criteria referred to : 1) evidence of enteric encephalopathy; 2) liver diseases; 3) renal diseases; 4) history of steroid intake; 5) heart disease; 6) known allergy to any substance; 7) multiple trauma or organ injury; 8) any gynecological etiology. Patients who were not willing to include in the study or who did not complete the inclusion criteria were also excluded from the study.

**Procedure**

On admission, detailed history was taken regarding pain, fever, vomiting, abdominal distention and thorough local examination was done. All routine blood tests and relevant radiological

investigations were done. Patients were resuscitated with the intravenous fluids, O<sub>2</sub> inhalation 4-6 liters/min and commenced broad spectrum intravenous third generation antibiotics (Ceftriaxone and Sulbactam). At the time of intervention, a sample of peritoneal fluid was collected in a sterile culture vial and transported to the Microbiology Department. It was inoculated on MacConkey's blood agar, incubated at 37 degree Celsius for 18 hrs. Next day identification of the organism was done by gram staining, biochemical reactions, and then the isolate was subjected to antibiotic sensitivity testing and the colony count. After the definitive surgery, the patients were randomly put into one of the two groups; 1) in group I, the peritoneal cavity was washed with 1 liter of saline. Then 200 ml (100ml of SOS diluted to 200ml with normal saline) of SOS was put in the peritoneal cavity; 2) in group II, after surgery (simple closure, resection and anastomosis etc.) the peritoneal cavity was washed with 1 liter of normal saline. Then the abdominal cavity was closed after putting 200 ml of normal saline; drains were placed and clamped for one hour (Figure 1). This was allowed to remain in the peritoneal cavity for 1 hour and the abdomen was closed. Drains were clamped during this period so that the SOS does not escape. Post-operatively, the culture was tak-



**FIGURE 1.** Lavage with Super oxidized solution with drains clamped

en on third day through the drain and was sent in a sterile vial to the Microbiology Department. It was inoculated on MacConkey's and blood agar, incubated at 37 degree Celsius for 18 hours. On next day, if growth present then identification of the organism was done by gram staining, battery of biochemical reactions. Then the isolate was subjected to antibiotic sensitivity testing and the colony count.

In post-operative course the antibiotics were given in all the patients i.e. Ceftriaxone, amikacin, metronidazole and antitubercular treatment in cases of tubercular pyoperitoneum (according to the renal status). The drain output was noted daily and also its character (serous/purulent). Drains were removed when output < 50 ml and serous. Day of drain removal was noted. If two drains were present then day of removal of both drains was noted separately. TLC, DLC and serum electrolytes were done as routinely. Day of recovery of bowel sound was noted and observed by hearing 3 to 4 bowel sounds per minute by stethoscope just right to the umbilicus. In the post-operative period, fever if present and its duration were recorded. Patients were followed for any complications such as superficial wound infection, burst abdomen, faecal fistula. Number of days for which the patient kept nil per orally. Number of days for which the patient stayed in the hospital was recorded. The day of stitch removal was noted. The data was recorded as per the proforma. The results were then compiled, analyzed and statistically evaluated.

### Sample size

There were 290 patients who had received optimal therapy for peritonitis were included in our study and after having screening test, 50 patients were excluded as 37 patients did not meet the inclusion criteria and 13 patients were not willing to participate in our study. The patients subsequently underwent further tests and filled the form about basic characteristics data for population study such as demography, laboratory data, and radiological tests mainly chest x-ray and ultrasonography of the abdomen.

### Randomization and Blind

Our study was a double blind randomized clinical trial, in which the evaluator did not know about the category of subject groups. We did not

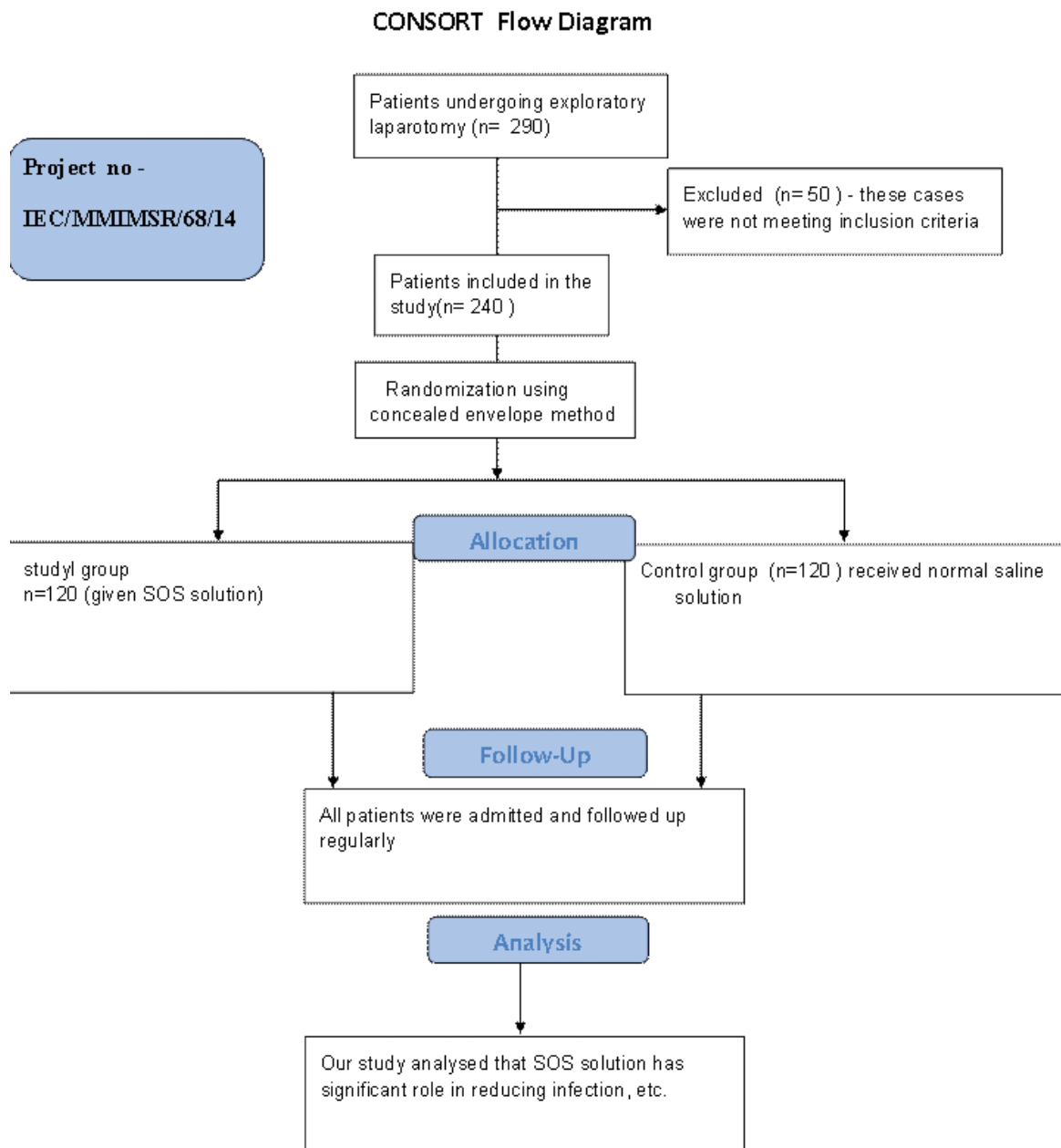
know whether the patients diagnosed as peritonitis were in the group receiving SOS lavage or normal saline lavage therapy. A concealed envelope was used for the randomization and the subjects were divided into 2 groups, i.e. there were 120 patients in the group I and other 120 patients in the group II. The study participants were recruited by the treating single surgeon and his team following the study protocol. The diagnosis was confirmed and included in the study as per the protocol.

Statistical Analysis - Statistical analysis was performed for all outcomes including primary, secondary and safety outcomes. Data were processed using mean value (standard deviation) and were tested with unpaired mean difference (median). The data of our study was analyzed using a computer software program of SPSS version 22.0.

Study Protocol - Patients diagnosed with peritonitis who received the peritoneal lavage with two different solutions were studied. They were then randomly selected to receive SOS lavage and normal saline lavage. An evaluation was subsequently conducted in 6-8 weeks following the therapy. Our study was conducted in keeping with Helsinki declaration and was supported by ethical clearance. The ethical clearance was issued by institutional ethic committee MM Institute of Medical Sciences and Research, Mullana, (Ambala), India with project number IEC/MMIMSR/68/14. All patients were obliged to sign informed consent before participating in our study. □

## RESULTS

The study was conducted from December 2014 to November 2015 In the Department of Surgery. Figure 2 shows a flow chart for participants in the study. Outcome measures of peritoneal lavage in peritonitis cases were documented after the treatment. Based on the results in the study, we found that most of the cases were male in both groups (males: 72.0% and females: 28.0%). On analysis according to the site of perforation, ileal perforation was observed in 11-40 years of the age group; duodenal perforation was almost equally divided in all the age groups while gastric perforations were usually found in more than 30 year of the age group. The heavy preponderance of males could be



**FIGURE 2.** Flow diagram showing the participants details

due to more use of intoxicating substances like alcohol, smoking, irregular meals, more outdoor life and eating spicy foods. In both the groups, the common complaints were pain abdomen, abdominal distention, vomiting and altered bowel habits. Total 40% patients had history of fever and 8.0% patients presented with shock, all were resuscitated and then surgery was done.

The most common site of perforation and bacterial growth was seen in gastric 98 (40.83%), duodenal 29 (12.08%), ileal 77 (31.25 %), ap-

pendicular 12 (5.8%) followed by jejunal 18 (7.5%) and colonic perforation 6 (2.5%) in both the groups (Table 5). All the patients were monitored postoperatively for the bacterial load, fever, type of discharge through the drain; day of appearance of bowel sounds, wound pain, superficial wound infection, and the wound dehiscence. The data was tabulated in the different tables and analyzed using chi square test and p-value. Bacterial load was calculated in different types of perforations and this data was tabu-



FIGURE 3. Bacterial growth on cultural plate

lated. According to calculation, bacterial load was higher in group II compared to the group I (Table 6). The significant reduction in the bacterial load was observed in most of the patients of the group I (Figure 3). From the above observations, we can say that peritoneal lavage with super-oxidized solution have good results on reducing bacterial growth and infection rate compared to normal saline lavage only.

Superficial wound infection rate was less in the group I (in 88 patients it was absent and present in 32 cases after the lavage) as compared to

Site of Perforation	Infection	Group I			Group II		
		Mild	Moderate	Heavy	Mild	Moderate	Heavy
Ileal perforation	Absent	3			2		
	Present	16	10	8	13	13	10
Duodenal Perforation	Absent	5			4		
	Present	4	2	4	2	5	3
Gastric Perforation	Absent	4			3		
	Present	12	14	14	14	15	13
Primary Peritonitis	Absent	0			1		
	Present	0	3	0	1	0	0
Jejunal Perforation	Absent	2			1		
	Present	3	1	3	3	2	2
Appendicular Perforation	Absent	1			1		
	Present	1	2	2	1	2	2
Colonic Perforation	Absent	2			1		
	Present	1	1	2	2	2	2

TABLE 5. Comparison of bacterial growth indifferent types of perforation during surgery

Site of Perforation	Infection	Group I (OXUM)			Group II			Combined
		Mild	Moderate	Heavy	Mild	Moderate	Heavy	
Ileal perforation	Absent	16			07			Chi square p = 0.039
	Present	12	08	02	12	12	08	
Duodenal Perforation	Absent	14			08			Chi square p = 0.035
	Present	01	0	0	01	04	01	
Gastric Perforation	Absent	18			08			Chi square p = 0.039
	Present	12	11	08	15	16	10	
Jejunal Perforation	Absent	08			02			Chi square p = 0.015
	Present	01	0	0	04	01	02	
Appendicular Perforation	Absent	04			03			Chi square p = 1.000
	Present	01	01	0	01	01	01	
Colonic Perforation	Absent	05			03			Chi square p = 0.545
	Present	0	0	1	0	1	2	

TABLE 6. Comparison of bacterial load in different types of perforation after 72 hrs of surgery

Factors noted		Group I	Group II	P value
Wound infection	Absent	88	72	0.040
	Present	32	48	
Wound pain	Absent	78	61	0.036
	Present	42	59	
Wound site Discharge	Serous	96	53	<0.001
	Purulent	24	67	
Bowel Sounds	Mean	4.92	5.8	<0.001
	Std. deviation	1.08	1.17	
Average day of drain removal	Mean	5.46	7.33	<0.001
	Std. deviation	2.59	2.25	
Hospital Stay	Mean	11.73	13.48	>0.05

TABLE 7. Effects of the solutions in both groups

the group II (in 72 patients it was absent but in 48 patients infection was seen) and statistically significant with p-value (0.040%). Wound pain was found in 59 patients in group II and in 42 patients in group I. This difference was found to be statistically significant with p-value 0.036. Hence we concluded that SOS is effective in reducing the wound pain by reducing the infection rate. On analysis of the post-operative fever, there were only 47.5% patients in group I compared to 52.0% patients in group II who had fever (Table 7). So it was observed that SOS reduces the infection rate by decreasing the post-operative fever but there were no major significant changes. The mean day for bowel sounds was  $4.92 \pm 1.08$  in the group I and among the group II it was  $5.8 \pm 1.17$ . By conventional criteria, this difference is considered to be statistically significant (p value <0.001). The drain was removed earlier in the group I than the group II. The mean in the group I was 5.46 and in the group II 7.33 (p value <0.001). The mean duration of hospital stay for group I was 11.73 days and 13.48 days for the group II. So, there is no difference observed in drain and hospital stay. In postoperative period, 3 patients in group I and 4 in group II had wound dehiscence, 1 patient in group II needed reexploration, 2 presented with incisional hernia in group I and two patients expired in group II as they presented

Complications	Group I	Group II
Wound dehiscence	3(2.5%)	4(3.33%)
Reexploration	0	1(0.83%)
Incisional Hernia	2(1.66)	0
Death	0	2(1.66%)

TABLE 8. Major complications encountered in postoperative period in two groups

with irreversible shock and could not be reviewed (Table 8). □

## DISCUSSION

The role of peritoneal lavage in the treatment of the peritonitis has been known to surgeons since time immemorial. Recently, to improve the clinical outcome without inducing chemical related toxicity to the peritoneum, IOPL with a neutral pH solution and low chlorine content (<70 ppm) is evaluated on the post-operative course. These types of solutions are referred to SOS. Some studies have suggested that use of SOS with the normal saline for irrigation in case of peritonitis has synergy (1). In cases of severe intra abdominal sepsis like peptic perforation, enteric perforation, appendicular perforation & gangrene gut, there is a very high rate of surgical site infection (SSI) inspite of use of higher antibiotics. Surgeons are able to control systemic infection but SSI still remains a challenge where incidence may be as high as 60-70% (5). There are also studies which used large amount of saline solution as IOPL in peritonitis cases to reduce the risk of infection. But there are very few studies who observed the results of the SOS with normal saline in peritonitis cases, as our study revealed that SOS is very effective in peritonitis cases. SOS is a hypotonic solution with an osmolarity of 13 mOsm/L and containing Hypochlorous acid, Sodium hypochlorite, Chlorine dioxide, Ozone, Hydrogen peroxide, and Sodium chloride. These solutions have been used in humans for cleansing of ulcers, mediastinal irrigation, peritoneal lavage and hand washing (6).

SOS fits within the described comprehensive therapy by contributing to the corrective mode, as a moistening, irrigation, and debridement solution. This enables Oxum to then perform within the maintenance mode by keeping the environment free of pathogenic micro-organisms. The mean age of patients was 40.5 years, ranged

from 13–80 years and standard deviation was 15.6 (7). The most common cause of perforation peritonitis was acid peptic disease 45 %, (perforated duodenal ulcer (43.6%) and gastric ulcer 1.3%), followed by small bowel tuberculosis (21%) and typhoid (17%) as studied by other group (8). A study was done on 229 patients diagnosed with gastroduodenal perforation and the common cause of perforation was peptic ulcer (9).

The IOPL is widely practised & choice of fluid varies among surgeons but its benefits are unclear. Surgeons were asked about the volume and the type of lavage fluid used, under various circumstances. In the dirty abdomen (gross pus or faecal peritonitis), 47% used saline as the lavage fluid, 38% aqueous betadine, 9% water and 3% antibiotic lavage. Similar results were found in the case of a contaminated abdomen (i.e. a breached hollow viscus). The successful management of the septic abdomen rests on at least 3 tenants – systemic antibiotics, control of the source of infection and the aspiration of gross contaminants. But there is a little good evidence in the literature to support IOPL in the management of the septic abdomen (6,10). In our study, 85% of the patients in the group I and 84% of patients in the group II showed positive cultures. Postoperatively, drain fluid was taken in all the patients. In the group I, out of 120 patients, bacterial load was found absent in 62 patients after 72 hours. This difference was found to be statistically significant ( $p$  value  $< 0.039$ ). The bacterial load was reduced less in group II as compared to group I. This shows that super-oxidized solution is very effective in controlling intraperitoneal infections. This fact is also supported by other study who showed that SOS caused reduction in bacterial load ( $t=2.7$ ,  $p<0.05$ ) (1). The average length of hospital stays were less in study group as compared to the control group. At the University of California, Landa et al (6) used pure cultures of *Staphylococcus aureus*, *Escherichia coli*, *P. aeruginosa*, *Salmonella typhi* and *Candida albicans* to evaluate in vitro antimicrobial efficacy testing of super-oxidized water (SOW). They described that SOW have broad microbiocidal activity, including bacteria, viruses, fungi and spores. These SOW have also passed different biocompatibility tests required by international agencies for wound care products, including: dermal, inhalatory, oral and peritoneal toxicities:

skin sensitization; skin and ocular irritation; intracutaneous reactivity and even genotoxicity tests (11). The study was done to assess the effect of intraoperative PVI application compared with no antiseptic solution (saline or nothing) on the SSI rate. Intraoperative PVI application significantly decreased the SSI rate (relative risk 0.58, 95 per cent confidence interval 0.40 to 0.83;  $p = 0.003$ ) (12). Another authors reported that hand disinfection using SOW is 7.5% more effective than povidone iodine. Although it has a very fast antiseptic activity on hands, it has a major disadvantage on alcoholic hand rubs due to its long drying time (13).

The main cause of death in the their series of patients was septicemia (25%) leading to multi organ failure. Therefore contamination is a crucial consideration in patients with peritonitis and problem of mortality is a problem of infection (14). But we want to also add that burst abdomen or other complications depend upon the technique used for closure, and on systemic factors (15). Overall, SOS achieved good source control in first week of treatment as shown by a potent microbial load reduction and a shorter hospital stay in the study group in comparison to the historical control group (16). SOW is among the broad spectrum disinfectants with its promising antimicrobial activity on microorganisms. They believe that SOW can be used efficiently to prevent hospital-acquired infections provided that further efficacy studies are done, and validated application methods are used (17).

Novel technologies:

- SOS are electrochemically processed aqueous solutions manufactured from pure solution which is rich in reactive oxygen species
- OXUM has a superoxidized solution with neutral pH and a longer shelf life ( $>12$  months). It rapidly reacts and denatures lipids and proteins of bacterial cell wall.
- OXUM also has antimicrobial effect and used in various diseases such as in diabetic foot, venous and pressure ulcer, burns. □

## CONCLUSION

SOS is a useful adjuvant therapy in peritonitis of any cause along with normal saline. This study proves that SOS is safe and effective in reducing postoperative complications like wound infection, pain and hence early recovery. SOS



requires no special handling or disposal. It has been demonstrated that there is remarkable reduction in common signs of inflammation like oedema, erythema and remarkable increase in signs of healing of the ulcer i.e. granulation and fibrin formation. □

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