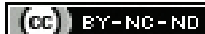


# Saline versus Metronidazole Peritoneal Lavage in Operated Cases of Peritonitis- A Longitudinal Study

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## ABSTRACT

**Introduction:** Perforation peritonitis is a fairly common surgical problem. Despite recent advances in surgical practice, postoperative minor and major complications are common in patients of peritonitis. Intraoperative peritoneal lavage is an important operative management and the choice of fluid can affect the outcome.

**Aim:** To compare the outcomes of peritoneal lavage using normal saline versus metronidazole in cases of perforation peritonitis in patients undergoing laparotomy, with respect to surgical site infections, sepsis, wound dehiscence, hospital stay.

**Materials and Methods:** The present study was a longitudinal study done on 80 patients, divided in two groups with 40 cases in each group. In one group, peritoneal cavity was lavaged with 2 L of normal saline and closed after putting drains. In the other group, peritoneal cavity was lavaged with 2 L normal saline mixed with 100 mL (500 mg) of metronidazole and abdomen

was closed in layers after placing two drains, kept closed for one hour after abdominal closure. Chi-square test was used, and  $p < 0.05$  was considered as level of significance.

**Results:** The mean age of patients in metronidazole group was  $47.72 \pm 15.64$  years, and was comparable to mean age  $45.92 \pm 15.26$  years in saline group, difference was not significant ( $p = 0.6039$ ). Male/female in Metronidazole and Saline groups were 31/9 and 30/10, respectively. It was observed that the patients in metronidazole group had less surgical site infections (22.5%) compared to saline group 42.5% ( $p = 0.056$ ), less sepsis (20% vs 62.5%) ( $p < 0.001$ ), less wound dehiscence (5% vs 15%) ( $p = 0.136$ ), and shorter hospital stay with a mean  $\pm$  SD of  $9.975 \pm 2.25$  and  $11.82 \pm 2.85$  days ( $p = 0.0019$ ).

**Conclusion:** The metronidazole lavage is better than saline lavage. However, larger multicentric randomised controlled trials need to be done.

**Keywords:** Hospital stay, Laparotomy, Perforation peritonitis, Postoperative complications, Sepsis

## INTRODUCTION

The peritoneum is the most extensive serosal membrane of the body composed of two main segments. One covering the internal surface of the wall of the abdomen, including the diaphragm and pelvis, called the parietal peritoneum, and other covering the surface of intra-abdominal organs, called the visceral peritoneum. The surface area of the peritoneum is nearly  $2 \text{ m}^2$ , which is approximately equal to the area of the skin. The peritoneal cavity normally contains only about 75 mL of fluid to serve as lubrication between abdominal viscera and wall [1].

Peritonitis is an inflammatory response which occurs as a result of infectious, ischaemic and perforating injuries of Gastro-Intestinal Tract (GIT) and genitourinary system. Peritonitis can be: (a) primary peritonitis, when source of peritoneal infection is from outside the peritoneal cavity and the infection is often monomicrobial; (b) secondary peritonitis, when source of infection is intra-abdominal usually a perforated hollow viscous organ; or (c) tertiary peritonitis that develops following treatment of secondary peritonitis [2]. The prognosis and outcome of peritonitis depend upon the interaction of many factors including patient-related factors, disease specific factors and diagnostic and therapeutic interventions [3].

After initial resuscitation, the main treatment is explorative laparotomy and correction of underlying cause along with intraperitoneal lavage and drainage [4-6]. Various fluids have been used for lavage. One of them is metronidazole which is an antibiotic and antiprotozoal drug. It inhibits nucleic acid synthesis by disrupting the Deoxyribonucleic Acid (DNA) of microbial cells. There are published studies comparing efficacy of saline, metronidazole, chloramphenicol, cephalosporin and imipenem lavage [7-13]. Bhushan C et al., found significant reduction in sepsis and

mortality after antibiotic lavage [9]. Other studies found reduction in respect of surgical site infection, sepsis, postoperative abscess formation in antibiotic lavage group compared to saline group, but those differences were not statistically significant [8,10,11,13]. Imipenem lavage was found to have statistically significant reduction in wound infection, intra-abdominal abscess, and sepsis compared to saline lavage [12]. In view of inconclusive results in the literature, this study was done as an attempt to find if metronidazole lavage offers a significant advantage vs saline lavage in patients of perforation peritonitis undergoing laparotomy in tertiary care hospital.

## MATERIALS AND METHODS

This was a longitudinal study done on 80 patients (40 in each group) of perforation peritonitis. The study was done at Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India, from November 2018 to December 2019. The ethical approval was obtained from the Institutional Ethical Committee (IEC) vide letter number AU/EC/FM/142/2018.

Eighty patients of perforation peritonitis were divided in two equal groups. One group received metronidazole 100 mL plus 2 L normal saline lavages and the second group received 2 L normal saline lavage. In both groups, drains were kept closed for one hour postoperatively. Results were compared with respect to surgical site infection, intra-abdominal abscess, sepsis, wound dehiscence and hospital stay.

**Inclusion criteria:** All patients with perforation peritonitis diagnosed and confirmed based on Ultrasound/ Contrast Enhanced Computed Tomography (USG/CECT) abdomen to have pneumoperitoneum and free fluid who underwent laparotomy. All patients who gave written informed consent for enrollment in the study.

**Exclusion criteria:** Patients who had co-morbid conditions like diabetes, cirrhosis, chronic kidney failure and steroid use.

Patients who visited the study institute with clinical features of peritonitis (such as pain abdomen, distension, vomiting) were clinically examined, and diagnosis was confirmed using erect radiograph of the abdomen with the evidence of the gas under diaphragm in most of the cases. The USG abdomen was done in some cases and in some cases CT of abdomen was done. Routine blood investigations were done as well. Patients were managed with intravenous fluids and antibiotics and optimised for surgery. The condition of the patient and prognosis were explained to the patient and patient relatives in their own language.

### Study Procedure

Cases were divided in two groups (alternate patient in the next group)- plain saline lavage group and metronidazole lavage group. Plain saline lavage group received intra-peritoneal lavage with 2 L of normal saline. Metronidazole lavage group received intra-peritoneal lavage using 2 L of normal saline mixed with 100 mL (500 mg) of metronidazole. The lavage was done for 20 minutes and after closure of perforation. Different operators were involved in different cases. Cases were followed-up till the discharge or death of the patient. Postoperative complications were noted. Postoperative hospital stay was noted.

**Postoperative course:** All patients were given institutional care in the postoperative period. Regular monitoring of vitals and input output was done. Necessary investigations were done and follow-up was done and pain management was also done as well. Patient was encouraged active and passive limb movement and ambulation. Physiotherapy was done for chest and limbs thrice a day. All patients performed monitored incentive spirometry, thrice a day, till their hospital stay in the postoperative period. The antibiotics given postoperatively were the same in all patients (piperacillin/tazobactam 4.5 gm i.v. 8 hrly, amikacin 500 mg i.v. 12 hourly, and metronidazole 500 mg i.v. 8 hourly for seven days).

The wound was primarily dressed with sterile surgical gauze and covered with occlusive adherent bandage. The primary dressing was removed after 48 hours, and daily dressing done with povidone-iodine solution. The wound was inspected and expressed for signs of infection (sinus formation, seroma formation and pus formation any discharge or bleed). Sutures were cut in case of any collection or frank discharge, secondary suturing was done later after the control of infection. Swab cultures were taken in case of any purulent discharge. Drain output was monitored daily 24 hourly for amount and character of the content (serous, purulent, blood). Drain was removed when output was less than 50 mL and serous in nature. Auscultation of abdomen was done for presence of bowel sounds. Auscultation was done over right para-umbilical region and hearing of bowel sounds for one minute. Stitches were removed on postoperative day 12.

### STATISTICAL ANALYSIS

Statistical Analysis was done using Statistical Package for the Social Sciences (SPSS) 24.0. Descriptive and inferential statistics were performed using Chi-square test, and  $p < 0.05$  was considered as significant.

### RESULTS

Maximum number of cases in both the groups were in the age group  $< 40$  years. Mean age in both the groups was comparable [Table/Fig-1].

The most common cause of perforation was ileal perforation (32.6%), followed by gastric perforation (21.3%) and duodenal

Age group (years)	Metronidazole group	Saline group	p-value
$\leq 40$	15 (37.5%)	18 (45%)	0.6039
41-60	15 (37.5%)	14 (35%)	
$> 60$	10 (25%)	8 (20%)	
Mean $\pm$ SD (years)	47.72 $\pm$ 15.64	45.92 $\pm$ 15.26	
<b>Gender</b>			
Male/Female	31/9	30/10	

[Table/Fig-1]: Age and gender distribution.

perforation (12.5%). The cases with rectal perforation were less (1.3%) [Table/Fig-2].

The patients of metronidazole group had a shorter hospital stay as compared to normal saline group, and the difference was significant [Table/Fig-3].

Cause	N (%)	Normal saline group, n (%)	Metronidazole group, n (%)
Gastric perforation	17 (21.2)	8 (20)	9 (22.5)
Duodenal perforation	10 (12.5)	4 (10)	6 (15)
Jejunal perforation	5 (6.2)	3 (7.5)	2 (5)
Ileal perforation	26 (32.6)	11 (27.5)	15 (37.5)
Appendicular perforation	11 (13.8)	7 (17.5)	4 (10)
Caecal perforation	5 (6.2)	3 (7.5)	2 (5)
Colonic perforation	5 (6.2)	3 (7.5)	2 (5)
Rectal perforation	1 (1.3)	1 (2.5)	0
Total	80 (100)	40 (100)	40 (100)

[Table/Fig-2]: Cause of peritonitis.

Hospital stay (days)	Metronidazole, n (%)	Saline, n (%)	p-value
$< 10$	25 (62.5)	13 (32.5)	0.0019
$> 10$	15 (37.5)	27 (67.5)	
Mean $\pm$ SD	9.975 $\pm$ 2.25	11.82 $\pm$ 2.85	

[Table/Fig-3]: Comparison of hospital stay.

There was a 20% reduction in incidence of surgical site infection in metronidazole group as compared with normal saline group; 5% reduction was seen in incidence of intra-abdominal abscess in metronidazole group as compared with normal saline group. Incidence of sepsis was higher in normal saline lavage group. Incidence of mortality and wound dehiscence was also higher in normal saline lavage group [Table/Fig-4].

Parameter	Saline lavage group, n (%)	Metronidazole lavage group, n (%)	p-value
Surgical site infection	17 (42.5)	9 (22.5)	0.056*
Intra-abdominal abscess	5 (12.5)	3 (7.5)	0.456
Sepsis	25 (62.5)	8 (20)	0.001*
Wound dehiscence	6 (15)	2 (5)	0.136

[Table/Fig-4]: Comparison of outcomes in two groups.

\*A p-value  $< 0.05$  is considered to be statistically significant

### DISCUSSION

Perforation peritonitis is a common surgical emergency. Despite all advances in surgical field these patients still have a significant post operative complication rate contributing to morbidity and mortality. Peritoneal lavage is essential step in surgery for perforation peritonitis. Choice of fluid used for lavage can have an effect on postoperative complications. In this study, mean age of patients were 46.82 $\pm$ 15 years. Majority of the patients were male. Ileal perforation was the leading cause of peritonitis followed by gastric perforation and duodenal perforation. All patients had perforation peritonitis and received either saline or saline +metronidazole lavage. Metronidazole lavage proved better in all aspects however

Parameter	Present study	Sulli D and Rao MS [10]	Choudhary V and Dhankar AA [11]	Santosh CS et al., [12]	Baig A and Kumar MK [14]	Sarada B et al., [15]	Saha H et al., [16]	Meena R et al., [17]
Lavage used	Saline and metronidazole	Saline and metronidazole	Saline and metronidazole	Saline and imipenem	Povidine-iodine and metronidazole	Povidine-iodine and metronidazole	Iodine versus normal saline	Super oxidised solution versus normal saline
Mean age	46 years	37 years	37 years	36 years	33 years	44.6 years	Most patients in 30-40 year age group	40 years
Most common cause of peritonitis	1. Ileal perforation 2. Duodenal perforation	1. Duodenal perforation 2. Ileal perforation	1. Duodenal perforation 2. Ileal perforation	1. Duodenal perforation 2. Stomach perforation	1. Duodenal ulcer 2. Stomach perforation	1. Duodenal ulcer 2. Stomach perforation	1. Duodenal ulcer 2. Stomach perforation	1. Ileal perforation 2. Duodenal perforation
Surgical site infection	42.5% and 22.5%	40% and 26%	25% and 4%	33.33% reduction in imipenem group compared to saline group	12% more reduction with metronidazole	20% more reduction with metronidazole	22% more reduction with povidine-iodine	No significant difference
Intra abdominal abscess	12.5% and 7.5%	12% and 10%	10% and 8%	23.33% reduction in imipenem group vs saline group	No significant difference	2% in both	No significant difference	No significant difference
Sepsis	62.5% and 20%	28% and 18%	30% and 20%	23.33% reduction in imipenem group vs saline group	No significant difference	No significant difference	No significant difference	14% reduction in superoxidised lavage group

**[Table/Fig-5]:** Comparison of outcomes in published studies [10-12,14-17].

difference was found to be statistically significant in sepsis and shorter hospital stay.

Bhushan C et al., also found significant reduction in mortality in antibiotic lavage group [9]. Sulli D and Rao MS reported a decreased incidence of infection sepsis hospital stay and mortality in metronidazole group, but the difference was not statistically significant for any parameter [10]. Choudhary V and Dhankar AA found reduction in wound infection, sepsis, abscess formation and mortality in metronidazole group vs saline group but the difference was not statistically significant [11]. Santosh CS et al., compared imipenem with saline lavage and found statistically significant reduction in wound infection intra-abdominal abscess, sepsis and mortality in imipenem group [12].

**Surgical site infection:** In this study, there was 20% reduction in incidence of wound infection in metronidazole group, however the difference was not statistically significant ( $p=0.056$ ). On reviewing the published studies, superoxidised solution lavage did not offer any advantage over normal saline lavage. While metronidazole lavage has been found to reduce wound infection more than povidine-iodine and normal saline lavage. Best results have been obtained with imipenem lavage (33% reduction in wound infection and difference statistically significant) [12].

**Intra-abdominal abscess:** There was 5% reduction in incidence of postoperative intra-abdominal abscess in metronidazole group, however, it was not statistically significant ( $p=0.456$ ). In previous studies also, no significant difference were found with superoxidised solution lavage, metronidazole lavage, povidine-iodine lavage. The only drug which showed significant reduction in intraperitoneal abscess formation was imipenem lavage [12].

**Sepsis:** There was 42.5% reduction in sepsis in metronidazole group which was statistically significant ( $p<0.001$ ). In other studies when metronidazole lavage was compared with normal saline lavage, there was reduction in sepsis, but when metronidazole lavage was compared with povidine-iodine lavage, no significant reduction in sepsis was found [14-16]. Imipenem lavage was the best, with 23.3% reduction in sepsis and difference was statistically significant [12]. Table/Fig-5 [10-12, 14-17], shows the comparison of different parameters in present study with other studies [10-12,14-17].

**Hospital stay:** In this study, there was shorter hospital stay in metronidazole group, and the difference was statistically significant ( $p=0.0019$ ). Similarly, Schein M et al., also reported a lesser

hospital stay (10 days) in chloramphenicol lavage group than in saline group (13 days) [8].

### Limitation(s)

The surgeries were not performed by a single surgeon hence operator bias was a limitation of the study.

### CONCLUSION(S)

As per this study, peritonitis was most common in middle age group (31-40 years). The majority of the patients were male. Ileal perforation and duodenal perforation were the leading causes. Primary closure of perforation with peritoneal is main treatment. Metronidazole based lavage is definitely better than saline lavage and the difference is statistically significant in respect of sepsis and hospital stay. However, larger multicentric randomised controlled trials should be done to further establish this.

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