

Original Research Article

Efficacy of imipenem lavage versus saline lavage in perforation peritonitis

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ABSTRACT

Background: Surgical treatment for perforation peritonitis is still believed to be demanding and complex in spite of the advent of better surgical technique, antimicrobial therapy and intensive care support improving the outcome of such cases. However, the specific details of the pre-operative, intra-operative and post-operative management have always been very controversial and debatable. This study aims to evaluate the efficacy of peritoneal cavity irrigation with imipenem solution in patients with perforation peritonitis and compare it with standard saline wash.

Methods: This study was conducted in a tertiary care teaching hospital from November 2015 to April 2017 and included 90 patients aged between 12 and 60 years who are operated for perforation peritonitis. Patients are divided into 3 groups and underwent post laparotomy irrigation as follows saline and fluid drained, saline and then imipenem wash at a concentration of 1mg/ml and fluid drained after 5 minutes, saline and then imipenem wash at a concentration of 1 mg/ml and drain was clamped for 1 hour. The patients were then observed for post-operative complications.

Results: There was a statistically significant reduction in post-operative wound infection (33.33%), intra-abdominal abscess (23.33%) and sepsis (23.33%) in group 3 when compared to other two groups. Group 3 had a much lower mortality rate (3.33%) when compared to the other two (16.67% and 6.67% respectively.)

Conclusions: Addition of Imipenem to normal saline for intraoperative peritoneal lavage has much satisfactory post-operative outcome. Further studies with larger sample size are needed to accurately assess the statistical significance of the same.

Keywords: Imipenem, Laparotomy, Perforation peritonitis, Peritoneal lavage, Post-operative complications

INTRODUCTION

Perforation peritonitis is the most common surgical emergency in India. Despite advances in surgical techniques, antimicrobial therapy and intensive care support, management of peritonitis continues to be highly demanding, difficult and complex. The spectrum of etiology of perforation continues to be different from that of western countries and there is paucity of data from India regarding its etiology, prognostic indicators, morbidity and mortality patterns.¹ Mortality of secondary

peritonitis was as high as 90% in the early 20th century and is still 30-50% despite advances in antibiotics, surgical technique, radiographic imaging, and resuscitation therapy.² Evaluating patients who have hollow viscus perforation remains one of the most challenging and resource-intensive aspects of acute surgical care. Missed diagnosis and late intervention are frequent causes of increased morbidity and mortality, especially in patients who survive the initial phase of insult. Hence successful treatment requires a thorough understanding of anatomy, microbiology,

pathophysiology of the disease process and in-depth knowledge of the therapy, including resuscitation, antibiotics, source control and physiologic support.

Surgical closure of the perforation and intra operative peritoneal lavage has been the cornerstone in the management of patients with peritonitis. Peritoneal lavage reduces the bacterial load, thereby reducing the incidence of post-operative surgical site infection and sepsis. Different types of fluids have been used for peritoneal lavage in peritonitis patients. These include sterile water, warm saline, aqueous povidone iodine and saline with antibiotics.

In the past 50 years, numerous antibiotics and antiseptic solutions like ampicillin, metronidazole, doxycycline, cefazolin, cephogran, cephalothin, cephaloridine, bacitracin, lincomycin, gentamicin, kanamycin, and Dakin's solution have been used as irrigation solution for the treatment of peritonitis; however, there are still controversies about their effectiveness. There is a general agreement that antibiotic lavage is safe, but there has been little evidence to support its efficacy compared to the control group.³

A recent retrospective study by Hesami MA et al found that peritoneal irrigation with imipenem solution (1 mg/mL) was more beneficial, compared to irrigation with normal saline, in decreasing the risk of post-operative SSI.⁴ This suggests that imipenem may be a good choice as a peritoneal washing solution, because it is a wide spectrum antibiotic with highly bactericidal activity on microorganisms causing peritonitis, including facultative gram-negative enteric bacteria and obligate anaerobe rods. There is a lack of prospective research regarding whether abdominal cavity irrigation with imipenem solution would decrease the rate of post-operative surgical site infections.

This study aims to evaluate the efficacy of peritoneal cavity irrigation with imipenem solution in patients with hollow viscus perforation and compare it to saline irrigation with respect to post-operative outcomes.

METHODS

All patients aged between 12 to 60 years operated for hollow viscus perforation between November 2015 and April 2017 in Victoria Hospital, Bangalore were included in the study after taking the necessary consent. However, patients with immunodeficiency, co-morbidities such as diabetes, cardiovascular, renal, pulmonary and hepatic diseases and pregnant/lactating females were excluded from the study. Patients requiring re-laparotomy for postoperative peritonitis due to anastomosis leakage were also excluded from the study.

Patients coming with clinical features of peritonitis were assessed by thorough clinical examination. Diagnosis was confirmed by erect X-ray of the abdomen in most of the

cases with the evidence of free gas under the diaphragm. USG abdomen was done in some cases. Investigations like haemoglobin, total count, differential count, blood urea, serum creatinine, liver function test (serum albumin) were done. Patients underwent exploratory laparotomy and necessary surgical correction was done depending upon the intra-operative decision of the surgeon. After which they underwent peritoneal lavage before closure.

Cases were randomly divided into three groups:

Group 1: After laparotomy, abdominal wash given with saline and fluid drained.

Group 2: After laparotomy, abdominal wash given with saline and then imipenem wash at a concentration of 1mg/ml and fluid drained after 5 minutes.

Group 3: After laparotomy, abdominal wash given with saline and then imipenem wash at a concentration of 1mg/ml and drain will be clamped for 1 hour.

Cases were followed up till the discharge or death of the patient. Post-operative complications- wound infection, intra-abdominal abscess, sepsis, faecal fistula, need of relaparotomy and death and post-operative hospital stay were noted. Data was tabulated and the results in various groups were compared with each other.

RESULTS

This study consisted of 90 patients who were divided into 3 groups according to abdominal lavage intraoperative

- Group 1: Patients with saline wash.
- Group 2: Patients with saline and imipenem wash.
- Group 3: Patients with retained imipenem wash (achieved by clamping the drain for 1hour).

The highest number of cases belonged to the age group of 21-30yrs (Table 1).

Majority of cases were males (88.9%) with a male to female ratio 8:1.

Table 1: Age specific distribution of cases.

Age group (years)	No. of cases	Percentage
<20	12	13.3
21-30	28	31.1
31-40	21	23.3
41-50	17	18.9
51-60	12	13.3

Most common site of perforation encountered was at the duodenum (40%) (Figure 1) followed by stomach (32.2%) and then ileum (14.4%) (Figure 3 and Table 2).

In the group 1 (saline lavage group) incidence of wound infection was 50%. 30% of the patients had intra-abdominal abscess. Sepsis was noted in 30% of patients.



Figure 1: Duodenal Perforation.



Figure 2: Ischaemic Bowel Disease.



Figure 3: Ileal Perforation.

Table 2: Site of hollow viscus perforation.

Site of perforation	No. of patient	Percentage
Gastric	29	32.2
Duodenum	36	40
Jejunum	6	6.7
Ileal	13	14.4
Appendix	7	7.8
Gall bladder	1	1.1

16.67 % of patients developed faecal fistula during the post-operative period. Mortality was highest (16.67%) in this group. And there was a need of relaprotomy for 20% of patients Table 3.

Table 3: Outcome of Group 1 (patients with saline wash).

Outcome	No. of cases	Total cases	Percentage
SSI	15	30	50
Intraabdominal abscess	9	30	30
Sepsis	9	30	30
Fecal fistula	5	30	16.67
Death	5	30	16.67
Need for relap	6	30	20

In the group 2 (Patients with saline and imipenem wash group) incidence of wound infection was 33.33%. 10% of the patients had intra-abdominal abscess. Sepsis was seen in 10% of patients. 10% of patients developed fecal fistula during the post-operative period. Mortality was 6.67% in this group and none of them required relaprotomy Table 4.

Table 4: Outcome in Group 2 (Patients with saline and imipenem wash).

Outcome	No. of cases	Total cases	Percentage
SSI	10	30	33.33
Intraabdominal abscess	3	30	10
Sepsis	3	30	10
Fecal fistula	3	30	10
Death	2	30	6.67
Need for relaparotomy	0	30	0

Group 3 (patients with retained imipenem wash) showed the least rates of complications. The incidence of wound infection dropped to 16.67% where as 6.67% of the patients had intra-abdominal abscess and sepsis was seen in 6.67% of patients. Mortality was the lowest at 3.33% and none of the patients developed fecal fistula or required re-laparotomy Table 5.

Table 5: Outcome in Group 3, Patients with retained imipenem wash (achieved by clamping the drain for 1hour).

Outcome	No. of cases	Total cases	Percentage
SSI	5	30	16.67
Intraabdominal abscess	2	30	6.67
Sepsis	2	30	6.67
Fecal fistula	0	30	0
Death	1	30	3.33
Need for relaparotomy	0	30	0

There was a 16.67% reduction in the incidence of wound infection (SSI) in Group 2 when compared to Group 1, which is further reduces to 33.33% in Group 3 compared to Group 1, which is statistically significant with a P value - 0.023. Incidence of intra-abdominal abscess reduced by 20% in Group 2 when compared to Group 1,

which is further reduces to 23.33% in Group 3 compared to Group 1 which is statistically significant with a P value-0.026. 20% reduction was seen in the incidence of sepsis in Group 2 when compared to Group 1, which is further reduces to 23.33% in Group 3 compared to group 1 which is statistically significant with a P value-0.026.

Table 6: Comparison of outcome in all three groups.

Outcome	Group 1		Group 2		Group 3		P value
	No.	%	No.	%	No.	%	
SSI	15	50	10	33.33	5	16.67	0.023
Intraabdominal abscess	9	30	3	10	2	6.67	0.026
Sepsis	9	30	3	10	2	6.67	0.026
Fecal fistula	5	16.67	3	10	0	0	0.07
Death	5	16.67	2	6.67	1	3.33	0.09
Relaprotomy	6	20	0	0	0	0	.001

There was a 6.67% reduction in the incidence of faecal fistula in Group 2 when compared to Group 1, which is further reduces to 16.67% in Group 3 compared to group 1 with no faecal fistula formation in Group 3, which is statistically insignificant with a P value-0.07 (Table 6). ANOVA test shows statistical significance of advantages of imipenem lavage (Group 2 and 3) over saline lavage (Group 1).

DISCUSSION

The treatment of peritonitis is associated with a high morbidity and mortality. The usual treatment of the peritonitis consists of fluid replacement, nasogastric suction, IV antibiotics and operative intervention. Operation consists of suction of the fluid, which has collected in the peritoneal cavity, and definitive procedure for the pathology of the peritonitis Figure 4 and Figure 5 (closure of perforation, closure bypass, resection and anastomosis or appendectomy etc.). This is followed by peritoneal lavage and then the abdomen is closed with drain/drains.



Figure 4: Graham's omental patch repair of prepyloric gastric perforation.

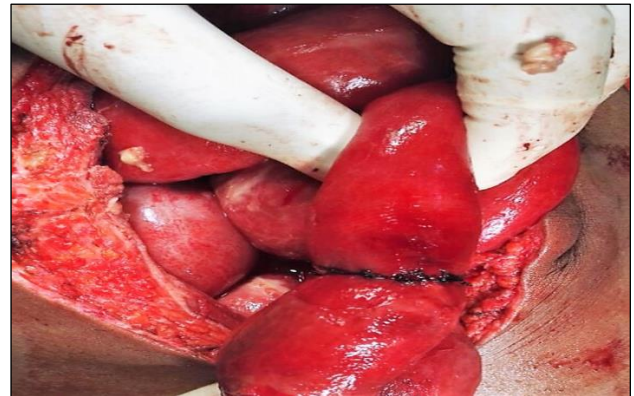


Figure 5: Resection and anastomosis in ileal region.

90 patients were included in this study. Patients were randoml assigned into three groups:

- After laparotomy, abdominal wash will be given with saline and fluid will be drained
- After laparotomy, abdominal wash will be given with saline and then imipenem wash at a concentration of 1mg/ml and fluid will be drained after 5 minutes
- After laparotomy, abdominal wash will be given with saline and then imipenem wash at a concentration of 1mg/ml and drain will be clamped for 1 hour.

Results were compared between the three groups.

Age

In this study it was found that maximum number of cases were in the age group of 21 to 30 years. Mean age of patients in this study was 32.83 years. This is comparable to the age distribution found by Sheeraz Khan et al where

maximum patients were in the age group of 31-40 years and mean age was 37 years.⁵

Surgical site infection

In the present study there was 33.33% reduction in SSI in retained imipenem lavage (Group 3) in comparison to saline lavage (Group1) which is statistically significant (P value: 0.00617) while in group 2, there was reduction in SSI by 16.67% in comparison to saline lavage group 1 which is not significant (P value 0.19). Similarly, Khan S et al reported 20% reduction in incidence of wound infection, when superoxide solution was used for IOPL.⁵ On contrary, Schein et al did not find any difference in incidence of wound infection when chloramphenicol was used for IOPL.⁶

Intra-abdominal abscess

In the present study there was 23.33% reduction in intra-abdominal abscess in group 3 in comparison to saline lavage group1 which is statistically significant (P value – 0.019) while in group 2 saline and imipenem lavage there was reduction in intra- abdominal abscess by 20% in comparison to saline lavage group 1 which is significant (P value 0.05).

Fowler R reported 16% reduction in the incidence of intra-abdominal abscess when Cephaloridine was used for IOPL.⁷ Hesami et al conducted a study where imipenem was used for IOPL for cases of perforation peritonitis and had a statistically significant decrease in SSI and intra-abdominal abscess.⁸

Sepsis

In the present study there was 23.33% reduction in systemic sepsis in retained imipenem lavage (Group 3) in comparison to saline lavage (Group 1) which is statistically significant (P value: 0.019) while in Group 2 saline and imipenem lavage there was reduction in sepsis by 20% in comparison to saline lavage group (1) which is significant (P value 0.05).

Silverman et al performed a study, where he compared IOPL with saline vs tetracyclines. His study did not show any significant decrease in post-operative sepsis in contrast with our study.⁹

faecal fistula

In the present study there was 16.67% reduction in faecal fistula in retained imipenem lavage (group 3) in comparison to saline lavage (group 1) which is statistically significant (P value – 0.019) while in group 2 saline and imipenem lavage there was reduction in faecal fistula by 16.67% in comparison to saline lavage (group1) which is not significant (P value 0.44).

Khan S et al reported 2.5% reduction in the incidence of fecal fistula in the study group, when superoxide solution was used for IOPL (not statistically significant).⁵

DiVincenti and Cohn conducted a similar study comparing saline wash to kanamycin wash. They concluded that there were reduction post-operative complications like SSI, sepsis and fecal fistula.¹⁰

Mortality

In the present study there was 13.34% reduction in death in retained imipenem lavage (group 3) in comparison to saline lavage (group 1) which is statistically not significant (P value 0.085) while in group 2 saline and imipenem lavage there was reduction in death by 10% in comparison to saline lavage (group1) which is also not significant(P value 0.227).

Schein (1990) found no significant difference in mortality of patients treated with or without intraperitoneal lavage with chloramphenicol.⁶ Rambo (1972) also found no difference in the number of deaths when intraperitoneal irrigation with cephalothin was used.¹¹ On the contrary Mc Kenna et al (1970) and Bhushan et al (1975) found significant reduction in mortality in patients treated with antibiotic lavage.^{12,13}

Need of relaparotomy

In the present study there was 20% reduction in need of relaprotomy in group 3 and group 2 in comparison to saline lavage (group 1) which is statistically significant (P value - 0.00982).

A meta-analysis done in 2002, concludes that by just performing IOPL, there was a decrease in the need for re-laparotomies. When compared with our study we saw no re-laparotomies were needed when an imipenem wash was given.

CONCLUSION

The study was done on 90 patients presenting with features of peritonitis due to hollow viscus perforation and eventually getting operated at Victoria hospital and B and LCH. Patients were randomly divided into three groups:

- Saline lavage group
- Imipenem lavage group
- Retained imipenem lavage for 1 hour.

Simply by addition of Imipenem especially retained (Group 3) to normal saline for intraoperative peritoneal lavage, beneficial effects in terms of reduction in incidence of SSI, intra-abdominal abscess, systemic sepsis, faecal fistula formation, death and need of relaprotomy were seen. Further studies with larger sample size are needed to accurately assess the statistical

significance of the beneficial role of Imipenem intra-operative peritoneal lavage in treatment of patients with peritonitis.

Continuous peritoneal lavage, which is being frequently used for acute pancreatitis, can also be studied for its role in perforation peritonitis in the similar lines. IOPL is also gaining importance in cancer surgery, though further evaluation for the same is required.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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