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Intraoperative Peritoneal Lavage in Peritonitis: Normal Saline vs Metronidazole

[1]Hira Aslam, [2]Muhammad Khurram Jameel, [2]Pir Muneeb, [1]Aneeqa Nasir Qureshi, [2]Fawad Hameed, [3]Muhammad Ammar, [2]Maham Qazi, [4]Abrar ul Hassan Pirzada

[1]Department of Surgery, Mayo Hospital, KEMU, Lahore
[2]Department of Surgery, ANMC / Chaudhary Muhammad Akram Hospital, Lahore
[3]Department of Urology, Chaudhary Muhammad Akram Hospital, Lahore
[4]Department of Plastic Surgery, ANMC / Chaudhary Muhammad Akram Hospital, Lahore, Pakistan

ABSTRACT

Introduction: Globally, acute generalized peritonitis ranks among the top surgical emergencies. Different studies have been conducted to show the amplitude of peritonitis worldwide eliciting a huge impact on overall patient morbidity and mortality. Largely peritonitis is caused by a gastrointestinal perforation or anastomotic leak. In peritonitis, anaerobes & gram-negative organisms are mostly responsible for sepsis and morbidity due to the overactive inflammatory cascade by endotoxins which is amenable to timely intervention.

Aims & Objectives: The study's aim was to evaluate whether using normal saline or metronidazole solution during intraoperative peritoneal lavage (IOPL), results in a lower rate of postoperative wound infection.

Place and Duration of Study: This study was undertaken at the South Surgical Ward, Mayo Hospital Lahore for 6 months from February 2nd, 2021, to August 1st, 2021.

Material & Methods: Consecutive sampling strategy followed by a randomized controlled trial were used to induct and provide intervention to 90 patients aged 15-65 years with peritonitis caused by hollow viscus perforation. The patients were subdivided into 2 groups A& B(n=45 each).Two liters of normal saline were used for peritoneal lavage in group A, while two liters of normal saline were combined with 200 mL of metronidazole solution and administered to group B. intraoperatively.Baseline physiological parameters such as age, sex, BMI , intra operative surgical parameters as duration of operation and post-operative course were recorded till discharge. On 10th POD, patients returned to OPD for further monitoring. An infection was diagnosed if the patient had post-operative symptoms such as a high temperature, increased TLC, wound discharge, redness, or pain. Data was entered and analyzed using SPSS version 23.

Results: A majority (54.44%) of the patients were young adults. Mean age of 37.33 ± 10.53 years of patients in the metronidazole group was comparable to mean age 40.04 ± 11.96 years in the saline group, difference was not significant (p=0.067). Male/female ratio in Metronidazole and Saline groups were 17/25 and 10/18, respectively. Patients who received intraperitoneal lavage with normal saline were more likely to develop wound infections (17/45) (37.78%), while only 3/45) (6.67% of those who received metronidazole solution did so (p 0.0001).

Conclusion: Based on the results of this experiment, using metronidazole solution for intraoperative peritoneal lavage instead of normal saline reduces the occurrence of postoperative wound infection.

Keywords: peritonitis, postoperative wound infection, intraoperative peritoneal lavage

INTRODUCTION

Globally, acute generalized peritonitis ranks among the top surgical emergencies[1]. It is more common in Third World nations. The prevalence of perforation is low (0.6% - 4.9%) in developed nations but high (33% - 63%) in West Africa[2]. 554 persons were discovered to have peritonitis in a study that took place over three years in India[3]. Researchers in Pakistan have conducted studies with similar methods, with one study reporting 650 cases in a just 9 months[4]. Most cases of peritonitis are caused by a gastrointestinal perforation or anastomotic leak[5]. In the case of peritonitis, anaerobes and gram-negative organisms are mostly responsible for sepsis and morbidity due to the overactive inflammatory cascade brought on by the release of endotoxins[5].Clinical evidence is used to identify peritonitis. Diagnosis can be achieved via upright plain x-ray of the abdomen, USG, or CT scan. This is often done through diagnostic laparoscopy nowadays[6].Resuscitation, diagnosis, prompt exploration, treatment of the underlying cause, and extensive surgical peritoneal lavage have always been the cornerstones of peritonitis therapy regimens (IOPL)[7,8]. Regular IOPL is performed to lessen bacterial contamination and burden. Even though large volumes of normal saline are used in IOPL, the rates of sepsis, wound infection, and mortality remain alarmingly high. Another method

of reducing bacterial count and the associated risk of bacterial contamination and surgical site infection is intra-abdominal antibiotic lavage[9].Antibiotic solutions like ampicillin, doxycycline, lincomycin, gentamycin, and many others have all been employed before for this function[10]. Metronidazole a synthetic antimicrobial drug has been infrequently used. Working through diffusion of its nitro group into bacterial and protozoal cells it destabilizes DNA and electron transport chains to produce a bactericidal and antiprotozoal effect. This mechanism of action sets it apart as an effective weapon against anaerobes[11]. Metronidazole and sterile water solution is used in IOPL. This will specifically target anaerobes which alone normal saline cannot do. Indian research into post-operative wound infections showed a significantly reduction in these employing metronidazole solution as IOPL. Lavage with normal saline resulted in a 21% infection rate, while metronidazole solution resulted in a 15% infection rate[7]. Another study indicated that whereas 42% of wounds became infected after being lavaged with regular saline, only 30% did so after being treated with a metronidazole solution. Also, the difference was not statistically significant ($p>0.05$)[7]. Even though normal saline has been used for IOPL for a long time, post-operative wound infection is still a problem .The use of antimicrbial and antibiotic lavage, has thus shown conflicting scientific data regarding reduction of postoperative wound infection rates. Patients presenting within 72 hours of developing peritonitis will be the focus of this study, as opposed to all peritonitis patients in previous research. As a result of this research, our community will have local data for the use of metronidazole solution as IOPL, which will decrease chances of sepsis and wound infection and the length of time patients spend in the hospital in our setup.

MATERIAL AND METHODS

The study's goal was to evaluate the efficacy of intraoperative peritoneal lavage (IOPL) with either normal saline or metronidazole solution in reducing wound infection. The investigation employed a randomized controlled trial using consecutive sampling as its study strategy. This study was executed in the South Surgical Ward of the Surgery Department of Mayo Hospital in Lahore. The time frame for this study was from February 2nd, 2021, to August 1st, 2021. The sample size of this study was determined by calculating the expected proportion of wound infection in the normal saline group at 6.53% and in the metronidazole group at 26.3%, using a significance threshold of 5% and 80% power of test, respectively. This yielded a total of 90 patients (45 in each group). Patients between the ages of 15 and 65 years of both sexes, and those diagnosed with peritonitis related to hollow viscous perforation (from trauma or any other cause) met the inclusion criteria used in the sample strategy. Patients with primary or spontaneous peritonitis (based on clinical examination and history), and patients with peritonitis related to solid organ injury (on clinical examination) were not eligible for this study.

Ninety (90) patients meeting the aforementioned criteria were enrolled after obtaining Ethics Board approval vide 756 /RC/KEMU dated 4/1/2021 for the data collection process. Before the operation, everyone gave their informed consent. Characteristics such as age, gender, body mass index, and time since peritonitis diagnosis were considered. Patients were equally divided into two equal groups by random lottery method. Two (2) liters of normal saline were used for peritoneal lavage in group A, while two liters of normal saline were combined with 200 mL of metronidazole solution for group B. Using general anesthesia; a single surgical team performed all procedures with the help of the assisting researcher. All the time spent during operation was recorded. Patients were monitored in the operating rooms and released from the facility after a period of 72 hours following surgery. After 10 days, patients returned to OPD for further monitoring. Patients were diagnosed with wound infection if they experienced post-operative complications such as fever, increased TLC, wound discharge, redness, and pain (as per operational definition). Proformas were used to record all of this data. Infections that developed in patients' surgical wounds after surgery were treated according to accepted medical practice.

Statistical Analysis:

All the information was entered into SPSS 23. Age, body mass index, length of peritonitis, and surgical time were some of the quantitative factors provided as means +/- standard deviations. Qualitative factors such as gender and postoperative wound infection were given in the form of frequency and percentage. The Chi-square test was used to examine the difference in rates of infection after surgery between the two groups. The cutoff for significance was set at a 0.05 probability level. The information was separated into groups based on variables such as age, gender, body mass index, length of peritonitis, and length of surgery. After the groups were divided into strata, the chi-square test was used to compare them based on the presence of postoperative wound

infection. The cutoff for significance was a P value of 0.05.

RESULTS

Patients included in the study were between 15 to 65 years with overall mean age of 38.67 ± 12.31 years.The mean age of group A was 40.04 ± 11.96 years and 37.33 ± 10.53 years in group B. Out of 90 patients 32 (35.56%) were males and 58 (64.44%) were females with male to female ratio of 1:1.8. Mean duration of peritonitis was 42.24 ± 12.01 hours. In Table-1 Mean BMI was 28.48 ± 2.92 kg/m^2. Mean operative time being 62.34 ± 11.56 minutes.

Frequency of postoperative wound infection with normal saline was found in 17/45 (37.78%) and in metronidazole solution in intraoperative peritoneal lavage was found to be 03/45 (6.67%) patients (p-value = 0.0001).

		Group A (n=45)		Group B (n=45)		Total (n=90)	
Age distribution for both groups (n=90)	Age	No. of patients	%age	No. of patients	%age	No. of patients	%age
	15-40	24	53.33	25	55.56	49	54.44
	41-65	21	46.67	20	44.44	41	45.56
	Mean ± SD	**40.04 ± 11.96**		**37.33 ± 10.53**		**38.67 ± 12.31**	
Distribution of patients according to duration of peritonitis	Duration (hr's)	**Group A (n=45)**		**Group B (n=45)**		**Total (n=90)**	
		No. of patients	%age	No. of patients	%age	No. of patients	%age
	≤36	19	42.22	18	40.0	37	41.11
	>36	26	57.78	27	60.0	53	58.89
	Mean ± SD	**41.40 ± 12.21**		**43.44 ± 11.28**		**42.24 ± 12.01**	
Distribution of patients according to BMI	BMI (kg/m^2)	**Group A (n=45)**		**Group B (n=45)**		**Total (n=90)**	
		No. of patients	%age	No. of patients	%age	No. of patients	%age
	≤27	15	33.33	17	37.78	32	35.56
	>27	30	66.67	28	62.22	58	64.44
	Mean ± SD	**28.98 ± 3.21**		**28.04 ± 2.67**		**28.48 ± 2.92**	
Distribution of patients according to operative time	Operation (min)	**Group A (n=45)**		**Group B (n=45)**		**Total (n=90)**	
		No. of patie	%age	No. of patients	%age	No. of patie	%age
		nts				nts	
	≤60	16	35.56	18	40.0	34	37.78
	>60	29	64.44	27	60.0	56	62.22
	Mean ± SD	**63.84 ± 11.94**		**61.89 ± 11.39**		**62.34 ± 11.56**	

Table-1: Different Parameters of Patients and their Results

Table-2 shows the ratio of wound infection with respect to various parameters. The stratification of postoperative wound infection with respect to age groups has significant P value (0.002) in group A patients with younger population between 15-40 years.Similarly statistically significant difference was found in postoperative wound infection among both genders having female predominance in group A. Postoperative wound infection according to duration of peritonitis is more common among ≥ 36 hours of Group A, while it is nil in Group B.The impact of higher BMI (≥27) on postoperative wound infection in group A is statistically important with significant P value (0.0001), while it is nil in metronidazole group (B). Lastly, the postoperative wound infection again was significantly reduced in patients of metronidazole group irrespective of duration of surgery with P value (0.005& 0.018).

In Fig-1 Comparison of the frequency of postoperative wound infection with normal saline versus metronidazole solution in intraoperative peritoneal lavage is shown.

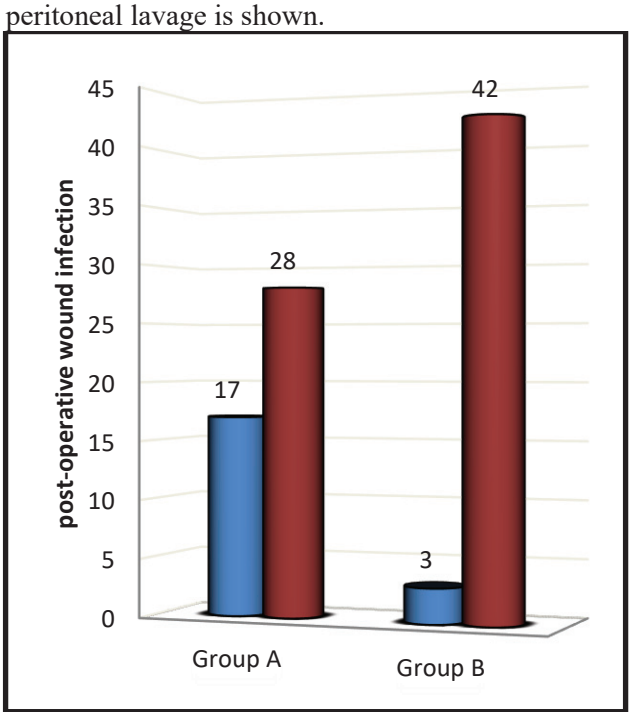

Fig-1: Comparison of the frequency of postoperative wound infection with normalsaline (A) versus metronidazole solution (B) in IOPL

ound infection with respect to age	Age of patient (yrs)	Group A (n=45)		Group B (n=45)		P-value
		Post-operative wound infection		Post-operative wound infection		
		Yes	No	Yes	No	
	15-40	12	13	02	22	**0.002**
	41-65	05	15	01	20	**0.067**
wound infection with respect to gender	**Gender**	**Group A (n=45)**		**Group B (n=45)**		**P-value**
		Post-operative wound infection		**Post-operative wound infection**		
		Yes	No	Yes	No	
	Male	05	10	00	17	**0.010**
	Female	12	18	03	25	**0.011**
wound infection with respect to duration	**Duration (hrs)**	**Group A (n=45)**		**Group B (n=45)**		**P-value**
		Post-operative wound infection		**Post-operative wound infection**		
		Yes	No	Yes	No	
	≤36	04	14	03	16	**0.618**
	>36	13	14	00	26	**0.022**
wound infection with respect to BMI	**BMI (kg/m^2)**	**Group A (n=45)**		**Group B (n=45)**		**P-value**
		Post-operative wound infection		**Post-operative wound infection**		
		Yes	No	Yes	No	
	≤27	04	13	03	12	**0.810**
	>27	13	15	00	30	**0.0001**
wound infection with respect to operative time	**Operative time (min)**	**Group A (n=45)**		**Group B (n=45)**		**P-value**
		Post-operative wound infection		**Post-operative wound infection**		
		Yes	No	Yes	No	
	≤60	07	11	00	16	**0.005**
	>60	10	17	03	26	**0.018**

Table-2: Ratio of Wound Infection with respect to Various Stratified Parameters of Patients.

DISCUSSION

Acute widespread peritonitis is a surgical emergency that poses significant treatment challenges. It is crucial to identify and treat sepsis as soon as possible so that the underlying cause can be addressed[14].In the past, since laparotomy on purpose had not yet been achieved in the operating room; early treatment of peritonitis had to rely on medical interventions. Rest, purgatives (particularly magnesium sulphate), fasting, lemon juice, cold therapy, and very limited opium use were all recommended for treating peritonitis[15]. In a later presentation, Mikulicz argued in favor of abdominal opening. He also popularized the use of drainage tubes and a 2% thymol solution for "toilet of the peritoneum," in which the unclean intestines are sponged clean. In another Study of Tait, the solution of blood and warm water was introduced in the abdomen and all internal organs washed until the water ran clear. Amniotic fluid, 25% glucose, water, saline, and different antibiotics were some of the fluids utilized in peritoneal lavage and aspiration in the past[16]. Peritoneal lavage can lessen the number of germs in the body by dilution, which in turn decreases the risk of infection and septic shock at the wound site. Saline lavage significantly decreases the numbers of aerobic and anaerobic bacteria in peritoneal fluid and provides an estimate of the debris load in the wash fluid[17]. This research was carried out to evaluate the efficacy of intraoperative peritoneal lavage with either normal saline or metronidazole (Nitroimidazoles) solution on the incidence of wound infection following perforated hollow viscus peritonitis surgery.

To compare, our study found that 17/45 (37.78%) patients who had intraoperative peritoneal lavage with normal saline developed postoperative wound infections, while only 3/45 (6.67%) received intraoperative peritoneal lavage with metronidazole solution (p 0.0001).

In contrast, a trial indicated that the Metronidazole lavage group had a lower rate of wound infection than the saline lavage group, the difference was statistically significant (p0.05)[12]. A further investigation found a 26.3 percent infection rate in the Metronidazole lavage group compared to 6.5 percent in the saline lavage group (p0.05)[13]. Harpreet Singh, Malika Agrawal, Naveen Singh[18] reported that incidence of 50% (21 out of 42) of wound infection when no local drug was used as compared to 30% when metronidazole was used. Dalvi et al[19] reported 20% reduction in incidence of wound infection with use of intraoperative topical metronidazole. Similarly, Khan et al[20] reported 20% reduction in incidence of wound infection, when superoxide solution was used for IOPL. On contrary, Schein et al did not find any difference in incidence of wound infection when chloramphenicol was used for IOPL[21].

The etiology of postoperative wound infection is complicated by the heterogeneous nature of these

parameters which include both patient factors (age, gender, BMI) and procedural factors (duration of surgery, prior infection due to long peritonitis timing)[29].Reviewing published data, shows that most researchers have not reported different parameters of patients like age, gender, BMI, time of peritonitis and duration of surgery in developing postoperative wound infection. In our study however parameters like higher BMI and increasing duration of surgery had statistically proportionate P values 0.0001, .018, 0.005 respectively in metronidazole group (B).Which may infer that increasing operative time and higher BMI are possibly factors for greater peritoneal infection which responds significantly better to metronidazole than normal saline. Moreover, metronidazole was significantly more effective in reducing peritonitis linked postoperative wound infection between the ages of 15-40 and in all genders. Increasing age above 40 however did not respond significantly better to metronidazole versus normal saline (p.067) probably due to the presence of likely comorbidities such as diabetes. An important point noted was that metronidazole was substantially more effective in eliminating prolonged peritonitis linked wound infection than normal saline (p value 0.0001) because of its specific antigram-ve bacterial action[11] Peritoneal lavage was found to be therapeutically effective in a study conducted by Nathens and colleagues[22].Similarly positive findings were seen in a trial using peritoneal irrigation and local antibiotics by Hau T et al. and colleagues. Lavage with antibiotics for irrigation has been found in experimental tests to significantly reduce mortality in cases of peritonitis[23]. Some studies have failed to show any advantage of peritoneal lavage over simple systemic antibiotics[24]. It has been proposed that peritoneal dialysis fluid is an appropriate lavage agent since it is gentler on the mesothelial cells than regular saline (0.9% sodium chloride)[25]. Metronidazole, gentamicin, cephalosporin, lincomycin, ampicillin, kanamycin and doxycycline and the antiseptics povidine iodine and chlorhexidine have all been studied with conflicting results.[26]In a review of 15 studies by Josie Chundamala J et al, and James G et al. Wright showed a definite reduction of surgical site infection (SSI) with povidine iodine when compared to saline or no irrigation[26].

In all above studies, we can conclude that surgical wound infections after laparotomy of peritonitis are the leading cause of morbidity, poor quality of life and increase length of hospital stay. Thus creating the physically, financially and mentally impact on patient's family[27]. This necessitates thinking the ways to reduce SSI after laparotomy not only in infected abdomen but also in other laparotomy for any reason. Metronidazole is thus an effective drug to use in SSI against gram-positive and gram-negative anaerobic bacteria, as well as gram-positive anaerobic bacteria that produce spores . It has been used both alone and in conjunction with other antibiotics in peritoneal lavage, and both methods have been shown to be safe and effective[28].

Limitations

This was a single center study having a relatively small sample size and mostly 3,4 surgeons performed all operations. Future larger clinical trials at more centers are necessary for comprehensive information on the use of metronidazole for IOPL in peritonitis.

CONCLUSION

This study concludes that the frequency of postoperative wound infection is less using metronidazole solution in intraoperative peritoneal lavage as compared to normal saline use. So, we recommended that metronidazole solution should be used routinely in intraoperative peritoneal lavage in order to prevent the post-operative wound infection.

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The Authors:

Dr. Hira Aslam,
Senior Registrar,
Department of Surgery,
Mayo Hospital KEMU, Lahore.

Dr. Muhammad Khurram Jameel,
Assistant Professor,
Department of Surgery,
ANMC/CMA Hospital, Lahore.

Dr. Pir Muneeb,
Assistant Professor,
Department of Surgery,
ANMC/CMA Hospital, Lahore.

Dr. Aneeqa Nasir Qureshi,
Senior Registrar,
Department of Surgery,
Mayo Hospital KEMU, Lahore.

Dr. Fawad Hameed,
Associate Professor,
Department of Surgery,
ANMC/CMA Hospital, Lahore.

Dr. Muhammad Ammar,
Senior Registrar,
Department of Urology,
ANMC/CMA Hospital, Lahore.

Dr. Maham Qazi,
Senior Registrar,
Department of Surgery,
ANMC/CMA Hospital, Lahore.

Dr. Abrar Ul Hassan Pirzada,
Associate Professor,
Department of Plastic Surgery,
ANMC/CMA Hospital, Lahore.

Corresponding Author:

Dr. Muhammad Khurram Jameel,
Assistant Professor,
Department of Surgery,
ANMC/CMA Hospital, Lahore.
Email: khurramjameel999@gmail.com