Single Dose vs Multiple Dose Prophylactic Antibiotic to Prevent Early Port-Site Infection in Elective Laparoscopic Cholecystectomy

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ABSTRACT

Introduction: Laparoscopic cholecystectomy (LC) is the gold standard treatment of symptomatic cholelithiasis. The need of the hour is to understand the fact that PSI is a totally different subset of infection and antibiotics are not a solution to this problem. The core issue of "prevention" is the principal solution. The study was undertaken to revalidate these well known facts with an effort to bring about a radical reform to this "social" rather than clinical problem.

Material and Methods: The study comprised of 60 patients admitted for elective LC. The first thirty patients undergoing elective LC were given single dose (SD) ciprofloxacin (500 mg) within an hour between the induction and making of the first port. While the control group received ciprofloxacin (500mg) post-operatively in the ward from ward nurses (MD). Operation-room anesthetic assistant administered prophylactic antibiotics at induction of anaesthesia to all the patients.

Results: Of the 30 cases that received single dose prophylactic antibiotic pre-operatively, 16.67% were males and 83.3% were females. And, of the 30 cases that received multiple dose prophylactic antibiotic pre as well as post-operatively, 10% were males and 90% were females. Analysis showed that there was no statistically significant difference across the groups in regard to the duration of preoperative hospital stay. Of the 30 cases that received single dose prophylactic antibiotic pre-operatively, only one patient suffered gross contamination during the surgery.

Conclusion: The rate of early PSI after administration of single dose ciprofloxacin (500 mg) intravenously at induction of anesthesia and multiple dose ciprofloxacin (500 mg given thrice or four times) intravenously post-operatively for two or three days in addition to peri-operative dose is comparable in elective laparoscopic cholecystectomy. Furthermore, hospital cost can be reduced with single dose antibiotic regimen. So single dose of ciprofloxacin 500 mg can be used safely in elective cases of laparoscopic cholecystectomy to avoid infection at port site.

Keywords: Cholelithiasis, Laparoscopic Cholecystectomy, Prophylactic Antibiotic, Ciprofloxacin, Port-Site Infection

INTRODUCTION

Laparoscopic cholecystectomy (LC) is the gold standard treatment of symptomatic cholelithiasis. Its advantage over open cholecystectomy has been well established (level 1 evidence).[1] Smaller incisions (ports), cosmesis, early recovery, patient"s satisfaction and cost effectiveness are the numerous advantages of LC. Unlike any other surgery, surgical site infection (SSI) is an integral part of LC. This is termed as port site infection (PSI) in LC.[2] Unlike SSIs in open surgery, PSI after laparoscopic surgery obviates all its advantages and is frustrating to the patient and night mare for the surgeon. The unsightly wound and nagging indolent infection continues for days with minimal response to common antibiotics. This decreases the quality of life of the patient with added cost. Apart from the other well known causes, the primary cause of PSI in our country includes insufficient and ineffective sterilization of reusable trocars.[2,3] This leads to colonization of the wound with native skin commensals which rarely produce infection in an otherwise healthy patient.[2] At times exogenous agents like contaminated water used for cleaning instrument are responsible for PSIs.[2,3] Being unusual organisms they respond poorly to usual antibiotics.[1-3] Often the culture report is negative. As such multi dose postoperative antibiotics have minimal role to provide relief from PSI. Though these facts are well established, surgeons still continue to use multiple doses of post operative antibiotics in CDC classified class 1 and 2 LC.[1-3] On the other hand it is also true that despite improved sterilization techniques and other laparoscopic surgical technical reforms PSI still exists.[1-3,4] Social taboo, lack of confidence in part of the surgeon and other industry driven facts, which are beyond the scope of this discussion, are reasons behind such inappropriate and irrational use of postoperative multiple dose antibiotics. It has been proved beyond doubt that a single preoperative dose of antibiotic is sufficient to prevent SSI in LC.[1-4] The need of the hour is to understand the fact that PSI is a totally different subset of infection and antibiotics are not a solution to this problem. The core issue of "prevention" is the principal solution. The

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study was undertaken to revalidate these well known facts with an effort to bring about a radical reform to this "social" rather than clinical problem.

Current research aimed to study about efficacy of single dose prophylactic antibiotic administered at induction of anaesthesia versus multiple dose of post-operative antibiotics to prevent early Port-site infection in patients undergoing elective laparoscopic cholecystectomy for uncomplicated cholelithiasis, to study the cost–effectiveness between two groups and to find out the factors which can prevent early PSI

MATERIAL AND METHODS

A prospective longitudinal observational study was conducted at Bankura Sammilani Medical College, a tertiary referral center in southern part of rural Bengal from first of May 2018 to 30th of June 2018. The study was approved by the institutional ethics committee of the college. All patients aged between 18 to 65 years suffering from symptomatic documented gallstones on ultrasonography and undergoing LC were included in the study. Patients with complicated gall stones (cholangitis, choledocholithiasis, and pancreatitis), age less than 18 years or more than 65 years, hypersensitivity to ciprofloxacin, pregnant or nursing women, patients with renal impairment, severe hepatic disease, immune-compromised status, steroid therapy, obese, diabetes mellitus, tuberculosis, septicemia defined by Systemic inflammatory response syndrome (SIRS), patient with contaminated and dirty abdominal surgeries, duration of surgery more than three hours and those who required conversion to open cholecystectomy were excluded. Those who did not consent to be included in the study were excluded. All the patients were examined and investigated prior to their surgery, and the information needed was recorded.

The study comprised of 60 patients admitted for elective LC. The first thirty patients undergoing elective LC were given single dose (SD) ciprofloxacin (500 mg) within an hour between the induction and making of the first port. While the control group received ciprofloxacin (500mg) post-operatively in the ward from ward nurses (MD). Operation-room anaesthetic assistant administered prophylactic antibiotics at induction of anaesthesia to all the patients.

All LCs were performed under general anaesthesia with endotracheal intubation by the surgeons experienced in the procedure. Prior to standard preoperative disinfection methods the operative field and umbilicus was thoroughly cleaned with savlon and spirit. The abdominal skin was then prepared with 10% povidone-iodine solution. Laparoscopic instruments were sterilized as per hospital protocol before procedures by autoclaving with the instruments wrapped in heavy tetra sheets. Aseptic precaution was maintained throughout the procedure. After dissection of gall bladder from GB fossa, epigastric port was used for extraction of gall bladder; those found difficult due to thick wall or large stone size for extraction were retrieved through umbilical port. Patients were monitored postoperatively in recovery room for two hours and then send to post anesthesia care unit as per our existing practice. For postoperative analgesia, injection paracetamol 500 mg intravenously, every eight hours, was administered on the day of operation, and was switched to oral paracetamol 500 mg and from next day. Oral feeding was started after twelve hours of surgery. Drip was stopped once oral feeding was tolerated with cannula being locked in situ. Patients in Group SD were discharged on third postoperative day after first dressing if vitals were stable, no features of peritonitis was present, and patients tolerated oral feeds. Patients in Group MD were discharged on third postoperative day after receiving antibiotics for 48 hours. Patients from both groups were advised to follow up in surgical out-patient clinic on tenth post operative day for suture removal and 30th postoperative day with reports of histopathology of resected gallbladder. Status of wound was recorded and managed accordingly and dressing of wound in case of pus. Pus was subjected for culture and sensitivity testing. Patient's demographics and clinical characteristics including gall bladder perforation and bile/stones spillage during surgery, use of suction, status of wound were recorded in a pre-designed proforma.

Collected data were compiled in Microsoft excel sheets, coded and analyzed. Continuous data were summarized and described by mean, median and standard deviation (SD). Categorical variables were presented via proportion. Data display was done with the help of tables and various charts like bar diagram, sector diagram. Continuous variables were checked for their normality distribution by using Shpiro-Wilk test. If in the initial test continuous data were found to have skewed distribution then those data were transformed into their log value and the transformed data set were again tested for normality distribution by the same test. If the data set still remained skewed then the non-parametric test for continuous variables was applied for their analysis. For drawing statistical inference regarding the interrelationship between variables Chi-square test, Fisher"s exact test, Odds ratio (OR) with its 95% confidence interval (CI) were adopted for the categorical data and Unpaired "t" test was used for the continuous variable showing to have normal distribution. Continuous data which was proved to have skewed distribution were tested by non-parametric test for continuous data like Mann Whitney U test. P value of <0.05 was considered to be statistically significant at 95% CI with 5% precision. Statistical soft ware package IBM SPSS Statistics 22 version was used for the purpose of data analysis.

RESULTS

Baseline characteristics of the participants

Of the 30 cases that received single dose prophylactic antibiotic pre-operatively, 16.67% were males and 83.3% were females. And, of the 30 cases that received multiple dose prophylactic antibiotic pre as well as post-operatively, 10% were males and 90% were females. As per the statistics, there was no significant difference between the groups in respect of distribution of genders among them. [Table 1 and Fig.1]

Groups	Gender		Total No. (%)	χ^2, df, p	OR (95%CI)
	Male No. (%)	Female No. (%)			
Study	5 (16.67)	25 (83.30)	30(100.0)	0.58,1,0.447	1.80(0.32-10.81)
Comparison	3 (10.00)	27 (90.00)	30(100.0)		
Total	8 (13.33)	52 (86.67)	60(100.0)	—	—

Table-1: Distribution of study subjects according to their gender (n=60)

Age Group (years)	Groups		Total No. (%)	χ^2, df, p	OR (95% CI)
	Study No. (%)	Comparison No. (%)			
Up to 40	16 (57.14)	12 (42.86)	28 (100)	1.07,1,0.301	1.71(0.55-5.44)
40-50	7(38.89)	11 (61.11)	32 (100)		
50-60	5(50.0)	5 (50.0)			
≥60	2 (50.0)	2 (50.0)			
Total	30 (16.67)	30 (83.33)	60 (100)	—	—

Table-2: Distribution of participants according to study groups and age categories (n=60)

Groups	Age		Unpaired t, df, p
	Mean	SD	
Study	39.33	13.25	0.706, 58, 0.483
Comparison	41.77	13.45	
Total	40.55	13.29	—

Table-3: Distribution of study subjects according to study arm and average age (n=60)

Variables		Groups		Total No. (%)	χ^2, df, p
		Study No. (%)	Control No. (%)		
Marital Status	Single	4 (50)	4 (50)	8 (100)	0.0,1,1.00
	Ever Married	26 (50.98)	26 (49.02)	52 (100)	
Residence	Rural	27 (48.21)	29 (51.79)	56 (100)	0.612
	Urban	3 (75)	1 (25)	4 (100)	
Education	Illiterate	23 (46.94)	26 (53.06)	49 (100)	1.0,1,0.317
	Literate	7 (33.33)	4 (66.67)	3 (100)	
Occupation	Unemployed	24 (48.98)	25 (51.02)	49 (100)	0.11,1,0.739
	Somehow employed	6 (50)	5 (50)	4 (100)	

Table-4: Distribution of participants according to some socio-demographics (n=60)

Groups	History of Laparotomy		Total No. (%)	χ^2, df, p
	Present No. (%)	Absent No. (%)		
Study	4 (13. 33)	26 (86.67)	30 (100)	0.16,1,0.688
Comparison	3 (10.00)	27 (90.00)	30 (100)	
Total	7 (11.67)	53 (88.33)	60 (100)	—

Table-5: Distribution of participants according to their history of Laparotomy (n=60)

Groups	Mean Rank	Sum of Ranks	Mann Whitney U	Z, P
Study	28.50	855.00	990.00	1.211, 0.226
Comparison	32.50	975.00		

Table-6: Distribution of participants as per pre-operative hospital stay (n=60)

Groups	Mean Rank	Sum of Ranks	Mann Whitney U	Z, P
Study	30.20	906.00	441.00	0.136, 0.891
Comparison	30.80	924.00		

Table-7: Distribution of participants as per Interval between administration of Antibiotic and making of Laparoscopy Port (n=60)

Groups	Mean Rank	Sum of Ranks	Mann Whitney U	Z, P
Study	27.68	830.50	365.500	1.273, 0.203
Comparison	33.32	999.50		

Table-8: Distribution of study subjects of according to the duration of operation

Groups	Mean Rank	Sum of Ranks	Mann Whitney U	Z, P
Study	34.45	1033.50	331.500	1.768, 0.077
Comparison	26.55	796.50		

Table-9: Distribution of Study Subjects of according to their Intra-operative Blood Loss

Groups	Mean Rank	Sum of Ranks	Mann Whitney U	Z, P
Study	31.00	930.50	435.000	0.275, 0.783
Comparison	30.00	900.00		

Table-10: Distribution of Study Subjects of according to their Post-operative Hospital Stay

Groups	Mean Rank	Sum of Ranks	Mann Whitney U	Z, P
Study	15.50	465.00	0.000	7.271, 0.000
Comparison	45.50	1365.00		

Table-11: Distribution of Study Subjects of according to their cost of antibiotic therapy (n=60)

Groups	Mean Rank	Sum of Ranks	Mann Whitney U	Z, P
Study	39.00	1170.00	195.000	4.355, 0.000
Comparison	22.00	660.00		

Table-12: Distribution of Study Subjects of according to their Number of Follow-up Visits (n=60)

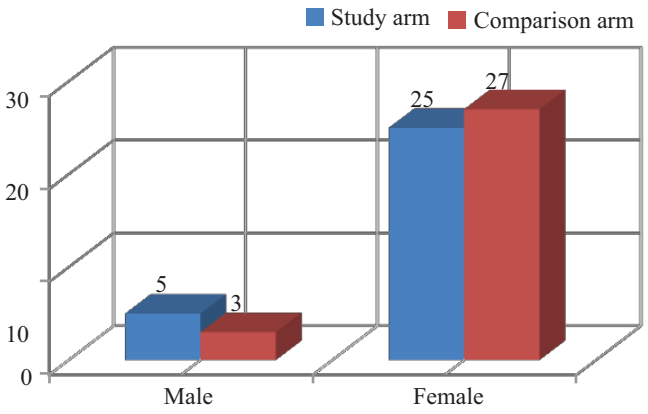

Figure-1: Distribution of participants as per gender

The table 2 shows that majority of the participants belonged to the lowest age group i.e. 40 years and below. However, after clubbing the age groups upto 40 years and performing Chi-square test of independence using 2×2 table the groups were revealed to be comparable in respect to the between group distribution of participants belonging to different age categories. This fact has also been reiterated by the findings of the table-3 which reveals no significant difference among participants of two groups in respect to their age.

Further analysis of data reflected the fact that the participants belonging to each group were also very much comparable in respect of certain socio-demographic characteristics. No such variable showed any statistically significant difference so far across the groups [Table 4].

Past Surgical History

Of the 30 cases that received single dose prophylactic antibiotic pre-operatively, 13.33% patients had previous history of laparotomy performed any time three months ago and, of the 30 cases that received multiple dose prophylactic antibiotic pre- as well as post-operatively 11.67% patients reportedly had previous history of laparotomy performed any time three months ago. However, there was no statistically significance difference between the groups in this respect [Table 5].

Current Surgical Infection: None of the patients had any current surgical infection.

Co-Morbidities: Similarly, none of the patients had any co-morbidity.

Current Clinical Condition: All the patients were hemodynamically stable and physically fit for surgery.

Analysis showed that there was no statistically significant difference across the groups in regard to the duration of preoperative hospital stay [Table-6].

Further analysis revealed that the groups were comparable in respect to the Interval between administration of Antibiotic and making of Laparoscopy Port [Table-7].

Adminstered dose of ciprofloxacin: All the patients of both group received a dose of Ciprofloxacin 500mg pre-operatively at the time of induction of anaesthesia.

Intra-Operative Events

No statistically significant between groups difference could be explored in regard to the duration of operation [Table-8].

The difference in intraoperative blood loss between the groups was statistically insignificant [Table-9].

Distribution of Study Subjects According to the Incidence of Gross Contamination: Of the 30 cases that received single dose prophylactic antibiotic pre-operatively, only one patient suffered gross contamination during the surgery. And, of the 30 cases that received multiple dose prophylactic antibiotic pre- as well as post-operatively, none of the patients had any gross contamination. None of the patients of either group had their duration of operation exceeding 3 hours and none of them suffered blood loss >1000 ml.

Post-Operative Events

Distribution of Study Subjects According to the Interval between Closure of Laparoscopic Port and First Dose of Post-Operative Ciprofloxacin: Of the 30 cases that received single dose prophylactic antibiotic pre-operatively, this criterion is not applicable for them. And, of the 30 cases that received multiple dose prophylactic antibiotics pre- as well as post-operatively, the average interval are 10.1667.

Distribution of Study Subjects According to the Interval between Wound Closure and First Wound Exposure: All the patients of both groups have the interval as 48 hours.

Distribution of Study Subjects According to Adequate Wound Cleaning: All the patients of both groups underwent adequate wound cleaning.

Distribution of Study Subjects According to Administered Dose of Post-Operative Antibiotic: Of the 30 cases that received single dose prophylactic antibiotic pre-operatively, this criterion is not applicable for them. And, of the 30 cases that received multiple dose prophylactic antibiotics post-operatively, all received 500mg of Ciprofloxacin.

Distribution of Study Subjects According to Incidence of Fever: None of the patients of either group suffered from fever.

Length of post-operative hospital stay was found to be comparable between the groups [Table-10].

Distribution of Study Subjects According to the Cost of Antibiotics: The cost of 1 infusion bottle of Ciprofloxacin 500mg is 14 rupees. Since the study group of 30 patients received a single pre-operative dose of Ciprofloxacin 500mg, their total cost of antibiotics is rupees 14 only. The comparison group received multiple doses of prophylactic antibiotic (ciprofloxacin 500mg), hence, their cost of antibiotics varied. The average cost is rupees 61.13.

A statistically robust difference across the groups was explored in respect of the cost of the antibiotic. The cost was revealed to be higher in comparison group [Table-11].

Follow-up

Incidence of PSI: None of the patients of either group developed early port-site infection (i.e. upto 7 days of follow-up).

The number of follow up visits was found to be higher among the participants of study group and the difference was proved to be statistically significant [Table-12].

DISCUSSION

The gold standard treatment of symptomatic cholelithiasis is laparoscopic cholecystectomy.[1,2,5-9] But in developing countries like India and especially in underdeveloped and rural medical colleges, open cholecystectomy is still considered the first line of treatment as facilities, cost-effectiveness and expertise are still a major concern.[5-9]

Cholecystectomy is a clean contaminated type of surgical procedure. The incidence of SSI without chemo-prophylaxis is about 20%.[6-9] Though post surgical prophylaxis is not advisable, the concept of pre-operative antibiotic prophylaxis is debatable.[10-13] Considering the high incidence of SSI without antibiotic prophylaxis and huge number of pro-prophylaxis evidence based data, single dose preoperative antibiotic prophylaxis is practiced worldwide.[7-9,10-13] This has been substantiated by numerous studies which concluded that antibiotic prophylaxis is effective in preventing postoperative wound infection. The continuing concerns even after numerous worldwide trials is because of the fact that SSI still prevails (0-7% in LC, 1-19% in open cholecystectomy) despite advancement in the field of operative instrumentation, technique and sterilization.[6,7,10–13] Most of the PSI (SSI in LC) are early and involve the epigastric port.[6-9] On the contrary this study is unique in the sense that none of the patients in the test group and control group developed PSI. In accordance with one of the published data it can be concluded that antibiotic prophylaxis do not seem to affect the incidence of PSI in LC which was one of the notable predictions of this study.[1] Symptomatic cholelithiasis is a disease of females (Female>Male) and the gender frequency in the study (83.3% - female, 16.6% -male) is similar to previous studies.[2,4,6-9,14] The incidence of PSI in single dose LC is 0-4% and 0-7% in multiple doses LC.[14–18] Though there was no PSI in the study but considering the level 1 evidence we would recommend single preoperative dose of antibiotic in LC.[11-13] The factors which were felt to be more important than antibiotic prophylaxis included shorter hospital stay, less postoperative time, less tissue handling, less blood loss and overall autoclaving as a method of sterilization rather than chemical sterilization of instruments though these were found to be statistically insignificant due heterogeneity in patient selection.[10–18]

Younger age of the patients (less than 40 years, 57.14% in study group, and 42.86% in control group) together with minimal basic education (75%) of the patients could have been a major cause of less incidence of PSI. Younger patients with better immunological status and educated patients with better ability to carry on post operative orders to keep wound clean following discharge. The study also reiterated the previous fact that previous laparotomy was not a major hindrance to laparoscopy as 11.67% of patients had past history of laparotomy in our study. Cost effectiveness of any surgical procedure is a major concern for a developing country like ours and in our study a statist ically robust difference across the groups was explored in respect of the cost of the antibiotic. The cost was revealed to be higher in the control group (Table-11). This was an important factor as we in our hospital use reusable trocars and instruments where 100% sterilization is mandatory to prevent PSI.

The choice of antibiotic ciprofloxacin, which is effective, readily available, cheaper, more half life and higher biliary concentration toget her with autoclaving rather than chemical sterilization also helped in reducing the cost.[19] With this simple approach we could not only reduce cost but nearly eliminated PSI in our study.

The study was not short of limitations. Short duration, less number of recruited patients due to time constrains and clinical heterogeneity in terms of defining early and superficial PSI, and patient recruitment where we have excluded patients with acute inflammation and associated medical pathology were some of the glaring shortcomings. This study will serve as a tip of the iceberg and help other investigators to unearth more important facts that would not only benefit the patient but also care providers in reducing surgical site infection in LC in a simple and cost effective manner in other institutions of our country.

CONCLUSION

The rate of early PSI after administration of single dose ciprofloxacin (500 mg) intravenously at induction of anesthesia and multiple dose ciprofloxacin (500 mg given thrice or four times) intravenously post-operatively for two or three days in addition to peri-operative dose is comparable in elective laparoscopic cholecystectomy. Furthermore, hospital cost can be reduced with single dose antibiotic regimen. So single dose of ciprofloxacin (500 mg) can be used safely in elective cases of laparoscopic cholecystectomy. There were some limitations in this study: the duration of study was too short (two months) and consequently, the sample size was quite small. Thus, it is difficult to draw any conclusion. Hence, further extensive study should be carried out with a larger sample size and longer duration. Nevertheless, it was observed that the cost of antibiotics was considerably low in the patients of the study group with t he efficacy to prevent early PSI being the same as with multiple dose antibiotic prophylaxis. Hence, we can conclude from our study that single dose antibiotic regimen can be safely practiced in elective laparoscopic cholecystectomy.

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