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RESEARCH ARTICLE

ROLE OF ANTIBIOTIC PROPHYLAXIS IN ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY: A PROSPECTIVE RANDOMIZED OBSERVATIONAL STUDY IN TERTIARY CARE CENTRE OF INDIA

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ABSTRACT

Cholecystitis is inflammation of the gallbladder. Symptoms include right upper abdominal pain, nausea, vomiting, and occasionally fever. The pain lasts longer in cholecystitis than in a typical biliary colic. Without appropriate treatment, recurrent episodes of cholecystitis are common. During this study 229 patients were admitted with chronic cholecystitis of which 12 patients were excluded before randomization. The remaining 217 were randomized with 106 in the group A and 106 in group B. 5 patients were excluded because of open conversion in both the groups (2 in group A and 3 in group B). **Preoperatively;** No significant differences existed between the 2 groups regarding sex, age; body mass index and ASA score. Also, the duration of LC surgery, incidence of intraoperative gallbladder perforations and spillage of bile or stones, incidence of intra-operative bleeding from either cystic artery or gall bladder fossa and mean postoperative hospital stay were found not significantly different between the 2 groups. The parameters studied were age group, placement of drains, bile leak, hospital stay, Asepsis score, Surgical site infections, postoperative antibiotic used (after 24 hrs). In SSI in Group A, 95 (89.6%) had no SSI and 11 (superficial 8, deep 2, organ specific 1, total 10.4%) had SSI. In Group B, 96 (90.6%) had no SSI and 10 (superficial 7, deep 2, organ specific 1, total 9.4%) had SSI (p value 0.818). In both the groups the difference in the incidence of surgical site infections was not statistically significant.Hence prophylactic antibiotics do not reduce the risk of infective complications in patients undergoing laparoscopic cholecystectomy in low risk group of patients.

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INTRODUCTION

Cholecystitis is inflammation of the gallbladder. Symptoms include right upper abdominal pain, nausea, vomiting, and occasionally fever. The pain lasts longer in cholecystitis than in a typical biliary colic. Without appropriate treatment, recurrent episodes of cholecystitis are common. Complications of acute cholecystitis include gallstone pancreatitis, common bile duct stones, or inflammation of the common bile duct. Open cholecystectomy reigned the most portions of last century as the treatment of choice for symptomatic gall stone disease (Kumar, 2011).

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Laparoscopic cholecystectomy usually requires 4 small incisions in the abdomen to allow insertion of operating ports. Recently, this procedure is performed through a single incision in the patient's umbilicus (Catarci, 2004; Uludag, 2009 and Higgins, 1999). This advanced technique is called Laparoendoscopic Single Site Surgery or "LESS" or Single Incision Laparoscopic Surgery or "SILS". In this procedure, instead of making 3-4 four small different cuts (incisions), a single cut (incision) is made through the navel (umbilicus). Through this cut, specialized rotaculating instruments (straight instruments which can be bent once inside the abdomen) are inserted to do the operation (Tocchi, 2000). The advantage of LESS / SILS operation is that the numbers of cuts are further reduced to one and this cut is also not visible after the operation is done as it is hidden inside the navel. Many authors believe that antibiotic prophylaxis may not be necessary in low-risk

patients undergoing elective LC. On the contrary, many other surgeons still use and recommend the administration of prophylactic antibiotics. One study documented in their chart review that 79% of patients who had undergone LC were given prophylactic antibiotics preoperatively (Ahmed, 2012). In case of acute cholecystitis, the general practice was to treat the patient with initial medical support followed by delayed planned laparoscopic cholecystectomy. If laparoscopic cholecystectomy can be performed in early stage of acute cholecystitis duration of hospital stay, possibility of further attack, incidence of gall stone related complications can be reduced. The most frequent complication in patient undergoing cholecystectomy is surgical site infection. SSI was reported in 10% to 23% of the patients who had been operated on or before the routine use of antibiotic prophylaxis, which was introduced in 1960. The SSI increases length of hospital stay and costs, decreases the quality of life (Kumar, 2013). Since 1960, antibiotic prophylaxis has been considered as the best intervention to prevent SSI in elective surgery. Antibiotic prophylaxis includes preoperative administration of wide spectrum antibiotics against the most frequent bacteria involved in surgical site infection, trying to get higher tissue levels of antibiotics at the surgical wound in order to avoid colonization and growth of micro-organisms. Cholecystectomy is considered as clean-contaminated surgery (Sanabria, 2010). Since 1986, with the use of laparoscopic technique surgical treatment of cholelithiasis has undergone a dramatic change. Although, this surgical method diminished the length and manipulation of the surgical wound, antibiotic prophylaxis use did not change. Recent clinical trials have re-evaluated the usefulness of antibiotic prophylaxis in laparoscopic cholecystectomy. In laparoscopic cholecystectomy the incisions are smaller, all manipulations of the excised organ are made through a trocar that isolates the surgical wound from the gall bladder and decreases the contact of the wound with the external environment. Nonetheless, there is no consensus about these considerations, and many surgeons (most of the surgeons) still use antibiotic prophylaxis in elective laparoscopic cholecystectomy. Antibiotic prophylaxis is used to reduce the risk of post- operative wound infections. Patients undergoing procedures associated with high infection rates, those involving implantation of prosthetic material, and those in which the consequences of infection are serious should receive perioperative antibiotics (Shah, 2012).

Cephalosporins (such as cefazolin) are appropriate first line agents for most surgical procedures, targeting the most likely organisms while avoiding broad spectrum antimicrobialtherapy that may lead to resistance and loss of useful gut flora (Loozen, 2017). Duration of prophylaxis should not exceed 24 hrs. Surgical site infections are of three types; Superficial, Deep incisional and Organ space infections. It is a type of health-care associated infections. Other types of health-care associated infections that may affect a surgical patient in postoperative period include Respiratory tract infections, urinary tract infections, Bacteraemia (i.v cannula) and antibiotic related diarrohoea (Club, 1991). A Surgical Site infection may range from a spontaneously limited wound discharge within 7-10 days of an operation to the life threatening complications. Port site infection is of main concern following laparoscopic surgery. Port site infections may be classified as; Early PSI (<7 Days of surgery), Delayed PSI (>4wks of surgery) (Koc, 2003). Measures can be taken in the pre-operative, intra-operative and post-operative period to reduce the incidence of SSI. There have been many studies on this topic over last many years since the introduction of laparoscopy, but all studies concluded that there is requirement of large scale study with adequate sample size (Yan, 2011; Sharma, 2010). In this randomized controlled trial we will evaluate the role of antibiotic prophylaxis in elective laparoscopic cholecystectomy in prevention of SSI. Patients, who took part in this study, were categorized into 2 groups. patients in the “Antibiotic group” (Group A) were given a total of three doses of 1.5 gm of intravenous cefuroxime: the first, just before skin incision, and the second and the third at 12 h and 24 h, respectively, after the operation. If an operation took over 3 h, a further dose of antibiotics were given intravenously. Patients in the “No Antibiotic” (Group B) group received no antibiotics. Then postoperatively patient was followed up to 4 weeks for surgical site infections.

MATERIALS AND METHODS

STUDY AREA- Department of general surgery, Ramakrishna mission sevaPratisthan (Vivekananda institute of medical sciences)

STUDY POPULATION AND STUDY PERIOD - All patients undergoing elective laparoscopic Cholecystectomy, who was admitted as indoor patient on July2016 to June 2017

INCLUSION CRITERIA : Patients who were aged ≥ 18 yrs and ≤ 65 yrsand undergoing elective laparoscopic cholecystectomy

Exclusion Criteria: Excluded from the study are patients who

- Undergo emergency operation
- Concurrently undergo another surgery
- Use insulin or steroids regularly
- Have a history of allergy to antibiotics
- Be on haemodialysis
- Have taken antibiotics within 7 days prior to surgery
- Are younger than 18 years of age or more than 65 yrs of age
- Have severe comorbidities such as Child C liver cirrhosis, or were undergoing chemotherapy for malignancies.
- Have empyema (Intraoperative finding)
- Have Any infection detected >1 month after operation
- Any co-existing hepatobiliary pathology

Study Technique

Patients with gallbladder stones or polyps scheduled to undergo elective laparoscopic cholecystectomy were eligible for enrollment in the study. Patients were categorized into either of two groups (Based on randomization done by computer generated system), Patients in the Antibiotics group were given a total of three 1.5 gm doses of intravenous cefuroxime: the first, just before skin incision, and the second and the third at 12 h and 24 h, respectively, after the operation. If an operation took more than 3 hr, a further dose of antibiotics were given intravenously. Patients in the No antibiotics group did not receive any antibiotics. The study included all cases of low risk elective cholecystectomy patient admitted in the Department of General Surgery of VIMS &RKMSP during time period from July 2016 to June 2017.During this period 229 patients were admitted with calculus cholecystitis of which 12 patients were excluded before randomization.

Table 1. Distribution of asepsis score, ssi, bile leak, drain, postoperative antibiotic USED and SSI according to groups

		Antibiotic Group	Non Antibiotic Group	Total	P Value	Significance
ASEPSIS SCORE	<20	95(89.6)	96(90.6)	191(90.1)	0.818	Not Significant
	>20	11(10.4)	10(9.4)	21(9.9)		
	Total	106(100)	106(100)	212(100)		
SSI	NO	95(89.6)	96(90.6)	191(90.1)	0.818	Not Significant
	YES	11(10.4)	10(9.4)	21(9.9)		
	Total	106(100)	106(100)	212(100)		
BILE LEAK	YES	26(24.5)	29(27.4)	55(25.9)	0.638	Not Significant
	NO	80(75.5)	77(72.6)	157(74.1)		
	Total	106(100)	106(100)	212(100)		
DRAIN	YES	27(25.5)	26(24.5)	53(25)	0.874	Not Significant
	NO	79(74.5)	80(75.5)	159(75)		
	Total	106(100)	106(100)	212(100)		
POSTOPERATIVE	NO	95(89.6)	96(90.6)	191(90.1)	0.818	Not Significant
ANTIBIOTIC USED	YES	11(10.4)	10(9.4)	21(9.9)		
	Total	106(100)	106(100)	212(100)		
SSI	Superficial Infection	8(72.7)	7(70.0)	15(71.4)	0.990	Not Significant
	Deep Infection	2(18.2)	2(20.0)	4(19.0)		
	Organ Specific	1(9.1)	1(10.0)	2(9.6)		
	Total	11(100)	10(100)	21(100)		

The remaining 217 (156 females amd 61 males) were randomized with 106 in the group A (Antibiotic group) and 106 in group B. 5 patients were excluded because of conversion of laparoscopic to open cholecystectomy in both the groups (2 in Gp A and 3 in Gp B)

Surgical Procedure

Procedure – All the operations were performed by using 10 mm 30 degree telescope, single chip camera and halogen light source. Every Gall bladder was sent for histopathological examination. All the patients were operated under general anaesthesia with endotracheal intubation in supine position followed by antiseptic dressing (using 10% povidone iodine in each case) and draping. Umbilical port was made by Open technique and 10 mm trocar port was introduced. Pneumoperitoneum was created by CO2 insufflation .The abdomen was fully insufflated using the preset pressure 12-15 mm of Hg with 3 to 5 litre of CO2. The abdominal wall was kept elevated manually to prevent any injury during trocar placement. The laparoscope was introduced through umbilical port and adjacent areas were looked for any injury. Other organs were inspected for any gross pathology. The patient was then tilted to reverse trendlenberg position with 15 degree rotation to the left side. The epigastric trocar port was introduced under visual control through epigastric port.2 additional 5 mm port were created one in rtmidclavicular line and one in antr axillary line. Dissector was introduced through epigastric port. After dissection of posterior and anterior fold gently using the dissector, Calots triangle was exposed. The structures forming the triangle and contents were clearly identified. Cystic duct and artery were skeletonized and anterior and posterior windows were made. The neck of GB was dissected away from liver bed using blunt dissection. The cystic duct and artery were found to be entering the GB only. The duct and artery then clipped separately with 3 clips and 2 clips separately. Duct and artery were cut leaving 2 and 1 clips away from GB. The duct and artery were examined for any leakage. GB was then separated from Liver bed by electrosurgical probe to coagulate small vessels and lymphatics. After removal of GB from liver bed, it was held by a grasper and kept over the superior surface of Liver. The Liver bed was checked for any bleeding or bile leakage. If necessary, diathermy was used.GB fossa and adjacent area were irrigated and sucked to dry.

Then the gall bladder was kept in a sterilized plastic packed and exctracted through epigastric port using large claw extractor. Depending upon the intraoperative condition, A nasogastric suction tube of 18 fr diameter was introduced through lower antr axillary port and kept in hepatorenal pouch. Umbilical port was checked by inserting the camera through epigastric port. Laparoscope was withdrawn. 10 mm fascia was closed with port vicryl No.1 and skin was sutured by monofilament nylon.

Postoperative Care: Intravenous Diclofenac sodium was used as per body wt twice daily and SOS. Patients in antibiotic group received 2 extra doses of cefuroxime 1.5 grams (all of same brands). Feeding was resumed as soon as tolerated. Discharge of patients from hospital was based on clinical grounds. All patients were asked to attend surgical OPD after 1 week and then every 4 week after discharge for 3 months or emergency room SOS. The patients were followed upto 30 days post operatively for study purpose. The method of follow up being outpatient visit twice in the postoperative period, once after 1 wk and next after 28-30 days postoperatively. In the outpatient visit patients were reviewed for infection by assessing the wound based on ASEPSIS SCORE. Patients were followed up for any surgical site infections on the basis of ASEPSIS SCORE. ASEPSIS SCORE more than 20 was considered to be significant.

RESULTS AND ANALYSIS

This study included all cases of elective laparoscopic cholecystectomy admitted in the Department of General Surgery of Vivekananda Institute of Medical Sciences during the time period from July 2016 to June 2017. During this study 229 patients were admitted with chronic cholecystitis of which 12 patients were excluded before randomization. The remaining 217 were randomized with 106 in the group A and 106 in group B. 5 patients were excluded because of open conversion in both the groups (2 in group A and 3 in group B). In both the groups patients were maximum in the range of 40-50, 32 in group A (30.2) and 35 in group B (33). Regarding sex distribution in Group A, 72 (67.1%) females and 34 (32.9%) males were there. In group B, 75(70.8%) females and 31 (29.8%) males were there (P value 0.655). Regarding bile leak in Group A, 26(24.5%) had bile leak and 80(74.5%) had no bile leak. In Group B, 29(27.4%) had bile leak and 77(72.6%) had

no bile leak (P value 0.638). Regarding requirement of drain placement in Group A in 27 (25.5%) drain was placed and in rest 79 (74.5%) no drain was placed. In Group B in 26 (24.5%) drain was placed and in rest 80 (75.5%) drain was not placed (P Value 0.655). Regarding ASEPSIS SCORE in Group A 95 patients (89.6%) had score <20 and in rest 11 score was >20. In Group B, 96 patients (90.6%) had score <20 and in rest 10 (9.4%) score was >20 (P value 0.818). Regarding postoperative antibiotics used, in Group A, 95(89.6%) no antibiotics were used and in rest 11 (10.4%) it was used. In Group B in 96 (90.6%) no antibiotics were used and in rest 10 (9.4%) it was used (P value 0.818). In SSI in Group A, 95(89.6%) had no SSI and 11 (10.4%) had SSI. In Group B, 96(90.6%) had no SSI and 10 (9.4%) had SSI (P value 0.818). Regarding age, mean age in Group A is 36.63 (SD 11.646), mean age in Group B is 39.07(SD 10.909). P value is 0.118. About hospital stay, in Group A mean 2.09(SD 0.991) in Group B mean 2.36(SD 1.189).P value is 0.080. Regarding the types of SSI, Superficial Infection in Antibiotic Group 8(72.7%) and in Non-Antibiotic Group 7(70%). Deep Infection in Antibiotic Group 2(18.2%) and in Non-Antibiotic Group 2(20%).Organ Specific Infection in Antibiotic Group 1(9.1%) and in Non-Antibiotic Group 1(10%) (P value 0.990) which is non-significant. Thus in both the groups there was no difference in incidence of surgical site infections.

DISCUSSION

With the advent of laparoscopic surgery, the outcome of surgery has improved in respect to hospital stay, less postoperative pain, early recovery and early ambulation. As prophylactic antibiotic has played a major role in prevention of septic complications in open surgery, its role has to be re-evaluated in laparoscopic surgery owing to its less morbidity as compared to open surgery. Similarly role of prophylactic antibiotics in prevention of surgical site infections need to be revaluated as previous studies showed that there is actually no role of prevention of surgical site infections in laparoscopic cholecystectomy. This is a prospective observational study trial at Vivekananda Institute of Medical Sciences from July 2016 to June 2017. The low risk patients who underwent elective laparoscopic cholecystectomy during this time period were categorized as the subject for the study. All candidates undergoing elective laparoscopic cholecystectomy were included in this study, by taking care of exclusion criteria. This prospective study was conducted to investigate the efficacy of cefuroxime (1.5 gm, three doses) as a prophylactic antibiotic to prevent surgical site infections in low risk patients undergoing LC. 217 Patients (156 females &61 males) included in the study were randomly divided into two groups (106 each). 5 were excluded from the study: Group A: patients received intravenous cefuroxime 1.5 gram (30 mins prior to incision, after 12 hrs postoperatively, 24hrs postoperatively) and Group B received No antibiotics. All patients were invited for examination on 7th and 28th postoperative day and postoperative complications were recorded and managed accordingly. Preoperatively; No significant differences existed between the 2 groups regarding sex, age; body mass index and ASA score. Also, the duration of LC surgery, incidence of intraoperative gallbladder perforations and spillage of bile or stones, incidence of intra-operative bleeding from either cystic artery or gall bladder fossa and mean postoperative hospital stay were found not significantly different between the 2 groups. The parameters studied were age group, placement of drains, bile leak, hospital stay, Asepsis score, Surgical site infections, postoperative antibiotic used (after 24 hrs). In SSI in Group A, 95 (89.6%) had no SSI and 11 (superficial 8, deep 2, organ specific 1, total 10.4%) had SSI. In Group B, 96 (90.6%) had no SSI and 10 (superficial 7, deep 2, organ specific 1, total 9.4%) had SSI (p value 0.818). In both the groups the difference in the incidence of surgical site infections was not statistically significant. All candidates undergoing elective laparoscopic cholecystectomy were included except patients with acute cholecystitis, obstructive jaundice, pancreatitis, pregnancy, cholangitis. Patients on immunosuppressive therapy due to any disease, concurrent antibiotic therapy, or known allergy to antibiotics were also excluded. This prospective study was conducted to investigate the efficacy of Cefuroxime (1.5gm three doses) as a prophylactic antibiotic to prevent surgical site infections in low-risk patients undergoing LC. 217 patients included in the study were randomly divided into two Groups (106 each),5 were excluded from the study because of conversion of laparoscopic to open cholecystectomy: Group A: patients received intravenous Cefuroxime (1.5gm three doses) within 30 minutes prior to incision,12 hours post-operatively and 24 hours post-operatively and Group B: received no antibiotic. All patients were invited for examination 7th and 28th post-operative days and any post-operative complications were recorded and managed.

Conclusion

Pre-operatively; there was no significant differences existed between the 2 Groups regarding sex, age, body mass index and ASA score. Also, the duration of LC surgery, incidence of intra-operative gallbladder perforations and spill of bile or stones, incidents of intra-operative bleeding from either cystic artery or gall bladder liver bed and mean post-operative hospital stay were found not significantly different between the 2 Groups. Post-operatively there was no statistical difference regarding the surgical site infection between the two groups. Hence prophylactic antibiotics do not reduce the risk of infective complications in patients undergoing laparoscopic cholecystectomy in low risk group of patients.

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