

Prophylactic Antibiotic in Elective Laparoscopic Cholecystectomies: Is it Mandatory?

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Abstract

Background: Prophylactic Antibiotics is an efficient tool in reduction of surgical infection. One of the most prevalent surgeries in laparoscopic field is laparoscopic cholecystectomy (LC). Still the role of prophylactic antimicrobial in elective LC with low risk patients is unclear.

Aim of Study: This research was undertaken to evaluate the efficacy of prophylactic antibiotics in reducing surgical site infection (SSI) in elective LC.

Patients and Methods: During the period from November 2019 to November 2021, A randomized double-blind controlled trial was conducted in gastrointestinal and laparoscopic unit, Tanta University Hospital. Elective cholecystectomy for low risk patients with gall bladder stones were randomized into two groups. Group A patients received single dose of 1 gram of Ceftriaxone as a prophylactic antibiotic at induction of anesthesia while group P patients received a placebo of 10 ml isotonic sodium chloride. All patients were followed-up for 30 days.

Results: No significant difference were found between both groups in the percentage of superficial site infection (A versus P: 4 (2.1%) versus 8 (4%) $p=0.271$). In both groups, no cases was presented with deep site infection as sub-phrenic collection or distant infection in form of urinary tract infection or pneumonia.

Conclusion: Based on our findings, no role was found for prophylactic antibiotic in reducing the rate of surgical site infection for low risk cases who underwent elective LC.

Key Words: Prophylactic antibiotics – Surgical site infection.

Introduction

PREVENTION of postoperative infection is a fundamental agent in improving the outcome of surgical procedure. Administration of prophylactic antimicrobials is a process to prohibit postoperative infection and sepsis [1].

Prophylactic antimicrobial is considered as one of the most significant measures to decrease the rate of post-operative infection. These prophylaxis is specific to clean-contaminated and contaminated surgical interventions and in several clean interventions with implants, previous treatment with immunosuppressive and dangerous operations as cardiac or neurosurgery [2].

LC is the first modality for treatment of gall bladder stones over open cholecystectomy because of less morbidity and mortality, less intensity of pain, reduce extent of the hospital stay, minimize full cost of the surgical intervention and less chance for postoperative sepsis [3]. The rate of post-operative infection is very low (0.4-6.3%) in comparison to open maneuver (1-21%) [4] as the laparoscopic management is associated with small size wounds and less tissue injury [5].

This high rate of infection with open maneuver was decreased to (3-7%) by usage of prophylactic antibiotics [4], therefore, these antimicrobials are routinely used. However, the utilization of prophylactic antibiotics in minimal invasive maneuver remain vague in spite of its popularity [6].

In 2019 Barmhall et al., stated that perfect prophylactic antimicrobial should be cheap, well tolerated, disinfectant and covers the most organisms that may cause SSI with sufficient concentration all over the intervention [7].

SSI is categorized in to superficial, deep and organ/space according to the depth of affected tissue [8]. Infectious complications were explained by classic signs of local or systemic manifestations: temperature $>37.8^{\circ}\text{C}$ (not in the first day of surgery), tachycardia, signs of wound inflammation with or without purulent discharge [9].

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SSIs had many factors as: Firstly, the quantity of contamination of the bacteria during surgical intervention. Secondly, the time span of the intervention and lastly, related previous co-morbidities as immunosuppression, diabetes mellitus and mal-nourishment [10].

Aim of the work:

The aim of this study was to evaluate the necessity of prophylactic antimicrobial on prevention of SSI in low risk patients with elective LC.

Patients and Methods

Study design:

This was a prospective, randomized, double blinded, controlled trial on 392 eligible low risk surgical patients with symptomatic gall bladder stones and was scheduled for elective LC from November 2019 to November 2021 in gastrointestinal and laparoscopic unit, General Surgery Department, Tanta University.

Study population:

I- Inclusion criteria:

Low risk surgical patients underwent LC older than 18 years.

II- Exclusion criteria: (High risk patients):

Age less than 18 years or more than 75, LC as a part from another intervention, DM, hemodialysis, child C liver disease, ASA score equal or more than 3, allergy to ceftriaxone, Common bile duct or intrahepatic biliary stones, conversion to open maneuver, previous biliary tract surgeries or ERCP in the last week, acute cholecystitis in last 6 months and cholangitis or obstructive jaundice or biliary pancreatitis.

Blinding and allocation:

Patients were allocated randomly through closed envelopes and the results for every patient were delivered to anesthesiologist reliable for anesthetic maneuver, that gave antimicrobial or not without any awareness of the surgeon. Patients were sectioned into two categories: A (antibiotic group) taken prophylactic ceftriaxone 1gm intravenously at induction of anesthesia, P (placebo group) taken 10ml of normal saline intravenously.

Intervention:

Operations were performed to all patients with reusable laparoscopic instruments that were sterilized by Steranios 2% ECS. The skin was sterilized with a 10% povidone-iodine. Laparoscopic maneuver was performed with 4 - trocar technique.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0 Quantitative data were expressed as mean \pm standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- 1- Independent-samples *t*-test of significance was used when comparing between two means.
- 2- Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters.

Results

A total of 392 cases underwent elective LC in the period from November 2019 to November 2021 were divided into two categories: Antibiotic group (group A, which administered Ceftriaxone 1 gram at induction of anesthesia) and Placebo group (group P, which administered 10ml of normal saline prior to the surgery by the same time).

Out of total 392 patients in this research, 336 (85.72%) were females and 56 (14.28%) males. In group A, 168/192 were women and the rest were men while in the group P 168/200 were females and the rest of this group were males. Age of the patients in this literature ranged from 20 to 72 years with mean age 40.96 years (SD \pm 13.11) in group A while it ranged from 18 to 74 years with mean age 41.88 years (SD \pm 14.13) in group P. With usage of Pearson Chi-Square test, the *p*-value came to 0.504 (not significant).

Mean duration of the surgery was 42.7 minutes in the antibiotic group while it was 44.82 minutes in the placebo group with standard deviation of 14.79 and 19.04 respectively. By utilization of *t*-test for equality, the *p*-value became 0.220 and this difference between both categories was not statistically significant.

From all patients in this study who underwent LC electively. Superficial SSI were happened in 12 (3%) cases. Group A had 4 (2.1%) cases i.e., three in the umbilical port site and one in the epigastric port site while in group P, 8 (4%) cases had superficial SSI i.e., five in the umbilical port site and three in the epigastric port site. No significant difference was observed between both categories according to the issue of superficial SSI with *p*-value = 0.27. No sepsis, urinary tract infection, bronchopneumonia or deep SSI as sub-phrenic collection had occurred in all cases in both groups.

Table (1): Perioperative records.

	Antibiotic	Placebo	t-test	p-value
Age:				
Range	20-72	18-74	0.669	0.504
Mean ± SD	40.96±13.11	41.88±14.13		
Duration of surgery:				
Range	21-88	18-91	1.229	0.220
Mean ± SD	42.70±14.79	44.82±19.04		
BMI:				
Range	22-47	22.5-39	1.100	0.272
Mean ± SD	29.38±4.96	28.89±3.70		
			X2	p-value
Sex:				
Male:				
N	24	32	0.980	0.322
%	12.5%	16.0%		
Female:				
N	168	168		
%	87.5%	84.0%		
Abdominal Scars:				
No:				
N	88	116	5.905	0.052
%	45.8%	58.0%		
Infraumbilical:				
N	100	80		
%	52.1%	40.0%		
Supraumbilical:				
N	4	4		
%	2.1%	2.0%		
Result:				
Easy:				
N	136	124	3.422	0.064
%	70.8%	62.0%		
Difficult:				
N	56	76		
%	29.2%	38.0%		
Hospital stay:				
1 day:				
N	184	184	2.504	0.114
%	95.8%	92.0%		
2 days:				
N	8	16		
%	4.2%	8.0%		
Superficial infection:				
No:				
N	188	192	1.213	0.271
%	97.9%	96.0%		
Yes:				
N	4	8		
%	2.1%	4.0%		

Table (2): Surgical site infection (SSI).

	SSI infection		t-test	p-value
	No	Yes		
Age:				
Range	18-74	55-73	6.889	0.001*
Mean ± SD	40.63±12.99	66.67±8.63		
Duration of surgery:				
Range	18-91	31-91	0.025	0.980
Mean ± SD	43.53±16.59	51.67±29.06		
BMI:				
Range	22-47	24-31	1.233	0.281
Mean ± SD	29.18±4.40	27.60±2.74		
			X2	p-value
Sex:				
Male:				
N	56	0	2.063	0.151
%	14.7%	.0%		
Female:				
N	324	12		
%	85.3%	100.0%		
Abdominal Scars:				
No:				
N	200	4	2.246	0.325
%	52.6%	33.3%		
Infraumbilical:				
N	172	8		
%	45.3%	66.7%		
Supraumbilical:				
N	8	0		
%	2.1%	.0%		
Result:				
Easy:				
N	252	8	0.001	0.980
%	66.3%	66.7%		
Difficult:				
N	128	4		
%	33.7%	33.3%		
Hospital stay:				
1 day:				
N	356	12	0.807	0.369
%	93.7%	100.0%		
2 days:				
N	24	0		
%	6.3%	.0%		

Discussion

Antimicrobial overuse raises the cost of this type of intervention with many complications as Clostridium Difficile infection, allergic reaction that may reaches the level of anaphylaxis and the most serious complication is methicillin resistant Staphylococcus Aureus (MRSA) [11,12]. In 2014, Graham and his colleges reported that more than twenty thousand doses and greater than one hundred thousand sterling pound could be saved every year in England and Wales if there was a change in the

behavior of the laparoscopic surgeons and started to follow the guidelines in low-risk patients with absence of any morbidities [13].

Although in 2008 the Scottish Intercollegiate Guideline Network (SIGN) published that use of antimicrobial as a prophylaxis in low risk cases was forbidden, [11] thirty six percent of the surgeons still use antibiotics with increasing its dose in patients with co-morbidities. In 2010, Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Advocated that precautionary

antibiotics were reserved only for patients with co-morbidities with no rule for these prophylactics in routine patients [14].

As stated by Italian and British group in 2000, the low rate of infection following laparoscopic intervention can be assigned to early mobility of the patients, insignificant damage caused by surgery, faster restarting of the eating and keeping away from using antimicrobial prophylactically [15,16]. In 2004, Colizza and their colleges published that crucial complications related to infection such as sub phrenic abscesses, acute pancreatitis and leakage of bile attributed to practical issues as delicate surgical intervention rather than prophylactic antibiotics [17].

The superficial SSIs rate for LC has been described ranged from 0.4% to 6.3% [18] and it was very low in the comparison with open maneuver. [19]. Our result display that the rate of SSI post elective LC in low risk group was 3.06% for all candidates of this study, 2.1% for the antibiotic group and 4.0% for the placebo group that mean there was no considerable difference in the rate of the infection between both groups. No recorded cases presented with deep infection, sepsis and distant infection like pneumonia or urinary tract infection. Though prophylactic antimicrobials is considered as the main protocol in the open intervention to decrease the rate of SSI, its utilization in laparoscopic maneuver is still controversial.

Similar to our study, British group in 2000 published a prospective randomized trial about prevention of wound infection in elective LC and divided the population of this trial in two groups one received antibiotic prophylaxis and the other one removing the specimen by Endopouch. They found that all infection occurred in extracting port site equal in both groups. They concluded that prophylactic antimicrobial has no role in reducing the rate of infection as they discovered that all isolated microorganisms acting as a source of infection were commensals at the skin port site alternative to colonized diseased specimen [16].

Identical to our result, a group from Thailand in 2004 published a prospective randomized double-blind controlled trial on 299 scheduled cholecystectomies not only for low risk group but also for high risk category, they found that the difference between both groups was not statistically significant ($p=0.512$) [20]. Also, In 2008, a meta-analysis performed by Choudhary and his colleges on nine Randomized controlled trials (RCTs) stated that no better outcome was noted with patients receiving

prophylactic antimicrobial in comparison with who did not take any prophylaxis previous to LC [6].

In 2010, cochrane review performed by Sana-bria and his colleges said that no role of prophylactic antimicrobial in reducing the rate of both SSI and extra abdominal infection with elective LC in low risk group while it should be limited only for high risk patients [21]. A review of literature performed in 2021 by Shyam et al., concluded that the racehorse in reducing the rate of infection post elective LC in low risk cases was skin antiseptic rather than single dose antibiotic. Although prophylactic antibiotic once may not influence the cost or causing any resistance to the antibiotic, but cumulatively for all cases with low risk for infection post-operative they trusted that it would be a great load economically and non-essential wasting of the time of paramedical personnel [22].

Opposite to the current study, Japanese group in 2014 published a randomized controlled trial on 1037 patients who underwent elective LC comparing two groups (antibiotic and non-antibiotic) according to appearance of SSIs, distant infections and total infections. They found that all three types of infections were significantly less in antibiotic group in comparison with non-antibiotic group ($p=0.001$, $p=0.0004$ and $p=0.0001$) respectively. They also stated that hospital stay after intervention and medical costs during staying in the hospital were significantly lower in antibiotic group ($p=0.01$ and $p=0.047$) consecutively [23].

Contrary to our result, Chinese group in 2016 conducted a meta-analysis comparing prophylactic antibiotic and placebo in low risk patients who were scheduled for LC. This meta-analysis was conducted 5207 patients and included twenty one RCTs. They found that rate of SSIs and total infections were significantly lower with prophylactic antibiotic in comparison with placebo ($p=0.001$ and $p=0.001$). Also, they stated that hospital stay postoperatively were significantly lower in prophylactic antimicrobial group ($p=0.008$) [24].

Also, In 2018, Korean group published a systemic review and meta-analysis on 12121 patients in 34 studies comprising twenty eight RCTs, three retrospective and three prospective stated that antibiotic single dose prior to surgery help to decrease the rate of SSI ($p=0.003$) and superficial SSI ($p=0.002$) without any efficacy in reducing the rate of deep SSI ($p=0.98$) [25].

Conclusion:

In summary, the prophylactic antibiotics is not recommended in scheduled LC in low risk patients

as it hasn't any advantage in reducing risk of SSIs. Limited usage of prophylaxis help in decreasing the chance of occurrence of bacterial resistance and making laparoscopic intervention less expensive that reduce the economic burden especially in third world countries.

Limitations of this study:

Limitations of this study represented in small number of patients and this study was not a multi-centric study as it was limited to our department also the high risk patients was not assessed in our study as the study conducted on low risk cases also many factors not indulged in this work as gall bladder perforation during intervention.

Conflict of interest:

No conflict of interest has been declared.

Authors' contribution:

All authors had equal role in design, work, statistical analysis and manuscript writing.

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هل للمضاد الحيوى الوقائى فى حالات استئصال المرارة بالمنظار الزامى؟

المقدمة : منع الالتهاب البكتيرى الناشئ ما بعد الجراحة أمر أساسى لتحسين النتائج ما بعد الجراحية والتي تعتمد بشكل أساسى على استخدام المضادات الحيوية لتقليل نسب العدوى البكتيرية.

استئصال المرارة بالمنظار الجراحى فى حالات حصوات المرارة لهل اليد العليا حالياً على التدخل الجراحى التقليدى نظراً للآتى:

- قلة معدل حدوث المشا كل والوفيات بعد الإجراء الجراحى.
 - تقليل نسبة الالم الناشئ عن التدخل الجراحى.
 - تقليل فترة الاقامة بالمستشفى مما يقلل من النفقات الخاصة بالإجراء الجراحى وتقليل فرصة العدوى البكتيرية الناتجة عن التدخل الجراحى.
- باستخدام المضادات الحيوية فى التدخل الجراحى التقليدى تضاعلت نسبة العدوى لتصبح من إلى وبالرغم من شيوع استخدام هذه المضادات الوقائية فى حالات استئصال المرارة بالمنظار الجراحى الا أن دوره ما زال مجهولاً.

الفرض من البحث : تقييم ضرورة استخدام المضاد الحيوى الوقائى فى منع حدوث جميع أنواع الالتهابات البكتيرية فى حالات استئصال المرارة بالمنظار فى المرضى نوى معدلات الخطرة القليلة.

الاستنتاج : النهائى المضادات الحيوية الوقائية ليس لها أى دور فى تقليل معدلات العدوى البكتيرية المصاحب لاستئصال المرارة بالمنظار الجراحى. تقنين استخدام هذه المضادات يقلل من فرص حدوث المقاومة للمضادات الحيوية ويقلل من النفقات المصاحبة لهذا الاجراء وخاصة فى الدول النامية بالعالم الثالث.