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Post-Operative Infection Rate Between Single Dose Versus Multiple Dose Antibiotic Therapyin Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Objective: To compare the frequency of post-operative infection rate between single dose versus multiple dose antibiotic therapy in patients undergoing laparoscopic cholecystectomy.

Study Design: Comparative prospective study.

Place and Duration of Study: Surgical Department, Combined Military Hospital, Lahore Pakistan from Oct 2017 to Feb 2020.

***Methodology*:** Patients of both genders undergoing laparoscopic cholecystectomy for simple cholelithiasis were included. Group-A patients underwent laparoscopic cholecystectomy using single-dose prophylactic antibiotic therapy with 2-gram 3rd generation cephalosporin at the time of induction of anaesthesia. In contrast, Group-B patients underwent laparoscopic cholecystectomy using 2-grams of 3rd generation Cephalosporin intravenously at the time of induction of anaesthesia followed by intravenous 1-gram Ceftriaxone two doses 12 hours apart. All patients were followed up on the first post-operative day, and then 1-week and 2-week follow up were done for any surgical site infection.

Results: Patients in Group-A had a mean age of 37.12±6.53 years, while patients in Group-B had a mean age of 37.74±6.40 years. The post-operative infection rate in Group-A (single dose antibiotic therapy) was seen in 08 (4.28%), while in Group-B (multiple dose antibiotic therapies) was seen in 18 (9.63%) patients (p-value = 0.042).

Conclusion: This study concluded that the single-dose prophylactic antibiotic is as good as multiple-dose antibiotic therapy used as prophylaxis for the prevention of post-operative infection rate among patients with cholecystectomy done via the laparoscopic method.

Keywords: Antibiotic, Laparoscopic cholecystectomy, Surgical site infection.

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INTRODUCTION

Gallstones disease or cholelithiasis affects about 10% to 15% of the adult population of the world. Cholelithiasis was once considered a disease of the western population, but now it is becoming prevalent in developing countries due to changes in food habits.[1] In most cases, gall stones do not cause symptoms and are detected incidentally during an abdominal ultrasound.[2]

Several surgical procedures have been introduced for gallstone disease since the mid of the last century. The introduction of minimally invasive Laparoscopic cholecystectomy in 1989 increased the number of people undergoing gall bladder removal surgery manifolds.[3] Cholecystectomy has been a routinely performed procedure in surgical departments worldwide. The laparoscopically done procedure has become the gold standard and a popular alternative to open cholecystectomy in benign gallbladder diseases like cholelithiasis.[4]

Surgical site infections (SSIs) remain a common cause of various complications in the modern era. These infections are the third most common hospital-acquired infections and constitute 1/5th of all health-care associated infections. These surgery-related infections may pose a burden on the health system, hospitals and the patients and may lead to serious health-related consequences as well. Secondly, the injudicious use of antibiotics has also been related to many problems for patients and systems and plays a major role in multidrug-resistant bacteria. Over the past few years, emphasis has been laid on using fewer and single-dose antibacterial medications in order to avoid non-judicious use of antibiotics in surgical patients.[5]

In 2013 all the relevant organizations in the USA reached a consensus regarding the use of antibiotics in surgical patients and advocated the use of Cephalosporins as prophylactic antibiotics. The reason is that they are safe, effective, non-toxic, and have excellent antimicrobial activity and good tissue penetration.[5] Sutariya *et al*. in their study, revealed that the

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rate of SSI in the single dose Group was 4.4%, whereas that in the multiple-dose prophylactic antibiotic Group was 3.3%. This difference was statistically significant, suggesting that both single or multiple-dose antibiotics have been equally effective in terms of rate of post-operative SSI.[6] similar to findings by Kumar *et al*.[7] However, these findings were contrary to the study by Abro *et al*. concluded that multiple doses of antibiotics should be used instead of single-dose antibiotic prophylaxis to prevent surgical site infections. The incidence between single versus multiple dose Groups was 9.6% versus 6.7%, respectively (p=0.004).[8]

The objective of this study was to determine the efficacy of single-dose prophylactic antibiotic therapy against the practice in vogue in our hospital of using multiple-dose antibiotic therapy, which will help reduce the costs of antibiotics as well as avoid adverse side effects associated with antibiotic use and will also reduce the development of resistant strains.

METHODOLOGY

This Comparative prospective study was conducted at Surgical Department, Combined Military Hospital, Lahore, from October 2017 to February 2020. The sample size was calculated using the WHO sample size calculator using anticipated population propor-tion-1 = 9.6%,[8] and Anticipated population proportion-2 = 3.3%6. Therefore, the minimum sample size in each Group was calculated as (n) = 187 patients. A total of 374 patients were recruited for the study after calculating the sample size. Non-probability, consecutive sampling was used to gather the sample for this study.

A total of 374 patients from Combined Military Hospital, Lahore Pakistan, were admitted to surgical wards undergoing elective laparoscopic cholecystectomy for gallstone disease who met the inclusion and exclusion criteria and were enrolled in the study after taking permission from the hospital ethical review committee (IREB letter no.175/2020). In addition, written informed consent was taken from patients included in the study.

Inclusion Criteria: Patients of both genders undergoing elective standard 4-port laparoscopic cholecystectomy between 20 to 60 years with uncomplicated cholelithiasis were included in the study.

Exclusion Criteria: Patients with multiple co-morbid, Ca gall bladder, complicated cholelithiasis and ASA IV & V were excluded from the study.

The lottery method was used for randomization and dividing the patients into two Groups. Group-A patients were undergone laparoscopic cholecystectomy using single-dose prophylactic antibiotic therapy with 2-gram 3rd generation Cephalosporins at the time of induction of anaesthesia. In contrast, Group-B patients were undergone laparoscopic cholecystectomy using 2-grams of 3rd generation cephalosporin intravenously at the time of induction of anaesthesia followed by intravenous 1-gram Ceftriaxone two doses 12 hours apart. Operative times of all the patients were recorded, and postoperatively, all the patients were observed for post-operative infection. All patients were followed up on the first post-operative day, and then 1-week and 2-week follow-up was done for any SSI. Patients developing a fever, port-site redness and tenderness, wound discharge, wound gape, and wound abscess was considered SSI. Data in both Groups was recorded on a predesigned proforma.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Mean and standard deviation were calculated for the quantitative variables, i.e., age. Qualitative variables like gender were measured in terms of frequency percentages. The chi-square test was used to compare the infection rate in a single dose and multiple dose antibiotic Groups. The p-value of ≤0.05 was taken as significant.

RESULTS

A total of 374 patients were included in the study, 287 (76.74%) were female, and 87 (23.26%) were males. The mean age of all the study participants was 37.55±6.43 years, with Group-A patients having 37.12±6.53 years and Group-B having 37.74±6.40 years. The mean BMI was 29.26±2.41 kg/m^2. The post-operative infection rate in Group-A (single dose antibiotic therapy) was seen in 08 (4.28%), while in Group-B (multiple dose antibiotic therapies) was seen in 18 (9.63%) patients, as shown in Table-I (p-value = 0.042).

Table-I: Comparison of Frequency of post-operative Infection rate between Single Dose Versus Multiple Dose Antibiotic Therapy in Patients Undergoing Laparoscopic Cholecystectomy (n=374)

		Group- A (n=187)	Group- B (n=187)	p-value
		n(%)	n(%)	
Post-Operative Infection Rate	Yes	08 (4.28)	18 (9.63)	0.042
	No	179 (95.72)	169 (90.37)	

Association of post-operative infection rate with res-pect to age and gender was shown in Tables-II & III, respectively.

Table-II: Post-operative Infection rate with respect to Age(n=374)

Age of Patients (Years)	Group- A (n=187)		Group- B (n=187)		*p*-value
	Post-operative infection rate		Post-operative infection rate		
	Yes n(%)	No n (%)	Yes n(%)	No n(%)	
20-40	04 (2.13)	127 (67.9)	12 (6.4)	119 (63.6)	0.039
41-60	04 (2.13)	152 (81.3)	06 (3.2)	50 (26.7)	0.508

Table-III: Post-operative Infection rate with respect to Gender(n=374)

Gender	Group- A (n=187)		Group- B (n=187)		*p*-value
	Post-Operative Infection Rate		Post-Operative Infection Rate		
	Yes n(%)	No n(%)	Yes n(%)	No n(%)	
Male	01 (0.53)	42 (22.45)	03 (1.6)	41 (21.9)	0.317
Female	07 (3.74)	137 (73.3)	15 (8.1)	128 (68.4)	0.073

Association of post-operative infection rate with respect to BMI and ASA status was shown in Tables-IV & V, respectively.

Table-IV: Post-Operative Infection rate with respect to Body Mass Index(n=374)

Body Mass Index (kg/m²)	Group- A (n=187)		Group- B (n=187)		*p*-value
	Post-Operative Infection Rate		Post-Operative Infection Rate		
	Yes n(%)	No n(%)	Yes n(%)	No n (%)	
≤ 27	02 (1.06)	55 (29.41)	07 (3.7)	55 (29.4)	0.317
>27	06 (3.2)	124 (66.3)	11 (5.8)	114 (60.9)	0.073

Table-V: Post-Operative Infection Rate with Respect to ASA Status(n=374)

Asa Status	Group- A (n=187)		Group- B (n=187)		*p*-value
	Post-Operative Infection Rate		Post-Operative Infection Rate		
	Yes n (%)	No n(%)	Yes n(%)	No n(%)	
I	01 (0.53)	78 (41.7)	04 (2.13)	74 (39.5)	0.168
II	05 (2.7)	74 (39.5)	11 (5.8)	69 (36.8)	0.120
III	02 (1.06)	27 (14.4)	03 (1.6)	26 (13.9)	0.640

DISCUSSION

This is the era of laparoscopic surgery because its minimally invasive approach causes less trauma to the patients. Patients with any health-related condi-tions or doing any difficult jobs may undergo this type of surgery and recover in less time than the conven-tional methods. Surgical site infections have always been a problem for surgeons after surgery involving any body part. Patients can have increased morbidity and mortality after the surgery if they suffer from infections.[9]

Surgical site infection may ruin all the hard work done by the surgeon during the surgery. Multiple studies have concluded that prophylactic antibiotic use has not effectively prevented surgical site infections.[10-13] Multiple factors should be considered in order to find the right antibiotic to be used for surgical site infections. Targeted therapy with the safety of the patient in terms of side effect profile should be the most important consideration. Single antibiotic with a long half-life and minimum effective dose and dosing schedule may be the best option in most cases where appropriate.[14]

We conducted this study to compare the frequency of post-operative infection rate between single dose versus multiple dose antibiotic therapy in patients undergoing laparoscopic cholecystectomy. The age range in this study was from 20 to 60 years, with a mean age of 37.55±6.43 years. The mean age of patients in Group-A was 37.12±6.53 years, and in Group-B was 37.74±6.40 years. The majority of the patients, 262 (70.05%), were between 20 to 40 years of age. Out of these 374 patients, 287 (76.74%) were female, and 87 (23.26%) were males, with a male to female ratio of 1:3.3.

Post-operative infection rate in Group-A (single dose antibiotic therapy) was seen in 08 (4.28%) while in Group-B (multiple dose antibiotic therapies) was seen in 18 (9.63%) patients (*p*-value = 0.042). The study by Sutariya *et al*.[6] revealed that the rate of SSI in single dose Group was 4.4%, whereas that in the multiple-dose prophylactic antibiotic Group was 3.3%, and the rate of infection in both the Groups was found to be statistically insignificant suggesting that single-dose antibiotic is as effective as multiple-dose antibiotics in terms of rate of post-operative SSI,[6] Similar to findings by Kumar *et al*.[7]

In a study by Gallaghar *et al*. patients receiving multiple-dose antibiotics had slightly fewer infection rates than patients with single-dose antibiotics. However, the cost of multiple-dose antibiotics was six times higher than the cost of single-dose antibiotics.[14] Keeping in view their results and then our analysis, developing countries like ours need to quantify the risk versus benefit ratio in order to device local guidelines regarding prophylactic use of antibiotics in surgical procedures especially minimally invasive surgeries like laparoscopic cholecystectomy.

Nooyen *et al*. compared single and multiple doses for a three-day antibiotic course and found no statistically significant difference in preventing post-surgical infections.[15] Eduardo *et al*. studied more than 1000 patients and concluded that single-dose antibiotic has been equally effective as multiple-dose to prevent surgical site infections among patients undergoing

cardiothoracic surgery.[16] Abro *et al*. in a local study, summarized findings different from those mentioned earlier studied and concluded that multiple-dose antibiotics are more effective than singledose antibiotics in preventing surgical infections.[8]

Kufman *et al*. long ago, 184 conducted randomized controlled trials with gentamycin versus placebo. Gentamycin was given as a single dose and had a clear advantage over placebo for preventing surgical site infections.[17] Single dose of antibiotics emerged as equally effective, more cost-friendly, well tolerated and a preferred option as compared to multiple dose antibiotics in minimally invasive surgeries like laparoscopic cholesystecotmy.[18]

Meijer *et al*.[19] conducted a randomized, controlled, double-blind, multicenter trial, and they did not find any significant difference between the one-dose and multiple dose regimens in preventing post-operative wound infection. However, Waldvogel *et al*.[20] have suggested that SSI may be found even in clean surgery as numerous microbial factors play a role, and antibiotic prophylaxis for not more than 24 hours is sufficient to prevent it as the critical period for the development of infection is short. Therefore, the unnecessarily long post-operative antibiotic regimen should be avoided, and hospital costs should be lowered with single-shot antibiotics in clean and clean-contaminated surgeries.

CONCLUSION

This study concluded that the single-dose prophylactic antibiotic is as good as multiple-dose prophylactic antibiotic therapy in preventing post-operative infection rates in patients undergoing laparoscopic cholecystectomy.

Conflict of Interest: None.

Author's Contribution

RH:, MM: Conception, design analysis, interpretation of data, MRH:, MKT, AW, AE, ZK, SAR: Design analysis, interpretation of data.

REFERENCES

1. Tanaja J, Lopez RA, Meer JM. Cholelithiasis. [Updated 2020 Mar 4]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020.[internet] available at: https://www.ncbi.nlm.nih.gov/books/NBK470440/.
2. Dincel O, Goksu M, Hatipoglu HS. Importance of routine histopathological examination of a gallbladder surgical specimen: Unexpected gallbladder cancer. J Cancer Res Ther 2018; 14(6): 1325-1329. doi: 10.4103/0973-1482.187301.
3. Di Ciaula A, Portincasa P. Recent advances in understanding and managing cholesterol gallstones. F1000 Res 2018; 7(1): F1000-F1529. doi: 10.12688/f1000research.15505.1
4. Coccolini F, Catena F, Pisano M, Fagiuoli S, et al. Open versus laparoscopic cholecystectomy in acute cholecystitis. Systematic review and meta-analysis; Int J Surg 2015; 18 (1): 196-204.
5. Bratzler DW, Dellinger EP, Olsen KM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Heal Pharm 2013; 70(3): 195–283. doi: 10.2146/ajhp120568.
6. Sutariya PK, Thekdi PI. Single dose versus multiple dose prophylactic antibiotic in laparoscopic cholecystectomy: a comparative study Int Surg J 2016; 3(2): 633-636. doi: http://dx.doi.org/10.18203/2349-2902.isj20161135.
7. Kumar A, Patodia M, Pandove PK, Sharda VK, Pahwa S. Role of Antibiotic Prophylaxis in Laparoscopic Cholecystectomy: A Randomized Prospective Study. Ann Hepatobiliary Pancreat Surg 2013; 26(4): 209-211.
8. Abro AH, Pathan AH, Siddiqui FG, Syed F, Laghari AA. Single dose versus 24 hours antibiotic prophylaxis against surgical site infections. J Liaquat Uni Med Health Sci 2014; 13(1): 27-31.
9. Wolford HM, Hatfield KM, Paul P. The projected burden of complex surgical site infections following hip and knee arthroplasties in adults in the United States, 2020 through 2030. Infect Control Hosp Epidemiol 2018; 39(10): 1189-1195. doi: 10.1017/ice.2018.184.
10. Borchardt RA, Tzizik D. Update on surgical site infections: The new CDC guidelines. JAAPA 2018; 31(4): 52-54. doi: 10.1097/01.JAA.0000531052.82007.42.
11. National Collaborating Centre for Women's and Children's Health (UK). Surgical Site Infection: Prevention and Treatment of Surgical Site Infection. London: RCOG Press; 2008 Oct. [internet] available at: https://pubmed.ncbi.nlm.nih.gov/21698848/ # article-details.
12. Collins CR, Wick EC. Reflections on the Complexity of Surgical Site Infection Prevention and Detection from an Organizational Lens. Surg Infect (Larchmt) 2019; 20(7): 577-580. doi: 10.1089/sur.2019.135.
13. National Collaborating Centre for Women's and Children's Health (UK). Surgical Site Infection: Prevention and Treatment of Surgical Site Infection. London: RCOG Press; 2008, [Internet] Available at: https://pubmed.ncbi.nlm.nih.gov/21698848/# article-details.
14. Gallagher M, Jones DJ, Bell-Syer SV. Prophylactic antibiotics to prevent surgical site infection after breast cancer surgery. Cochrane Database Syst Rev 2019; 9(9): CD005360. doi: 10.1002/14651858.CD005360.pub4.
15. Nooyen SM, Overbeek BP, De la Riviere A, Storm AJ, Langemeyer JJ. Prospective randomized comparison of single-dose versus multiple-dose cefuroxime for prophylaxis in coronary artery bypass grafting. Eur J Clin Microbiol Infect Dis 1994; 13(2): 1033-1037. doi: 10.1007/BF02111823.
16. Eduardo T, Javier G, Santiago F, Bouza JME, Alvarez FJ. Comparative study of single-dose and 24-hour multi-ple dose antibiotic prophylaxis for cardiac surgery. J Thorac Cardiovasc Surge 2008; 136(3): 1522-1527. doi: 10.1016/j.jtcvs. 2008.05.013
17. Kaufman Z, Engelberg M, Eliashiv A, Reiss R. Systemic prophylactic antibiotics in elective biliary surgery. Arch Surg 1984; 119(1): 1002-1004. doi:10.1001/archsurg.1984.01390210006002
18. Shah YD, Thekdi PI, Raut S, Patel KG. Single shot versus multiple shot antibiotic therapy in patients undergoing laparoscopic surgery: our experience. Int J Res Med Sci 2013; 1(1): 252-256.doi:10.5455/2320-6012.ijrms20130818
19. Meijer WS, Schmitz PIM. Meta-analysis of randomized, controlled clinical trials of antibiotic prophylaxis in biliary tract surgery. Br J Surg 1990; 77(3): 283-290. doi: 10.1002/bjs. 1800770315.
20. Waldvogel FA, Vaudaux PE, , Lew PD. Perioperative antibiotic prophylaxis of wound and foreign body infections: microbial factors affecting efficacy. Rev Infect Dis 1991; 13(Suppl-10): S782-S789. doi: 10.1093/clinids/13.supplement_10.s782.