ORIGINAL ARTICLE

Comparison between one and Two Days Treatment with Intravenous Cefuroxime in Laparoscopic Cholecystectomy

RIZWAN AHMAD KHAN[1], FAREEHA KHALIQ KHAN[2],' SHAUKAT RABBANI[3]

ABSTRACT

Aims: To determine the effectiveness of cefuroxime prophylaxis in controlling the postoperative wound infection in laparoscopic cholecystectomy and to compare single day and multiple (two) days antibiotic prophylaxes by means of hospital stay and cost effectiveness.

Methods: 220 patients of laparoscopic cholecystectomy were studied. Patients were divided into two groups A and B comprising of 103 and 117 patients respectively. Group A was treated with three IV doses of cefuroxime 750mg tid. starting from 30 min before surgery and then oral therapy of 250 mg cefuroxime bid for 5 days was given. Group B received total six IV doses of cefuroxime 750mg t.i.d and then shifted to oral therapy for four days. Resultant observations were analyzed by Chi square test.

Results: In Group A, 5(4.85%) and in group B 19(7.69%) patients developed surgical site infections. Mean hospital stay of group A and group B was 2.14 and 2.21 days respectively. Overall cost effectiveness of group A is almost two times less than Group B.

Conclusions: From our study, it is concluded that the risk of post-operative wound infection in laparoscopic cholecystectomy can be effectively managed by one day t.i.d treatment of cefuroxime which has the benefit of patient compliance and less hospital stay of patient as well as is cost effective and ultimately increases the availability of health care provider and hospital bed for patients.

Keywords: Laparoscopic cholecystectomy, antibiotic prophylaxis, Cefuroxime, surgery

INTRODUCTION

Gall stones are very common with a prevalence of 10%[1]. Although the aphorism that gall stones arise in fat, fair, and fertile female in their forties, often holds true, stones can affect patients of all ages and both sexes. However, they are two to four times more common in women. Cholecystectomy is a procedure now commonly done by laparoscopic means and with the mortality well below 1%. In acute cholecystitis, cholecystectomy may be done early within 48 hours of the onset of symptoms either as a standard policy to avoid recurrent attacks of cholecystitis or because symptoms and signs have failed to resolve. Other surgeons routinely operate later (some 4-6 weeks after an attack). Operation in the interim period may be difficult because of inflammatory adhesions[1].

The infection is an invasion of the body by different microbial agents including virus, worms, bacteria, protozoa and fungi and various toxins produced by these pathogens and their reactions. These can enter in the body by many routes including topical route like animal bite or insect bite, can be transmitted sexually, by inhalation or by ingestion. Although significant methods have been developed for inhibiting and treating infectious diseases, still such transmissions remain a major cause of sickness and death, chiefly in regions of poor nutrition and sanitation[2]. Approximately 16 million different operative procedures are performed in the United States yearly[3] and recent study showed that Surgical site infections (SSIs) were the common healthcare-associated infection, accounting for 31% of all Hospital acquired infections (HAIs)[4]. According to the data of national healthcare safety network (NHSN) for period of 2006-2008 an overall SSI rate of 1.9% (16,147 SSIs from 849,659 operative procedures) was observed[5].

In order to minimize the incidences of postoperative wound infections the use of antimicrobial agents as a prophylactic measure is a common practice. Patients undergoing for surgical procedures in which the infection rate and consequences of infection are serious should receive preoperative antibiotics[6]. Such kind of treatment, rather than prophylaxis, is indicated for surgical procedures allied with evident preexisting infection (i.e., pus, necrotic tissue or abscess)[7].

Cephalosporins are preferred first line agents for many surgical procedures. This group has the capability to target the probable pathogens that may cause the infection. The use of broad-spectrum

[1]*Department of surgery, Shalimar hospital/ Shalimar medical & dental college, Lahore, Pakistan.*
[2]*Department of gynecology & obstetrics, Fatima Memorial Hospital, Shadman, Lahore Pakistan.*
[3]*Department of surgery, Lahore medical and dental college Correspondence to Dr. Rizwan Ahmad Khan, Assistant Professor, E-mail:drrizkhan@hotmail.com Contact: +92-3224496132*

antimicrobial agents is discouraged because it may lead to the development of antimicrobial resistance.[8] Features influencing the development of SSI's include, host defenses, preoperative care, bacterial inoculums and virulence and intraoperative management. Unluckily, an increasing number of resistant strains like *Candida* species and methicillin-resistant *Staphylococcus aureus* (MRSA) are usually involved in surgical wound infections. For patients who have recently suffered from infection with vancomycin-resistant *Enterococcus* (VRE) or MRSA, prophylaxis with Linezolid, or quinupristin/dalfopristin can be considered[9]. Common Pathogens likely to cause the post-operative infections at surgical site are almost the same as that of described by Chang and his collogues[10].

Random sampling of different SSI of the patients of the hospital showed some of the very common pathogenic strains including *Staphylococcal species, Coagulase negative Staphylococci, Streptococcus pneumonia, Streptococcal spp., Moraxella catarrhalis, Enterobacteriaceae, Haemophilus Influenzae.* Some strains of *Salmonella, Klebsiella, Proteus mirabilis,* and very uncommon *Citrobacter and Shigella species*

The best available and logical choice which is also clinically proved could be a broad spectrum second generation cephalosporin[11]. As for bacterial spectrum of SSI is concern, Cefuroxime which is a broad spectrum 2nd generation cephalosporin is one of the best fit antibiotic[12-13].

METHOD

A quasi-experimental study was conducted in the surgical unit of Shalamar Hospital Lahore from 1st July 2011 to 30th June 2013. Total 220 out of 325 patients without any gender discrimination were included in the study with gall stones.75(23%) patients out of 325 did not have the laparoscopic cholecystectomy, but had open cholecystectomy, that's why excluded from the study. Out of 250 patients with laparoscopic cholecystectomy, 30 patients were not included in the study because of random reasons mentioned in exclusion criteria. Remaining 220 patients were included in study. Patients of age ranging from 16 to 65 years with both genders for elective laparoscopic cholecystectomy were included in the study. Patients with COPD, diabetes, hypertension, hepatitis and jaundice were not included in the study. Similarly the smokers and the patients with the history of fungal skin infection, history of any drug toxicity or drug allergy, chronic renal failure and history of pancreatitis and acalculus cholecystitis were also excluded from the study. All the patients were admitted through the OPD in the surgical ward for laparoscopic cholecystectomy surgery. Permission was taken from the hospital's ethical committee for the study. The patients were thoroughly examined in the wards and all the routine and specific investigations were done to confirm the diagnosis. Detailed informed consent was taken from patient.

Group division: The patients were divided into two groups A & B randomly regardless of the gender and age. Group A comprises of 103 patients and was treated with three I.V doses of 750mg cefuroxime starting from 30 min before surgery and then two more doses with an in-between interval of 8 hours and then oral therapy with 250 mg bid cefuroxime was given for 5 days. Group B comprises of 117 patients and received total 6 IV doses of 750mg cefuroxime with an interval of 8 hours starting from first dose 30 min before the procedure then this group of patients was shifted to an oral therapy of cefuroxime 250 mg bid for four days (Table 3). Patients of both groups were kept under the observation for 48 hours in ward to find any postoperative sepsis or SSI.

Observational parameters: During the stay in hospital, bowel sounds and abdominal tenderness was assessed and recorded regularly, furthermore the body temperature, pulse, respiratory rate and blood pressure of the each patient was also recorded on pre-formed Performa. Then the patients were observed on the 7th, 14th, 28th, day in surgical OPD for fever, wound infection and other complications. The wound infection was characterized into three grades based on the severity (Table 1).

Statistical analysis: The data was collected on a pre-formed Performa and entered into SPSS software version 16 and analyzed. Mean±Standard deviation was calculated for age and hospital stay, frequencies and percentages were calculated for wound infection in both groups as well as the incidence of disease in both gender. To compare the frequency of wound infection in both groups, Chi Square test was used and a P-value < 0.05 was considered significant.

RESULTS

The results revealed that mean age of gall stone patients was 48.33 years with a S.D±10.3 years. Maximum numbers of patients were found in the age group of 46 to 60 years (Fig. 1). In group A, five patients (4.85%) developed SSI while 98 patients had normal wound healing. Three patients developed grade II infection while two patients developed grade III infection (Table 2). In group B, nine patients (6.69%) developed SSI out of which one patient developed grade I infection, five patients developed

grade II infection and three patients developed grade III infection. Upon comparing the results of both groups by applying Chi Square test a value 0.632 was obtained which was insignificant. Mean hospital Stay of Group A was 2.14 days with standard deviation of ±0.63 while mean hospital stay of group B was 2.21 days with standard deviation of ±0.79 (Table 2). In terms of cost effectiveness, including the cost of antibiotics, cost of hospital stay, medication expense and other expenditures at hospital of group B was almost twice as compared to group A.

Table 1: Grades of wound infection

Type of infection	Observations
Grade I	Little flushing and hardness of wound edges for which no intervention is needed
Grade II	Minor serous absolution from wound for which no intervention is needed
Grade III	Palpable and noticeable infection or pussy discharge from wound demanding repeated change of dressings and antimicrobial therapy

Table 2: Data of patients reported with infection

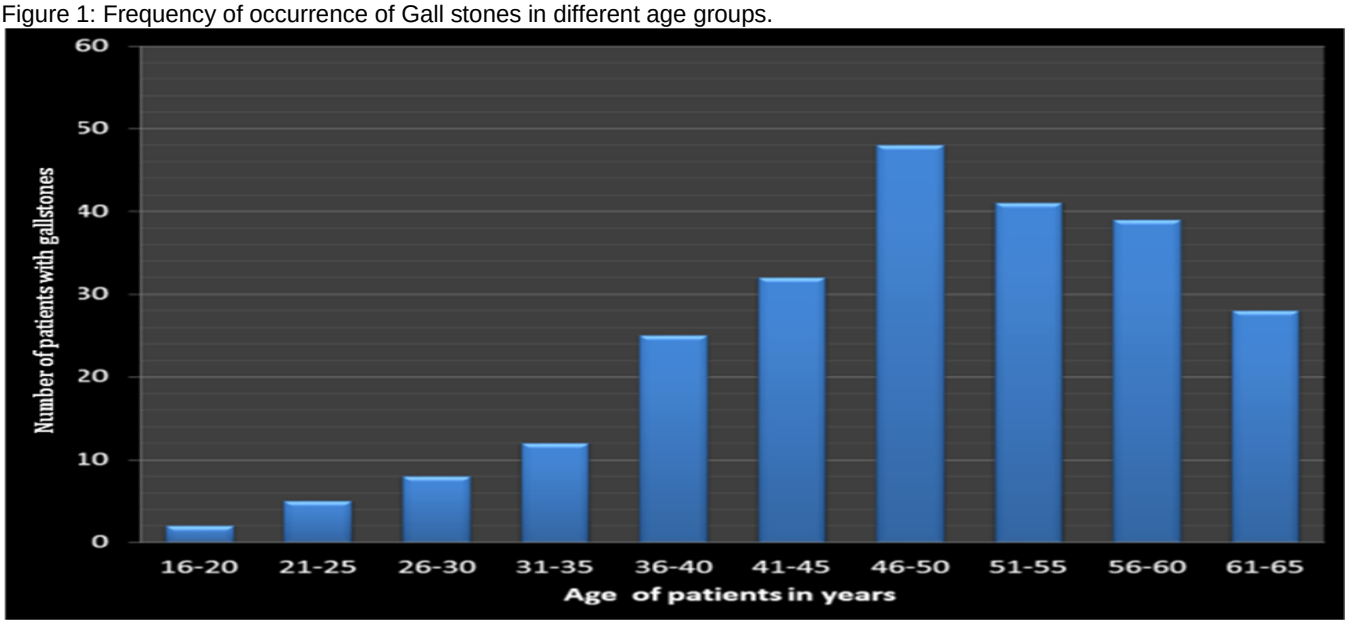
	Group A	Group B
Total patients	103	117
SSI reported	5(4.85%)	9(7.69%)
Grade I infection	0	1
Grade II infection	3	5
Grade III infection	2	3
Mean hospital stay	2.14±0.63	2.21±0.79

Table 3: Dose schedule of 750mg cefuroxime i/v and subsequent oral treatment with 250mg bid in both groups.

	Group A	Group B
1st dose	30min B.S.	30min B.S.
2nd dose	7.5-8.0 Hours A.S.	7.5-8.0 Hours A.S.
3rd dose	15.5-16 Hours A.S.	15.5-16.0 Hours A.S.
4th dose	Shifted to oral therapy of 250mg Cefuroxime bid	23.5-24.0 Hours A.S.
5th dose		31.5-32.0 Hours A.S.
6th dose		41.55-42.0 hours

B.S=Before Surgery, A.S=After Surgery, Pt.=Patient.

Figure 1: Frequency of occurrence of Gall stones in different age groups.



DISCUSSION

Gall stone is a very common problem all over the world, and present differently, ultimate treatment is surgery.[1] Laparoscopic cholecystectomy is very common elective procedure in general surgery. On an average annual admission with gall stones in major cities of Pakistan counts for 9.5-15% of the total Hospital admissions recommended for surgery.

Cephalosporins are preferred first line agents for many surgical procedures that target the most likely pathogens[7]. A study published in 2003 advised 2nd generation Cephalosporins prophylaxis for clean contaminated cases for ultra-short period[14]. Similarly the concept of chemoprophylaxis which is the base of our study is also recommended by the Bowater and his colleagues in the study published in 2009[15].

The results of our study showed that five patients (4.85%) developed wound infection in group A. Among these patients three patients developed grade II infection**,** and two patients developed grade III infection, all the patients in this group were receiving one day intravenous treatment of cefuroxime for prophylaxis. In group B which was

receiving cefuroxime through intravenous route for multiple (two) days for prophylaxis, nine patients (7.69%) developed wound infection. In this group one patient had Grade I infection, five patients had grade II infection and three patients had grade III wound infections. On comparing the results of both groups, the P value had shown statistically insignificant results. Even the group which received less number of intravenous doses showed better results than Group B. Compliance of patients of Group A was also much better than Group B. In a previous study same types of results with single dose of Cefotaxime for cholecystectomy were recorded[16]. Prophylactic use of cefuroxime for clean contaminated surgical procedures is thoroughly studied by Rashid A.S. and his colleagues[17] and documented same types of results even with single dose.

CONCLUSION

From our studies, it is concluded that there is no difference in one day (3 I/V doses) and multiple (two) days prophylaxis with 6 I/V doses of cefuroxime 750mg t.i.d in patients of elective laparoscopic cholecystectomy surgery in terms of post-operative surgical site infection. The risk of post-operative wound infection can be effectively managed by one day t.i.d. treatment prophylactic antibiotic (cefuroxime 750mg) which also has the benefit of cost effectiveness, patient compliance and reduced hospital stay of the patient which increases the availability of health care practitioner and number of beds for patients. Furthermore we recommend large scale multicenter studies in Pakistan to augment our conclusion**.**

Acknowledgements: This study was conducted In Shalamar Hospital with the encouragement of hospital staff and management.

REFERENCES

1. Text book of Clinical Surgery second edition by Henry and Thompson.
2. Nicas M, Nazaroff WW, Hubbard A. towards Understanding the Risk of Secondary Airborne Infection: Emission of Respirable Pathogens". *Journal of Occupational and Environmental Hygiene.* 2005; 2 (3): 143–154.
3. Data from the National Hospital Discharge Survey. Retrieved from http://www.cdc.gov/nchs/data/nhds/4procedures/2010pro_number percntage.pdf. [assessed on January 9, 2013]
4. Magill SS, Hellinger W, Cohen J, Kay R, Bailey C, Boland B et al. Prevalence of healthcare-associated infections in acute care facilities. *Infect Control Hospital Epidemiology.* 2012;33(3):283-91.
5. Yi M, Edwards JR, Horan TC, Berrios-Torres SI, Scott KF. Improving risk-adjusted measures of surgical site information for the National Healthcare Safety Network. *Infection Control Hospital Epidemiology.* 2011; 2(10):970-986.
6. Awad SS. Adherence to Surgical Care Improvement Project Measures and post-operative surgical site infections. *Surgical Infection.* 2012 Aug; 22 .
7. Condon RE, Schulte WJ, Malangoni MA, Anderson-Teschendorf MJ. Effectiveness of a surgical wound surveillance program. *Arch Surg.* 1983; 118: 303-7.
8. Antimicrobial prophylaxis in surgery (clinical practice guidelines). *Can Med Assoc J.* 1994;151(7):925-931.
9. Edwards FH, Engelman RM, Houck P, Shahian DM, Bridges CR. The society of thoracic surgeons practice guidelines series: antibiotic prophylaxis in cardiac surgery, part I: duration. *Annals Thoracic Surgery.* 2006; 81: 397-404.
10. Chang WT, Lee KT, Chuang SC, Wang SN, Kuo KK, Chen JS, Sheen PC. The impact of prophylactic antibiotics on postoperative infection complication in elective laparoscopic cholecystectomy: a prospective randomized study. *Am J Surg*2006;191:721-725.
11. Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the national surgical infection prevention project. *Am J Surg*2005;189:395-404.
12. Gillespie WJ, Walenkamp G. Antibiotic prophylaxis for surgery for proximal femoral and other closed long bone fractures. *Cochrane Database Systemic Review*. 2001;(1): CD000244.
13. Prokuski L. Prophylactic antibiotics in orthopaedic surgery. *J Am Academy Orthopaedics Surgery.* 2008; 16:283-293.
14. Pea F, Viale P, Furlanut MI. Antimicrobial agents in elective surgery: prophylaxis or "early therapy" *J. Chemother*. 2003 Feb; 15(1):3-11.
15. Bowater RJ, Stirling SA, Lilford RJ. Is antibiotic prophylaxis in surgery a generally effective intervention? Testing a generic hypothesis over a set of Meta-analyses. *Ann Surg.* 2009 249(4):551-6.
16. Zahid MA, Bakhsh R, Dar FS, Akhter N, Malik ZI. Comparison of single dose and three dose antibiotic prophylaxis with Cefotaxime sodium in cholecystectomy. *Journal Ayub Medical College Abbottabad.* 2003; 15:38-40
17. Rashid AS, Ahmad AK, Usman MF, Fatima I. Single versus 3-dose antibiotic prophylaxis in clean and clean contaminated operations. *Journal Ayub Medical College Abbottabad.* 2010; 22(4).