

ROLE OF PROPHYLACTIC GATIFLOXACIN IN LAPAROSCOPIC CHOLECYSTECTOMY – A COMPARATIVE STUDY WITH CEFTRIAZONE

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ABSTRACT

Objectives: The objective of this study was to evaluate and compare the effectiveness of gatifloxacin and ceftriaxone as prophylactic antibiotic in elective clean surgical procedures.

Methods: Sixty patients, undergoing laparoscopic cholecystectomy, were recruited consecutively and divided into two groups, that is, Group A and Group B of 30 patients each. In Group A, a pre-operative dose of injection ceftriaxone 1 g was administered intravenously half an hour before induction of anesthesia and second dose was given 12 h postoperatively. In Group B, pre-operative dose of tablet Gatifloxacin 400 mg was administered night before operation and another tablet postoperatively when the patient started orally in the evening. If not accepting orally then single intravenous infusion of Gatifloxacin was given in the evening.

Results: In Group A, one patient (3.33%) had grade 1 and two patients (6.66%) had grade 2 infection. Similarly in Group B, one patient (3.33%) had grade 1 and two patients (6.66%) had grade 2 infection. None of the patients in both the groups had severe post-operative wound infection (grade 3 and grade 4).

Conclusion: Prophylactic gatifloxacin is non-inferior to the “current gold standard ceftriaxone” as far as effectiveness of the drug is concerned. In addition, it had a similar side effect profile and was equally safe as a prophylactic antibiotic in preventing wound infection following routine elective laparoscopic cholecystectomy.

Keywords: Prophylactic antibiotic, Gatifloxacin, Ceftriaxone.

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INTRODUCTION

The study of surgeon's war against wound infection began with Hippocrates (460–370 B.C), though bacteria have infected human being since the origin of mankind. After discovery of penicillin in 1928 by Fleming, a method of removing bacteria that has already colonized the wound become available as a weapon to fight against infection to the surgeon. Subsequently, many other antimicrobial agents were discovered. The relatively newer ones include third-generation cephalosporins and the latest are fourth-generation fluoroquinolones. Nicolas [1] advocated that the first prophylactic dose of antibiotic should be given within 1 h before the operation. Antibiotic prophylaxis has shown to reduce the incidence of wound infection in intra-abdominal surgeries [2], routine surgical cases [3], and in elective laparoscopic cholecystectomy [4-6]. Surgery can now be performed very safely mainly due to advancements in anesthesia, improved surgical techniques, better post-operative care, and potent and advanced antimicrobials. However, post-operative wound infection still remains the most difficult and important problem of current surgical practices [7].

Public Health Laboratory Services of England in 1960 gave an infection rate of 10.30% in a survey of 21 British hospitals. According to Stone *et al.* [8], there are basic factors acting singly or in combination which are responsible for the development of post-operative wound infection. Strict asepsis is an ideal method to prevent post-operative infection that can barely be achieved, because it is impossible to eliminate bacteria completely from surgical environment.

Another way to prevent post-operative infection is use of prophylactic antibiotics [9]. Antibiotic prophylaxis refers to administration of

antibiotic agent to the patient without evidence of established infection with the objective of reducing subsequent post-operative septic complications. Thus antimicrobial treatment which begins before contamination is referred to as prophylaxis.

According to Stone *et al.* [9], and Plock [10], it is an accepted fact that antibiotics level must be present before or within couple of hours of contamination. Prophylaxis was not generally recommended for most clean surgical procedures like laparoscopic cholecystectomy, because post-operative wound infection has been reported in fewer than 3% of operations [11].

Recently, this traditional approach has been challenged. Careful post-operative surveillance has shown in this era of out-patient and short stay surgery and especially in Indian setup (overcrowding, poor hygiene, malnutrition, etc.), about 50% of wound infections are diagnosed after the patient has been discharged from the hospital [12]. Even in clean wounds, the risk of infection varies in patients from <1% to 16% [11].

Drugs to be evaluated for prophylaxis should be safe, potent, newer, non-toxic, cheap, and long acting with complete antimicrobial spectrum and less chances of resistance.

Ceftriaxone, a third-generation cephalosporin, is an ideal antibiotic with minimal side effects. It is a parenteral, broad-spectrum third-generation cephalosporin, and is active against Gram-positive, Gram-negative, and anaerobic pathogens. The antimicrobial activity of the drug is due to inhibition of cell wall synthesis. Peak plasma concentrations are achieved within half an hour after intravenous dose and it exceeds the MIC values of susceptible organisms by many-folds. The elimination half-life is 6–9 h in healthy subjects. It has dual route of

excretion, 45–60% is excreted unchanged in the urine and remainder is secreted in the bile [13]. It has got no significant drug interaction and is generally well tolerated.

Gatifloxacin, a fourth-generation fluoroquinolone, is a relatively newer antibiotic which is increasingly being used as a prophylactic perioperative antibiotic. It is a broad spectrum fourth-generation fluoroquinolone and is active against Gram-positive, Gram-negative, and anaerobic pathogens and the antibacterial activity of gatifloxacin results from inhibition of DNA gyrase and two topoisomerase 4. The drug has a long half-life (8 h), faster and more reliable action, once daily dosing with convenient oral and parenteral dosage forms. The absolute bioavailability of drug is 96%, peak plasma concentration of it usually occurs 1–2 h after oral dose. The drug achieves a peak serum conc. of 3.79 mg/l with single oral dose of 400 mg, which is more than 4 times the MIC level required to eradicate most of common pathogenic organisms. Drug undergoes limited biotransformation in liver and is excreted unchanged primarily by kidneys. It has no significant drug interactions and is generally well tolerated.

The aim of the study was to evaluate and compare the effectiveness of gatifloxacin and ceftriaxone as prophylactic antibiotic in elective clean surgical procedures and reduce the cost of surgery.

METHODS

The present study is a thesis project for the award of Masters in Surgery degree from the medical university. Ethical Committee and Scientific Committee approval was taken and the same was attached to the plan submitted to the University. On completion of the thesis, the same was submitted to the medical University in partial requirement for completion of the degree of M.S. General Surgery.

Sixty patients, undergoing laparoscopic cholecystectomy, were picked up consecutively in Rajindra Hospital, Patiala. A detailed history, clinical examination, and investigations were carried out in all these cases. Cases were allocated at random by computer generated random table into one of the two groups, that is, Group A and Group B.

Group A

This group consisted 30 cases undergoing laparoscopic cholecystectomy, one pre-operative dose of injection ceftriaxone 1 g was administered intravenously half an hour before induction of anesthesia and second dose 12 h postoperatively.

Group B

This group comprised 30 cases undergoing laparoscopic cholecystectomy. One pre-operative dose of tablet Gatifloxacin 400 mg was administered night before operation and another tablet postoperatively when patient started accepting orally in the evening. If not accepting orally then single intravenous infusion of Gatifloxacin was given in the evening. The pre-operative preparation of wound area was the same, that is, shaving the part a night before and washing it with soap and water. Povidine iodine 5% was used as antiseptic solution for preparing the site at the time of operation during the study.

Assessment

The site of wound/port site was inspected 48 h postoperatively and then every day until the removal of stitches. The patients were followed up weekly for 4 weeks for fever and pain in wound/port sites. Severity of wound infection was graded according to Robertson's classification (1958).

Grade 1	Minimal infection – redness about a stitch
Grade 2	Pustule about a stitch or minor infection of wound edges without separation and with no systemic reaction
Grade 3	Frank infection of a relatively small portion of wound with purulent discharge and some systemic reaction
Grade 4	Frank infection usually with systemic reaction or dehiscence of wound

Specimen of pus or wound exudates was taken from infected wounds/port sites and subjected to culture and sensitivity tests and appropriate treatment were started.

In the post-operative period, the side effects of Ceftriaxone/Gatifloxacin were recorded. Observations of Group A and Group B were compared to evaluate the efficacy of prophylactic antibiotics Ceftriaxone and Gatifloxacin in the prevention of post-operative wound infection. At the end, the results were analyzed and compared and available literature on the subject was reviewed.

RESULTS

A comparison of ceftriaxone and gatifloxacin, as observed in the present study, is shown in Table 1. The demographics and baseline characteristics of the two groups were comparable (Table 2). In Group A, one patient (3.33%) had grade 1 and two patients (6.66%) had grade 2 infection. Similarly in Group B, one patient (3.33%) had grade 1 and two patients (6.66%) had grade 2 infection. None of the patients in both the groups had severe post-operative wound infection (grade 3 and grade 4) (Table 3, Fig. 1).

DISCUSSION

Post-operative wound infection seldom causes death, yet it does prove to be an economic burden on the patient due to prolonged convalescence, prolonged hospital stay, additional expenditure, nursing care, and an unnecessary wastage of time.

Despite the increasing awareness regarding asepsis at the time of surgery, post-operative wound infection still continues to mar the result of an excellently performed surgical procedure.

To prevent these complications, trend is now shifting more and more toward prophylactic antibiotics. The infection rate described by different workers all over the world has differed considerably. The

Table 1: Comparison of ceftriaxone and gatifloxacin

Parameter	Ceftriaxone	Gatifloxacin
Mode of administration	Intravenous only	Intravenous and oral tablet
Cost	1 g – Rs 60 only	Tab. –Rs. 5.90 only Infusion Rs. 120 only
Side effects	Skin rash (1 patient only)	Nausea and vomiting (1 patient only)
Infection rate	3 out of 30 patient (10%)	3 out of 30 patient (10%)
Severity of infection	Grade I – 1 patient Grade II – 2 patients	Grade I – 1 patient Grade II – 2 patients

Table 2: Comparison of baseline characteristics between the two groups

Characteristic	Group A	Group B
No of patients	30	30
Males	3	3
Obese	12	10
Surgery duration >30 mins	25	25
Pre-operative stay > 5 days	3	4

Table 3: Comparison of rate of infection and severity of infection between the two groups

	Group A (%)	Group B (%)
Infection rate	3/30 (10)	3/30 (10)
Grade 1 infection	1/3 (33.3)	1/3 (33.3)
Grade 2 infection	2/3 (66.6)	2/3 (66.6)

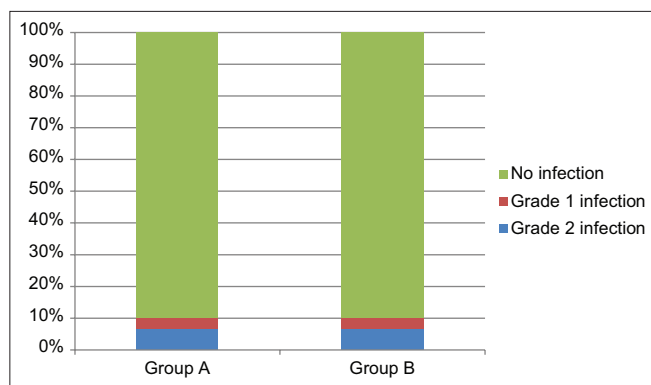


Fig. 1: Comparison of rate of infection and severity of infection between the two groups

variations in infection rate are due to different criterion for selection of patients, grading of infection, and antibiotics chosen.

The aim of the study was to evaluate and compare the effectiveness of gatifloxacin and ceftriaxone as prophylactic antibiotic in elective clean surgical procedures and reduce the cost of surgery. None of the patients in both the groups had severe post-operative wound infection (grade 3 and grade 4); however, in Group A, one patient (3.33%) had grade 1 and two patients (6.66%) had grade 2 infection. Similarly in Group B, one patient (3.33%) had grade 1 and two patients (6.66%) had grade 2 infection. None of these patients required any additional systemic antibiotic therapy and were managed successfully with local wound care.

The results were similar to study conducted by Colizza *et al.* [14], in which ceftriaxone was confirmed as the gold standard in biliary tract surgery. Ultra-short prophylaxis was enough in most cases. In their study, the authors had 4 complications (1.8% of 217 laparoscopic cholecystectomies), two of which were minor (infection of the umbilical access by *S. aureus*) and two major (1 biliary fistula [accessory duct] and 1 acute pancreatitis), both treated conservatively.

Similarly in another study by Kellum *et al.* [15] the authors concluded that a single pre-operative dose of ceftriaxone was as effective as multiple perioperative doses of cefazolin in the prophylaxis of infection associated with biliary tract surgery.

For decreasing the incidence of post-operative wound infection, it is, therefore, recommended that antibiotics should be commenced preoperatively, observing the basic principles of surgery such as complete asepsis, gentle tissue handling, and clean sharp dissection. Post-operative antibiotics for prolonged periods have no role in preventing wound infection in clean elective surgical procedures. There is not only increase in cost of treatment, but also increased incidence of toxicity and more likelihood of emergence of resistant strains of bacteria.

A Canadian study published in the New England Journal of Medicine in March 2006, claimed that gatifloxacin can have significant side effects including dysglycemia [16]. In view of this side-effect, some countries banned the systemic use of gatifloxacin, although it is still permitted in the topical form. The study was conducted at the time systemic gatifloxacin was not banned. The authors are of the view that in-patients who are given prophylactic gatifloxacin-one dose preoperatively and one dose postoperatively – are at least risk of side-effects and their sugars can be easily monitored. Gatifloxacin offers a cheap and effective alternative to ceftriaxone in resource-limited facilities, wherever the systemic use is permitted.

CONCLUSION

It is, hereby, concluded that prophylactic gatifloxacin is non-inferior and safe prophylactic antibiotic in preventing wound infection

following routine elective laparoscopic cholecystectomy as compared to ceftriaxone.

AUTHORS CONTRIBUTION

Anjna – Designing the study, collecting data, and analyzing the data. Tanveer Singh Kundra – Writing the manuscript. Jaspreet Kaur – Writing the manuscript. Lalit Kumar Garg – Analyzing the data.

CONFLICTS OF INTEREST

Nil declared by all authors.

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