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Is ceftriaxone being better broad spectrum antibiotic than cefotaxime, as prophylactic drug in abdominal surgeries - a randomized, prospective double-blind study

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Abstract

Although ceftriaxone and cefotaxime are highly effective third generation cephalosporins antibiotics, only few studies have compared their prophylactic efficacy, current study compares their prophylactic efficacy in abdominal surgeries.

Methods: A randomized, prospective double-blind study of 250 patients undergoing abdominal surgery, the prophylactic use of ceftriaxone and cefotaxime were compared. Intravenous cephalosporin 3rd generation were given dose of 1 g, was given at induction of anaesthesia, with intravenous metronidazole (500 mg), also being given for colorectal surgery. Data was statistical analysed at significance level of $p>0.05$ with 80% power of the study.

Results: Out of 250 patients 120 (48%) were given drug A (cefotaxime) and 130 (52%) were given drug B (ceftriaxone). Both male (55.2%) and female (44.5%) participants were in two arms. Operation category major surgeries was 54.16% and intermediate surgeries was 45.83% in two groups. This difference was mainly due to appendectomies, which were analysed separately and so do not confound the overall results of the study. Difference in the wound microbiology was done to staphylococcus aureus, epidermidis and species. In the group of cefotaxime 22 were staphylococcus aureus, 8 staphylococcus epidermidis and 4 were staphylococcus species. In the group of ceftriaxone 7 cases staphylococcus aureus, 2 staphylococcus epidermidis and 3 were staphylococcus species. The wound infections were 44 in cefotaxime group and 26 in

ceftriaxone group. Over all wound infection rate was 17.6% with cefotaxime and 10.4% with ceftriaxone.

Conclusions: Ceftriaxone may be more empirical having the additional benefits of reducing postoperative infections, being less dependent on desacetyl as an adjunct and providing a more effective prophylactic cover against microbes.

Keywords: Abdominal surgeries, Broad spectrum antibiotics, Cefotaxime, Ceftriaxone.

Introduction

Infections are more common in surgical procedures if standard operating procedure (SOP) is not followed. Infections, that are of critical importance to surgeons are of three types. First, some established infections may require operative treatment. Second, surgeon may be called on to treat infections that have been arisen from previous operations, Third, appropriate prophylaxis can prevent operative infections results from contamination at surgical field. The omission of anti-microbial prophylaxis, can result in development of surgical site infections 40 to 60% of upper gastrointestinal tract, haemorrhage exhibit post-operative wound infections when prophylactic anti-microbial was not used [1]. The appropriate use of antimicrobial agents may reduce post-operative complications and surgical site infections [SSI] [2]. Prophylactic use of anti-microbial agents may be useful in reducing SSI and other distant infections [3]. Gram positive, gram negative organisms and enterobacteria play an important role in surgical site infections. Staphylococci, on other hand found on the skin may end up infections in soft tissues, bones and joints. Many localized infections are caused by mixed populations of bacteria. Even when the organs have been isolated and identified it is always not clear which species are truly pathogenic and which are commensurate or contaminate [4]. A surgical infection can be fatal, if not treated by empirical therapy. Calculated antibiotic therapy may help to choose the antimicrobial drugs based on the spectrum of pathogens [5,6]. Current study demonstrates the efficacy of 3rd generation cephalosporin ceftriaxone over cefotaxime in treatment of surgical site infections when administered as a prophylactic drug in abdominal surgeries.

Materials and Methods

A total of 250 patients admitted into a general surgical unit of Surabhi Institute of Medical sciences and hospital, Siddipet, Telangana, for acute and elective open abdominal surgery were studied over a period of 18 months (2019-20) in a randomized, prospective, double-blind study. Patients aged 20 years and above over who met the conventional standards of antibiotic prophylaxis for their surgery were recruited for the study. Using a blocked randomized technique with stratification, the patients recruited to study were grouped into antibiotic A group and antibiotic B group. The “colorectal” stratification included all colorectal surgery and stomal surgery and the “noncolorectal” stratification included hepatobiliary, oesophageal-gastric duodenal surgery, small bowel surgery, appendicectomy, splenectomy and vascular surgery. 1gm of intravenous cephalosporin (cefotaxime and ceftriaxone) were given at induction of anaesthesia for all abdominal surgery asper protocol, intravenous metronidazole 500 mg, was also given at induction for those in the “colorectal” stratification. The identity of antibiotic A and antibiotic B was kept unknown until the completion of the study. Patients with active infections taking antibiotics prior to surgery and showing allergy to cephalosporin or metronidazole are excluded from the study to avoid the bias. The

institution's ethics committee approved the study and obtained written consent from the participants.

All patients were reviewed at a minimum of 30 days postoperatively, either as an inpatient or as an outpatient in surgical OPD. The surgical audit was done to ensure that all infections were included in the final study. Good laboratory practice (GLP) and Standard operating procedure (SOP) were followed to avoid the laboratory and operation theatre contamination. Wound swabs were cultured aerobically only, unless the Gram stain was consistent with an anaerobic or polymicrobic infection. Specimens from "deep" and sterile sites were cultured aerobically and anaerobically. Identification of Gram negative aerobic and facultative anaerobic bacilli was done by using a modified agar dilution, replica-plating method. Sensitivity testing of most aerobic pathogens was done by agar-dilution method, Himedia agar (Himedia laboratories) was used for the replica-plating method, except for methicillin sensitivity when Mueller-Hinton agar was used. Other aerobic organism sensitivity testing was performed by disc sensitivity. Drugs used in this study was of make Cipla as to maintain the proportion of drugs.

Statistical analysis: The study designed to test for 5% ($p<0.05$) of difference in infection rates between the two treatment groups, with a confidence Interval of 95% and with a power of 80%. Using a chi-square analysis with a two-tailed alternative hypothesis a sample size of 250 was used in both arms of the trial. Yates' correction and a two-tailed Fisher's exact test were used to correct for small numbers. The analysis was performed by using GraphPad prism version 6 (USA) and Microsoft excel.

Result

Out of 250 patients 120 (48%) were given drug A (cefotaxime) and 130 (52%) were given drug B (ceftriaxone). Mean and SD age of study participants was 49.9±21.5 in drug A group and 51.6±21.1 in drug B group. Both male (55.2%) and female (44.5%) participants were in two arms (Figure 1). Operation category major surgeries was 54.16% and intermediate surgeries was 45.83% in two groups. Patient and demographic data (Table 1) were comparable except that by chance cefotaxime was used more in both nonelective surgery and intermediate surgery. This difference was mainly due to appendectomies, which are analysed separately and so do not confound the overall results of the study. Difference in the wound microbiology was done to staphylococcus (aureus, epidermidis and species). In the group of cefotaxime 22 were staphylococcus aureus, 8 staphylococcus epidermidis and 4 were other staphylococcus species. In the group of ceftriaxone 7 cases staphylococcus aureus, 2 staphylococcus epidermidis and 3 were other staphylococcus species. The wound infections were 44 in cefotaxime group and 26 in ceftriaxone group. Over all wound infection rate was 17.6% with cefotaxime and 10.4% with ceftriaxone (Table 2).

Figure 1: Distribution of male and females in study participants

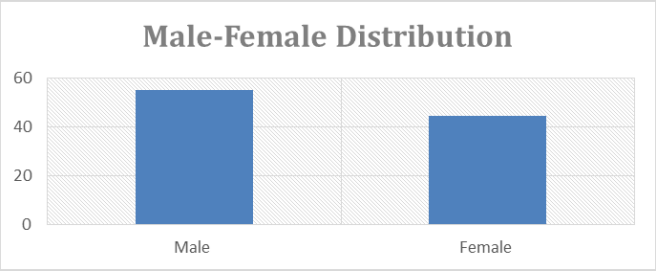

Table 1: Demographic and operative data of study participants

Drug Number of patients		Drug A group (Cefotaxime) (120)	Drug B group (Ceftriaxone) (130)	Total (250)	Total %
Age (Mean±SD)		49.6±21.5	51.6±21	250	100
Sex	Male	63 (52.5%)	75 (57.69%)	138	55.2
	Female	57 (47.5%)	55 (42.30%)	112	44.8
Operation category	Major surgeries	65 (54.16%)	76 (58.46%)	141	56.4
	Intermediate surgeries	55 (45.83%)	54 (41.53%)	109	43.6
Wound category	Clean	46 (38.33%)	47 (36.15%)	93	37.2
	Contaminated	66 (55%)	78 (60%)	144	57.6
	Dirty	08 (6.66%)	05 (3.84%)	13	5.2
Gastrointestinal anastomosis		45 (37.5%)	50 (38.61%)	95	38
Drains		15 (12.5%)	20 (15.38%)	35	14

Data presented as Mean±SD for age, % for all other parameters.

Table 2: Cultures of wound swabs from operative cases collected from study participants

Parameter	Cefotaxime	Ceftriaxone
Wound	44	26
Cultures	44	26
Microbe(staphylococcus)		
Aureus	20	06
Epidermidis	04	02
Species	04	00

Two-tailed chi-square test and two-tailed Fisher's exact test. P =0.01.

Table 3: Combined infections of study participants

Parameters	Cefotaxime	Ceftriaxone	p-Value
Infections (including other)	43	23	=0.01
Peritoneal and Distant	62	42	=0.002
Chest and urinary	40	20	=0.05

two-tailed chi-square test with yate's correction. P value >0.05.

Discussion

Cefotaxime and ceftriaxone are two injectable third generation cephalosporins commonly used in clinical practise as prophylactic measures to avoid bacterial infections and septicaemia. Despite of their similar spectrum of action they have different pharmacokinetic properties. Both of these antibiotics were effective as prophylactic agents in wound infection similar to that previously reported [7]. An interim analysis showed when these antibiotics are used as prophylactic measure

in an appendectomy has shown satisfactory results when cefotaxime is used alone as prophylactic drug and our study is in contradiction with this study. Previous studies by Lumely and Lung demonstrated the effectiveness of ceftriaxone alone is more effective and supports our study [8,9]. Cefotaxime combined with the desacetyl have shown better results in a vitro studies than when it is given single drug [10]. The better performance of ceftriaxone was because of its excellent TPI (tissue penetration index) and long life, in spite of differences in invitro activity. Although the overall frequency of wound infection was similar in both the groups, after the abdominal surgeries specially in appendectomy, further differences were observed in the frequency of organisms isolated and in the severity of infection [11] and we concluded the same in our study.

Microbes such as Staphylococcus aureus was more frequently isolated with cefotaxime and Staphylococcus epidermidis with ceftriaxone. It is difficult to eradicate Staphylococcus epidermidis present on the skin. Its presence in wound infections suggests that it may have the ability to colonize wounds when other bacteria are inhibited with the use of broad-spectrum antibiotics. Ceftriaxone was also effective in reducing the frequency of some infections, raises the possibility of being prophylactic antibiotic and play a greater role in prevention of wound infection alone. Previous studies demonstrated that use of ceftriaxone has reduced chest and urinary tract infections alone [12,13]. Animal and clinical studies have shown inconsistent results on anastomotic infections, possibility of an anastomotic infection resulting in an increase in collagenolytic activity [14,15] but animal and clinical studies have given inconsistent results [16]. The differences in anastomotic morbidity was probably due to chance of differences in blood supply and surgical technique, our study supports further evaluation of anastomotic infection with the use of ceftriaxone alone on its effects on anastomotic collagenase activity.

Prophylactic antibiotics optimal effectiveness should be at therapeutic tissue concentration at the time of bacterial contamination. Ceftriaxone with an excellent TPI and long half-life, results in a therapeutic tissue concentration, which is greater than that of cefotaxime [17] and is sustained for 24 hours [18]. On effectiveness of ceftriaxone in our study supports previous studies in eradication of bacterial effectiveness and minimization of bacterial synergism [19]. The bacterial contamination may occur within the first 24 hours of the completion of surgery. A reduced cough reflex, shallow breathing, and atelectasis may contribute to early postoperative colonization of the respiratory tract. Impaired emptying of the bladder and catheter trauma may also contribute to postoperative urinary tract infection [19]. The sustained antimicrobial cover given by a single intravenous dose of ceftriaxone may therefore contribute to reduce the incidence of postoperative infections remote to the wound.

Limitations of study: There were certain limitations with our study being a cross sectional study and both of the injectable drugs used were from same maker. More studies are warranted with larger sample size in elective surgeries with use of same drug combination from different makers.

Conclusion

Current study demonstrate the efficacy of third generation cephalosporin ceftriaxone on cefotaxime and may be better prophylactic antibiotic to be injected before surgeries as later is need to be given with desacetyl combination in abdominal surgeries.

Author's contribution- Dr. Vijayakumar has formulated the hypothesis, Dr. Mujahid Mohamed executed, statistical analysis and methods, Dr. Shobha Mohammed helped in writeup and Dr.CH BS Srinivas reviewed the article.

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