

COMPARISON OF SINGLE DOSE PROPHYLACTIC ANTIBIOTICS VERSUS FIVE DAYS ANTIBIOTIC IN CESAREAN SECTIONZeel Shah¹, N. S. Kshirsagar², Shikha Shah³**HOW TO CITE THIS ARTICLE:**

Zeel Shah, N. S. Kshirsagar, Shikha Shah. "Comparison of Single Dose Prophylactic Antibiotics versus five days Antibiotic in Cesarean Section". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 12, March 24; Page: 3123-3129, DOI: 10.14260/jemds/2014/2254

ABSTRACT: AIMS AND OBJECTIVES: To compare if single dose antibiotic is as effective as multiple doses in prevention of post-operative infection in caesarean section. To compare the cost effectiveness of drugs in both the groups. **MATERIAL AND METHOD:** This prospective randomized controlled study was carried out to evaluate the effectiveness of single dose antibiotic versus multiple doses in caesarean section. The study population consisted of 600 patients that were randomly allocated to single or multiple dose groups. All potentially infected cases were excluded from this study. All patients received inj Cefotaxime IV half hour before surgery. In addition the multiple dose group received antibiotics for five days post-operatively. Each patient in the study was observed till discharge for presence of any morbidity like endometritis, urinary tract infections, and wound infections. **STATISTICAL ANALYSIS:** Fischer exact test, unpaired t test used for analysis. **RESULTS:** There was no statistically significance in the rate of infections in both the groups. The rate of febrile morbidity, endometritis, urinary tract infection and wound infections were statistically not significant. However the difference in cost of antibiotic in both the groups was significant. **CONCLUSIONS:** Single dose antibiotics are effective as multiple doses in prevention of post-operative infections in caesarean sections Careful periodic surveillance of antibiotic prophylaxis is necessary to detect the emergence of drug resistant strains of bacteria in our institution because it caters to the needs of local population.

KEYWORDS: Cesarean section, prophylactic antibiotics, cefotaxime, infectious morbidity.

INTRODUCTION: Since the introduction of the first antibiotic, the risk of serious postoperative infections with associated morbidity and mortality has led the clinicians to use these agents for prophylactic purposes rather than depending upon their efficacy for the treatment of established infections.¹ There is an increase in the incidence of cesarean delivery and is the most commonly performed major surgical procedure.² Cesarean delivery is the most important factor associated with post-partum infection, and carries a 5-20 fold increased risk of infection compared with vaginal delivery.^{3,4} It is recommended that prophylactic antibiotic should be administered prior to surgical incision to reduce surgical site infections.⁵ Cochrane database of systemic reviews, The American College of Obstetrics and Gynecologists (ACOG) and the CDC recommend narrow- range first generation cephalosporin, like cefazoline, to be administered after the umbilical cord clamping for the prophylaxis against post – caesarean delivery.^{6,7}

The use of first generation cephalosporin such as cefazoline provides activity against Ureaplasmas and Mycoplasma but may cause and increase in the resistant organisms like anaerobes.^{8,9} Hence, there is rationale for adding agents such as metronidazole, clindamycin or azithromycin to extend the cover. Four RCT'S compared use of narrow range antibiotic prophylaxis with broad spectrum antibiotics regimens.¹⁰⁻¹³ compared narrow range with broad spectrum

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regimens. Broad spectrum were associated with a statistically significant reduction in infection rates,¹⁰ Cefotaxime a third generation cephalosporin, has been clinically useful in obstetrics and gynecology by virtue of its broad –spectrum coverage.

Post-operative infections comprise a major portion of morbidity experienced in obstetrics. Hence, increased cost of medical care and the increased demand of hospital beds have given added impetus to search for new methods to decrease post-operative morbidity and shorten the duration of hospital stay. The present study was conducted to compare the infectious morbidity with single dose and multiple dose antibiotics and assess the cost effectiveness.

METHODS: All the patients received inj cefotaxime half hour before cesarean section in addition to that the multiple dose group received inj cefotaxime till patient was nil by mouth followed by T Cefixime 200 mg till 5 days. The single dose group received the injection pre-operatively only.

Patient selection: All patients undergoing emergency and elective caesarean section at Krishna hospital.

Exclusion criteria:

- Patients known to be hypersensitive to Cefotaxime
- Diabetes, heart disease, pre mature of membranes, ante partum hemorrhage

Patient evaluation: The primary outcome measure was the incidence of febrile morbidity, defined as an oral temperature of >38 C on two occasions at least four hours apart, excluding the first 24 hours; it can be due to post-operative infection, which includes endometritis (fever, uterine tenderness, foul smelling lochia), wound infection (fever, cellulitis, exudates), pelvic abscess, peritonitis, urinary tract infections, chest infections.

Once febrile morbidity was identified, women were examined thoroughly to localize the potential source of infection. Urine analysis and total white blood cell count was done. Patients with superficial wound infections were treated with dressing only and deep ones were treated with dressing and resuturing. Antibiotics were added according to culture sensitivity. All patients were followed up to 7 days and discharged if no complications.

Ethics: The study received ethical clearance from the committee of research at Krishna hospital.

Statistical analysis: The data obtained were analyzed using descriptive statistics. Fischer exact test and unpaired t tests were used.

RESULTS: Six hundred subjects were enrolled in this study from May 2011 to May 2013. Demographic data are presented in table 1. Statistical analysis of the variables listed confirmed comparable groups. The most common indication for abdominal delivery was previous LSCS and most patients underwent emergency section. The statistical analysis of the two antibiotic regimens did not demonstrate any statistically significant differences in the post-operative morbidity or endometritis.

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Eleven of 300 patients (3.6%) in the single dose group developed febrile morbidity versus four patients (1.3%) in the multiple dose group. There was no significant difference in endometritis (4.3% in single dose group versus 3.6% in multiple dose group) and wound infections (5.6% in single dose group and 4.6% in multiple dose group), the p value ranging from 0.1 to 0.8. Patients with endometritis and wound infections were treated with additional antibiotics like inj ceftriaxone, inj amikacin, inj gentamycin, tab ciprofloxacin, tablet norfloxacin.

The average duration of hospital stay in both the groups was the same. However the cost of antibiotics was statistically significant in the two groups. The average cost in the single dose group was Rs 31 while in the multiple dose was Rs 240 with p value of 0.0001.

VARIABLES	SINGLE DOSE	MULTIPLE DOSE
Age (yr.)	24 +/- 4.1	25.7 +/- 5.3
gravidity	2.1 +/- 1.2	1.9 +/- 1.2
Registered patients	252	249
Emergency section	265	259
Elective section	35	41
Indications		
Prev LSCS	109	95
Oligohydraminos	38	41
Fetal distress	32	32
Pre eclampsia	42	40
Breech	34	23
others	45	69

TABLE 1: Demographic variables for the study population

VARIABLE	SINGLE DOSE (N=300)	MULTIPLE DOSE (N=300)	P VALUE
Febrile morbidity	11(3.6%)	4(1.3%)	0.1139
Endometritis	13(4.3%)	11(3.6%)	0.835
Urinary tract infection	7(2.3%)	5 (1.6%)	0.7721
Wound infection	16(5.6%)	14(4.6%)	0.8578
Other antibiotics used	44(14.6%)	33(11%)	0.222
Hospital stay	8.2	8.1	0.79
Average cost	31	240	0.0001

Table 2: Post-Operative Complications in the study

DISCUSSION: All patients in the study received antibiotics half hour before surgery and those in multiple dose received additional doses post operatively. In surgical practice there is a considerable variation in the timing of antibiotics. Classen et al have shown that the timing of antibiotic administration was critical in preventing post-operative wound infections.¹⁴ For most surgical procedure it is desirable to administer prophylactic antibiotic pre operatively before tissue injury and bacterial contamination. Subsequently, a retrospective cohort study of 1316 term, singleton cesarean delivery reported on a policy change in timing of antibiotic prophylaxis from post clamping

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to pre incision which resulted in a reduction of 60% in rate of SSI's and a 50% reduction in the rate of endometritis and 80% decrease in cellulitis.¹⁵

Since there is overwhelming evidence for the need and effectiveness of prophylactic antibiotics to prevent infections following cesarean delivery, the current debate focuses on the choice and timing of administration. In our study the incidence of febrile morbidity in the single dose group was 3.6% and in the multiple dose group was 1.3%. Though the incidence is lower in the multiple dose group the association is not significant. In another randomized trial comparing single versus three doses of the same drug as on this study, cefotaxime showed the incidence of febrile morbidity to be 14% in the single dose group and 20% in the three dose group.¹⁶ Hawrylyshyn et al found incidence to be 8.3% in single dose and 12.3% in multiple dose regimen.¹⁷

The incidence of endometritis in this study was 4.3% in the single group and 3.6% in the multiple dose group. Patients with endometritis were successfully treated with either Amikacin or Gentamycin. In a prospective study of 122 patients studied two dose of amoxicillin-clavulanic acid versus three doses of the same had 0% incidence of endometritis in the two dose and 1.6% in the three dose group.¹⁸ In the study by Noyes et al 293 patients received single dose of one of the three drugs cefazoline, ampicillin-sulbactam or cefotan.¹⁹ The incidence of endometritis with cefazoline regimen was 14.3%, with ampicillin –sulbactam was 7.4% and cefotan was 11.1%. The result was that single dose prophylaxis is equally effective as the multiple doses for controlling febrile morbidity.

The incidence of urinary tract infections (UTI) was found to be 2.3% in the single dose group while in the multiple dose group it was 1.6%. In a study by J Shetty et al the incidence of UTI in two dose group was 2% and 1% in the triple dose group.¹⁸ In our study 16 patients in the single dose group (5.6%) and 14 patients in the multiple dose group (4.6%) had wound infections. Only one patient from the multiple dose group had burst abdomen. In the multicentric trials evaluated by Hopkins L, Smail F in the Cochrane review compared various trials that compared different antimicrobial agents, comparison between the routes and the number of doses of drugs given⁶. The table 3 shows comparison of any single dose systemic regimen (pre, post, intra-operative) vs. any multiple dose regimen in terms of wound infections.

STUDY	TREATMENT n/N (%)	CONTROL n/N (%)	PETO ODDS RATIO
Galask	4/162 (6.4%)	4/79 (5%)	0.45
Roex	7/66 (4.2%)	2/72 (2.7%)	3.58
Tassi	3/100 (3%)	1/100 (1%)	2.67
Varner	3/20 (15%)	1/9 (11%)	1.37
Von Mandach	17/536 (3.1%)	20/516(3.8%)	0.81
Jakobi	0/50 (0%)	1/50 (2%)	0.14
Hawrylyshyn	1/64 (1.5%)	1/60 (1.6%)	0.94
Hartert	1/81 (1.2%)	0/58 (0%)	5.56
McGregor	4/46 (8.6%)	4/24 (16%)	0.46
Mc Gregor	5/195 (2.5%)	3/91 (3.2%)	0.76
Parsons	0/90 (0%)	1/62 (1.6%)	0.09
present	16/300 (5.6%)	14/300 (4.6%)	0.857

Table 3: Comparison of wound infections in other studies

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The results indicated that multiple dose does not offer any added benefit when compared with single dose regimen. The incidence of other infections like gastroenteritis and upper respiratory tract infections in the single dose group was 2% and in the multiple dose group was 1.6%. Out of the 600 patients that were studied in this study 44 patients required additional antibiotics in the single dose group while 33 patients required additional antibiotics in the multiple dose group. Patients in the single dose group required more additional antibiotics but the relation was not significant. The average duration of hospital stay in both the groups was same. The duration in the single dose group was 8.4+/- 3.3 days while in the multiple dose group was 8.1+/- 2.9 days. Clarke et al reported post-operative complications added 8.1 days to the duration of hospitalization. In our study also patients with post-operative complications were hospitalized for 12 -16 days as compared to those without complications.

The average cost of antibiotics in the single dose group is Rs 31+/- 100 while in the multiple dose group is Rs 240 +/-107. The association was found to be statistically extremely significant. Thus prolonged administration increases the cost.

Short term administration of antibiotics is as effective as long term administration in surgical prophylaxis.²⁰ In a report describing emergence of resistance to antibiotics; it was found that resistance developed in patients developed who were continued antibiotics for four days postoperatively compared to patients who received three perioperative doses. ²¹This showed that shorter course of antibiotic administration reduced the emergence of resistance. In our study half the patients received five day antibiotics post operatively.

Such prolonged administration may increase the cost, which includes the cost and costs of acquisition and cost of treating post-operative infections related to prophylactic failures related to development of resistance. Use and misuse of antibiotics not only affects individual patient also hospital and community environment. The prophylactic use of antibiotics in surgery may be limited to 1-2 doses of a suitable agent perioperatively and never more than 24 hours. If we can predict and administer additional antibiotic prophylaxis only to those population at high risk majority of the patients would be spared from unnecessary drug administration.

CONCLUSIONS: Pre-operative antibiotic prophylaxis ensures the therapeutic concentration of antibiotic in serum, tissues and wound during contamination. The antibiotic chosen should be active against the bacteria that will be encountered during the surgery. The drug should be administered for the shortest period to minimize the development of resistance. The drug should be safe and economical to the patient. Careful periodic surveillance of antibiotic prophylaxis is necessary to detect the emergence of drug resistant strains of bacteria in our institution because it caters to the needs of local population.

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