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RESEARCH ARTICLE

Single dose single antibiotic versus multiple doses multiple antibiotic prophylaxis in caesarean section, at a tertiary care centre

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ABSTRACT

Background: Surgical site wound infections and associated complications after caesarean delivery are important causes of maternal morbidity, increased duration of hospital stay and cost of treatment. Prophylactic antibiotic usage decreases the risk of these wound infections. Though single dose preoperative antibiotic prophylaxis is advocated, clinicians are hesitant to adopt this regimen due to differences in patient profile and uncertainty about asepsis. **Objectives:** To assess whether single dose pre-incision antibiotic prophylaxis is as effective as multiple doses for routine caesarean sections in a tertiary care centre. **Materials and methods:** This was a quasi-experimental study involving 320 women undergoing caesarean delivery at tertiary care centre. Eligible participants were divided into two groups. Group A received single dose antibiotic prophylaxis of ceftriaxone 1gm intravenously 30-40 minutes before caesarean section and group B received cefotaxime 1g+sulbactam 500mg 30-40 minutes before the caesarean, followed by cefotaxime+sulbactam and ornidazole intravenously for the first 3 post-operative days followed by oral cefixime for the next 5 days. Postoperatively, both groups of patients were followed up for febrile morbidity, infections including urinary, wound, endometritis, and others; and duration of hospital stay. These parameters were compared across the two groups. **Results:** There were 160 patients in each group. Baseline characteristics, indications for caesarean delivery, operative duration and difficulties were similar. Post-operative morbidities like fever (p=0.5) and wound infection (p=1) did not differ significantly. None of the women needed prolongation of hospital stay. **Conclusion:** Preoperative single dose antibiotic regimen was as effective as multiple dose multiple antibiotic regimen prophylaxis for routine caesarean delivery. Judicious use of limited antibiotics should be encouraged to decrease antibiotic resistance, with the added benefit of being economical.

Keywords: Antibiotic prophylaxis, caesarean delivery, infectious complications, single drug, surgical site infection.

Infectious complications after caesarean delivery are an important and substantial cause of maternal morbidity and increase in the hospital stay and cost of treatment. These infectious complications range from the mild to severe, and could sometimes be fatal. These include fever, wound infection, urinary tract infection, endometritis, pelvic abscess, septic pelvic vein thrombophlebitis, sepsis and septic shock [1]. The infection could also spread and result in life threatening peritonitis [2] or rarely manifest as anaesthetic infectious complications like meningitis or encephalitis [3].

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The most important source of microorganisms responsible for post caesarean infection is the genital tract, particularly if the membranes are ruptured. Commonly, culture of an infected wound results in polymicrobial isolation of organisms, which includes E. coli, Staphylococcus aureus, coagulase negative Staphylococci, Group B Streptococcus, other gram negative aerobic rods, Enterococcus faecalis, Gardnerella vaginalis, anaerobes and genital mycoplasma[4, 5].

The goal of administering prophylactic antibiotics is to have therapeutic tissue levels of antibiotic at the time of microbial contamination. Rather than sterilizing the tissue, antibiotic administration before the skin incision is aimed at decreasing the intra operative microbial load, so that the entry of a smaller load of micro-organisms which could occur, can subsequently be managed by the host immune response. This is achieved by giving broad spectrum intravenous antibiotics preoperatively such that peak serum and tissue concentration is achieved within 20 minutes [6]. Delayed administration reduces or eliminates the benefit of prophylaxis. Administration of antibiotics 20-30 minutes before the surgical incision appears to be optimal to maximize tissue and blood concentrations at the surgical site. The antibiotic of choice should be long acting, focused on the bacteria likely to be contaminating the surgical site, cost effective, and have a low incidence of adverse effects [7, 8]. However, there is considerable debate regarding the preferred antibiotic (narrow-spectrum versus broad-spectrum), number of doses (single dose versus multiple dose) and the timing of administration (pre-incision or post – umbilical cord clamping). Another parameter which should be considered is the risk of emerging bacterial antibiotic resistance, which increases with longer use [8, 9].

Several studies have explored these questions and guidelines are in place recommending best practices. Many of the standard guidelines including those by WHO, ACOG, ICMR and NICE, recommend single dose pre-incision antibiotic prophylaxis in uncomplicated caesarean deliveries, most also recommending cephalosporins as the preferred choice [10 - 13]. Despite recommendation by clinical guidelines and though there is enough literature proving the efficacy of single dose of single antibiotic prophylaxis being as effective as prolonged use of combination of antibiotics [14,15] it is not universally accepted and adopted. This may be due to the apprehension of the surgeons pertaining to the differences in patient profile handled or the infrastructure and functioning of the facility at which they serve. Our institution is a tertiary care centre, primarily catering to rural patients belonging to low socio-economic status. This study was undertaken to assess whether single dose pre-incision antibiotic prophylaxis can be proven to be as effective as multiple doses for routine Caesarean sections in such a clinical setting.

Materials and methods

This quasi-experimental study included a subset of the patients who were undergoing caesarean section from March to August 2018 at tertiary care centre, which acts as a referral centre for surrounding villages and mainly serves patients of economically weaker section. Sample size calculation was done using open epi software version 2.3.1. at 95% confidence level, 80% power of the study, according to study conducted by Prathima S [16]. Sample size calculated was 320, with 160 women in each group. Approval for the study was taken from the institutional ethics committee, approval number was SNMC/IECHSR/2017-18/A-55/1.1. The study duration was 6 months.

The antibiotic policy of two units of the OBG department resembled the two arms of the study, with the first unit practising single dose antibiotic prophylaxis and the second unit using multiple dose multiple drug prophylaxis. Patients who were to undergo caesarean section in these units were assessed for eligibility, informed about the study and consented. Exclusion criteria were hypersensitivity to any of the trial drugs, antibiotic administration within the previous 2 weeks, presence of chorioamnionitis, diabetes mellitus (both gestational and pre-existent), HIV/AIDS, tuberculosis, anaemia (Haemoglobin <7 g/dL), rupture of membranes >24 hours, intrauterine fetal death, urinary tract infection and duration of labour >12 hours. By virtue of admission to a particular unit, women were divided into Group A and Group B.

Baseline demographic, medical and obstetric data, including the indication for caesarean delivery was noted. Women in group A received single dose antibiotic prophylaxis with injection ceftriaxone 1gram (g) given intravenously 30-40 minutes before the surgery. Group B received injection cefotaxime 1g + sulbactam 500milligram (mg) intravenously 30-40minutes before the caesarean section, followed by injection cefotaxime 1g + sulbactam500mg and ornidazole 500mg intravenously twice a day for the first 3 post-operative days followed by oral cefixime 200mg twice a day for the next 5 days. Surgical and postoperative complications were noted in both the groups. Intraoperative methods used by different surgeons were noted. Suture material and technique of closure of the

abdomen was documented. All the patients were followed up in the post-operative period for evidence of infectious morbidity. Duration of use of intravenous cannula was noted. The following were recorded: Vital signs and temperature twice daily and abdominal examination once daily to note the size of the uterus and presence of tenderness (Table 1). The wound was inspected on the 4thand7thpostoperative day.

Table 1: Definitions used for outcome measures/ Infectious morbidity

Febrile morbidity	Temperature >38.0°C for ≥ 24 hours, excluding the first 24 hours
Urinary tract infection	5 pus cells per high power field or Positive urine culture, with or without dysuria and fever
Endometritis	Marked uterine tenderness and/or foul smelling vaginal discharge in association with fever

Surgical site infection (SSI) classification per Centre for Disease Control was used in this study. [17]

Superficial incisional SSI - only skin or subcutaneous tissue is involved, treated by antibiotics and dressing.

Deep incisional SSI - deep soft tissue (fascial and muscle layers) involved or occurrence of wound dehiscence managed by secondary suturing.

Organ/space SSI - involves any part of the anatomy (e.g. organs or spaces), other than the incision, that was manipulated or opened during surgery. Managed by exploration and closing.

Evidence of any other infection manifesting in the postoperative period was looked for, investigated and recorded. Use of additional antibiotics other than the antibiotics administered in the study regimen was also noted. Data in the two groups were compared. Statistical analysis was done using SPSS Version 22. Descriptive statistics were represented with percentages, mean and standard deviation. Independent t-test, Mann-Whitney U test, Chi-square and Fisher Exact tests were applied to find the significance. p≤0.05 was considered statistically significant.

Results

A total of 320 cases of caesarean delivery were recruited in this study. There were no differences in patients baseline demographic status. Mean age was 24.79±3.14 years in group A and 24.79±3.41 years in group B (p=0.06). Mean BMI in group A was 23.02±3.27 kg/m^2 and in group B it was 22.63±2.74 kg/m^2 (p= 0.25). Mean gestational age was 38.08±1.38 weeks in group A and 37.76±1.21 weeks in group B. 34.4% (n=55) in group A and 39.4% (n=63) in group B were primigravidae. The indications for caesarean deliveries in the two groups were comparable and are shown in table - 2. Most common indication in both the groups was previous caesarean section.

There was no statistically significant difference across the two groups regarding the number vaginal examinations performed. In both groups around 85% of participants underwent vaginal examination only once or twice. Notable intra-operative findings listed in table 3, were comparable in the two groups. Uterine exteriorisation for repair of uterine incision was done in 18 patients in group A and 12 patients in group B. Vicryl number 1 (Polyglycolic acid) was used in all cases for closing the uterus. Subcutaneous fat approximation was done for 3.8% (n=6) women in both the groups. Subcuticular sutures were used for skin approximation in 13.1% (n=21) patients in group A and 7.5% (n=12) in group B (p=0.14), and mattress sutures were used in the others. In most (92.5%) patients, skin closure was done with non-absorbable suture material, and in 7.5% delayed absorbable suture material was used. There was no difference in the mean operative time in the two

Table 2: Indications for Caesarean section

Indications	Group-A		Group-B	
	Count	%	Count	%
PE/E	5	3.1%	5	3.1%
PROM	7	4.4%	5	3.1%
Abruptio placenta	1	0.6%	1	0.6%
FGR	3	1.9%	4	2.5%
NRFS	21	13.1%	14	8.8%
CPD	12	7.5%	11	6.9%
Failure to progress	4	2.5%	4	2.5%
Maternal request	3	1.9%	5	3.1%
Previous LSCS not willing for VBAC	49	30.6%	65	40.6%
Previous LSCS with scar tenderness	3	1.9%	3	1.9%
Previous 2 LSCS	29	18.1%	8	5.0%
Obstructed labor	5	3.1%	4	2.5%
Malpresentation	2	1.3%	5	3.1%
Others	16	10.0%	26	16.3%

PE/E: Pre-eclampsia,/eclampsia, PROM: Premature rupture of membranes, FGR: Fetal growth restriction, CPD: Cephalopelvic disproportion, LSCS: Lower segment caesarean section, VBAC: Vaginal birth after caesarean delivery, NRFS: Non reassuring fetal status.

Table 3: Notable intra-operative findings

Parameters	Group A (n=160)		Group B (n=160)		p-value
	Frequency	Percentage	Frequency	Percentage	
Difficult extraction	6	3.8%	4	2.5%	0.52
Ascites	5	3.1%	2	1.3%	0.45
Extension of uterine incision	11	6.9%	15	9.4%	0.54
Scar dehiscence	6	3.8%	6	3.8%	1
Uterine rupture	1	0.6%	0	0.0%	1
Low-lying placenta/placenta previa	1	0.6%	1	0.6%	1
Significant adhesions	5	3.1%	8	5.0%	0.57
Distended bladder	3	1.9%	2	1.3%	1
Intra and Post- operative haemorrhage ≥2000 ml	3	1.9%	2	1.3%	1

Table 4: Post-operative morbidity

Parameters	Group A (n=160)		Group B (n=160)		p-value
	Frequency	Percentage	Frequency	Percentage	
Febrile morbidity	3	1.9%	8	4.9	0.13
Endometritis	2	2.5%	0	0.0%	0.49
UTI	1	0.6%	3	1.9%	0.25
RTI	7	4.4%	6	3.8%	0.78
Paralytic ileus	2	1.3%	0	0.0%	0.49

UTI-Urinary tract infection, RTI- Respiratory tract infection

groups. Intravenous cannula was removed after 36 hours in group A, whereas it was removed after 72 hours in group B.

Post-operative morbidities noted are listed in table 4. None of the patients had deep incisional or organ /space SSI. Superficial incisional SSI was seen in 1.9% (n=3) in group A and 2.5% (n=4) in group B (p=0.7). All these seven patients who developed wound infection had had use of non-absorbable mattress sutures. Overall, there was no statistically significant difference in postoperative morbidities in both groups. None of the patients suffered adverse drug effects in our study. Additional antibiotics were given in 2 patients in group A and 5 patients in group B (p=0.28). None of the participants required prolongation of hospital stay.

Discussion

This study proves that single dose pre-incision antibiotic prophylaxis is as effective as multiple drug, multiple dose antibiotic regimen in selected cases of caesarean section at low risk for infection, even in the low socioeconomic rural population served at our hospital. Prophylactic antibiotics have been recommended by many research workers. [6] Shaheen et al compared one day of antibiotic prophylaxis with seven days of antibiotic prophylaxis in elective caesarean sections in Pakistan and found no statistically significant differences in wound infections [18]. In a study by Bhattachan et al in Nepal which included both elective and emergency caesarean sections, wound infection rate was 1% and 0% in single dose and multiple doses respectively. Other studies have also found antibiotic prophylaxis to be effective in both elective and emergency caesarean sections [5, 19]. In our study also, we included both elective and emergency caesarean sections and found no deep incisional or organ /space surgical site infection. Superficial SSI was not significantly different across the groups.

Febrile morbidity in the study by Bhattachan et al was 2% and 6% in single versus multiple doses respectively [20], comparable to our study which had rates of 1.9% and 4.9% respectively. Higher rate of febrile morbidity in multi-dose antibiotic group could be related to a longer duration of retention of the intravenous cannula which would be required for longer administration of intravenous antibiotics. The resultant higher rates of phlebitis could be responsible for more febrile morbidity [21]. The longer use of the IV cannula could also lead to more serious infections gaining an intravenous access directly if asepsis is not maintained while handling. Brood et al reported a lower incidence of urinary tract infections in their study with the single dose regimen [9]. In our study also, postoperative urinary tract infection was seen in 0.6% in group A and 1.9% in group B. This non-significant increase in infections in the multiple dose group could be related to the longer duration of catheterization which is a routine practice in the clinical unit included as group B, rather than the antibiotic regimen. This prolonged catheterisation and increased UTI in group B could also be the reason for increased febrile morbidity. Other factors that have been proposed to potentially affect infectious morbidity are shaving of surgical site, uterine exteriorisation and suturing of subcutaneous tissue. In our study, shaving of surgical site before surgery was done for all the women in both arms. Uterine exteriorisation for closure of the uterus was done in 18 patients in group A and 12 patients in group B. CORONIS study which compared extra-abdominal versus intra-abdominal repair of uterine incision found no significant differences in complication rate and wound infection [22].

According to a cochrane review, subcutaneous tissue closure reduced wound morbidity including hematoma, seroma, wound infection and wound separation [23].In our study, subcutaneous tissue approximation was done for 3.8% (n=6) women in both the groups as per the recommendation that subcutaneous closure is required when subcutaneous tissue thickness exceeds 2cm [24]. Choudhary A et al [25] have reported that skin closure with subcuticular sutures, appears to be superior to closure with mattress sutures with regards to wound outcome. In our study, no wound complication was observed in the cases with subcuticular suture closure as opposed to 4.4% in those with mattress suture closure.

In addition to all the clinical parameters compared in this study, several other factors are also noteworthy. The cost related to antibiotic treatment in the single antibiotic, single dose regimen is approximately INR 70 and that in the multiple antibiotic regimen is INR 1100. In a country like India, where majority of the patients pay out of pocket for health care needs, costs which do not add to quality of health care would burden the common man. In addition, repeated doses of intravenous drugs add to the workload of the health

care personnel and could be responsible for some potential errors in dosing/ drug administration [26].

Strengths and Limitations of the study: There are several strengths of this study. It was conducted in a tertiary care hospital, handling a heavy case load, where most patients are of low socio economic status and rural background. Method of surgery for the caesarean section and postoperative nursing care was similar in both groups. Results found in our study would be applicable across majority of the hospitals with similar settings. There are also a number of limitations of this study. Elective and emergency caesarean delivery patients were not studied separately. Neonatal follow up was not done to evaluate the exposure to antibiotics which may adversely impact neonatal sepsis workup. Patients were not followed up for late onset infection related morbidity after their hospital discharge.

Conclusion

In our study, preoperative single dose antibiotic regimen was found to be as effective as multiple doses multiple antibiotic regimens for prophylaxis for routine caesarean delivery. Single dose antibiotic use reduces the cost of treatment and has the potential to decrease the emergence of antibiotic resistant micro-organisms. The findings of our study should be helpful in reassuring surgeons about the efficacy of the recommended prophylactic pre-operative antibiotics for routine surgeries, perhaps even extrapolated to non-caesarean surgeries.

Conflict of interest: None. **Disclaimer:** Nil.

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