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Role of Antibiotic in Clean Surgery among Obstetrics Patients in CIMCH: Single Dose Versus Seven Days Course

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Abstract

Background: Evidence suggests that during caesarean section, single-dose antibiotic prophylaxis has comparable efficacy to multiple-dose antibiotic prophylaxis but with a lower cost and risk of antibiotic resistance. However, most hospitals in Bangladesh, including the study site, are still using antibacterial medications perioperatively and postoperatively for a variable time. This study aimed to compare the effectiveness of single- versus multiple-dose antibiotic prophylaxis to prevent post-caesarean section infections.

Materials and methods: This open-label, randomized controlled trial involved 140 consenting patients subjected to a caesarean section at Chattagram International Medical College Hospital (CIMCH). They were distributed randomly into single-dose and multi-dose arms. Subjects in both arms received intravenous cefazolin (1g) after cord clamping; subjects in the multi-dose arm received additional parenteral doses 12 hourly for 24h and then cefixime, 200mg tablets twice daily for six days. The patients were monitored for twoweeks for evidence of wound infection and febrile morbidity.

Results: Both the groups were similar regarding their sociodemographic and clinical characteristics. There was no statistical difference in the incidence of febrile morbidity (7.1% versus 2.9%, p=.341) wound discharge (4.3% versus 3.9%, p=1.0) and wound infection (4.3% versus 1.4%, p=.62). The median duration of hospital stay was similar in both groups (3 days).

Conclusion: Single-dose cefazolin is as effective as multiple doses for antibiotic prophylaxis to prevent post-caesarean section infections. Adopting this approach would reduce the cost of prophylactic antibiotics, the workload for staff and antibiotic resistance.

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Introduction

Caesarean delivery is the delivery of a fetus through surgical incisions made through the abdominal and uterine walls. It is performed for many indications including maternal desire, elective and surgical life-saving procedures for mothers and babies in labor dystocia, abnormal or indeterminate fetal heart rate tracing, fetal malpresentation, multiple gestations, suspected fetal macrosomia or other emergencies.[1] The World Health Organization recommends a caesarean delivery rate of <15% for optimal maternal and perinatal outcomes due to the associated risks.[2] However, the prevalence of C-section deliveries remains high in many countries, and in Bangladesh, in an institutional setting, caesarean delivery has increased from 2.4% in1999-2000 to 7.5% in 2007 and 23% in 2014.[2,3] Delivery by caesarean section is associated with a 5 to 20 fold more significant risk of postpartum infections ranging from endometritis to urinary tract infection and wound infection, compared with vaginal delivery.[4] Prophylactic antibiotics have been associated with a 60–70% reduction in maternal infection among women who have undergone caesarean delivery.[5] A recent systematic review conducted by Pinto-Lopes et al reported no significant difference between single and multiple antibiotic doses in terms of preventing maternal infection after caesarean delivery.[6] Most of these studies were done in high-income nations. Studies have shown increased cost, a higher workload on the medical staff, and the risk of antibiotic resistance with long-term antibiotic prophylaxis with no additional benefit in preventing postpartum infections compared with short-term antibiotic prophylaxis.[7,8]

However, most obstetricians in developing countries seem unwilling to adapt to the evidence-based recommended single-dose regimen for surgical prophylaxis despite high awareness, perhaps from the fear of increased postoperative

infection in low resource environments even when there is no evidence to justify this robust and long-held belief.[9,10] We aimed to close the knowledge gap on the effectiveness of single-dose versus multiple-dose antibiotic prophylaxis to prevent post-caesarean section infectious morbidity. In addition to the elective cases, we included emergency caesarean deliveries, these cases have not been widely studied in other research done in the similar settings.

Materials and methods

This was an open-label randomized clinical trial. The study comprised pregnant women who had a caesarean delivery, either electively or due to an emergency,at the Department of Obstetrics & Gynaecology of CIMCH, Chattogram, Bangladesh. The study was conducted between 21st Jan 2021 and 20th Jan 2022. Ethical approval for the study was obtained from the Health Research Ethics Committee of the CIMC (Reference num: CIMC/IRB/02/21-15). According to the Declaration of Helsinki, written informed consent was obtained from the participants.

The inclusion criterion was pregnant women scheduled for caesarean section, either electively or due to an emergency, with no added risk for infection. The exclusion criteria were pregnant women with known allergy to cefazolin or cefixime, use of antibiotics in the preceding two weeks, patients with medical disorders (GDM, HTN, anemia, morbid obesity, Cardio-respiratory illness) obstetrical complications (Prolonged and obstructed labor, prolonged rupture of membrane, chorioamnionitis) and patients receiving corticosteroid or immunosuppressive treatment.

The sample size was determined by using the hypothesis testing of the equivalent trial that single-dose antibiotic is not worse than conventional seven days postoperative Antibiotic Prophylaxis (AP). If there is truly no difference between the two regimens, then 70 patients are required in each group to be 80% sure that the limits of a two-sided 95% confidence interval would exclude a difference between the conventional and experimental groups of more than 5%.[11]

Women who met the inclusion criterion were counseled and provided their consent to participate in the study. A focused history was obtained from the participants using a structured questionnaire. Surgery was performed with spinal anesthesia and Pfannenstiel incision. The study subjects were assigned randomly to one of the two parallel study arms: single-dose or multi-dose. Subjects in single-dosearms received cefazolin 1gm intravenously after cord clamping of the baby. A repeat dose was planned to be given if the patient's weight was more than 60 kg or blood loss exceeded 1500 ml because this factor has been shown to increase infectious morbidity during surgery.[12] Subjects in multi-dose arms received cefazolin 1 gm intravenously 12 hourly for 24 hours and later oral antibiotics cefixime, 200 mg twice daily given for six days. Wound dressings will be done on the 3rd postoperative day and checked for signs of wound infection like local erythema, induration, local temperature rise, or discharge. The wound was covered with mupirocin 2% ointment dressing. The inspection of the damage was repeated on the seventh postoperative day. Sutures were removed on the seventh postoperative day if there was no wound infection. If any deviation was noted, the sutures were released earlier, a wound swab was sent for culture and sensitivity, and start or change antibiotics with daily dressing was done. The participants were examined for indicators of infection beginning 24 h post-caesarean section, then every 12 hourly for 72 h until discharge. Following discharge, they were monitored and followed up via phone calls and inquiries made on the presence of any symptoms of infectious morbidity by the researchers for two weeks. Those with possible symptoms were invited to the hospital for an evaluation.

Wound infection was defined as partial or total dehiscence or the presence of purulent discharge from the wound with localized swelling, warmth, and tenderness with or without microbiological evidence.[13] Postoperative fever was defined by a temperature greater than 38℃ at least four hours apart on two or more occasions, excluding the first 24h after a caesarean section.[14]

The data were collected and then analyzed with SPSS Statistics version 23. The outcomes were analyzed with the per-protocol approach, meaning that the participants were diagnosed in the group in which they were randomized, with the exclusion of loss to follow-up. Categorical variables were analyzed using the chi-square test

or Fisher's exact test (Where appropriate) continuous variables were analyzed using Student's t-test or Mann-Whitney U test. p-value <0.05 was considered statistically significant.

Results

During the study period, 140 eligible women underwent caesarean section. Only one woman in the multi-dose arm was lost to follow-up before the 2-week postoperative follow-up. Most of the women were in the 20-29 age group in both arms, and there was no significant difference in the age distribution between the two groups (p = .291). The groups were similar in terms of their level of education, vocational activities, place of residence, and monthly family income (Table I).

Table I Sociodemographic characteristics of the study participants

Variables	Study groups		p-value
	Single-dose (n=70)	Multiple doses (n=69)	
Age group			
15-19	5 (7.1)	8 (11.6)	
20-24	23 (32.9)	31 (44.9)	
25-29	31 (44.3)	19 (27.5)	0.291*
30-34	7 (10.0)	8 (11.6)	
35-39	4 (5.7)	3 (4.3)	
Education			
No formal education	6 (8.6)	0 (0)	
Primary	34 (48.6)	30 (43.5)	0.058*
Secondary	19 (27.1)	26 (37.7)	
Higher secondary & above	11 (15.7)	13 (18.8)	
Occupation			
Housemaker	45 (64.3)	39 (56.5)	
Employed outside	16 (22.9)	20 (29.0)	0.632*
Students	9 (12.9)	10 (14.5)	
Residence			
Rural	40 (57.1)	47 (68.1)	0.181*
Urban	30 (42.9)	22 (31.9)	
Monthly family income			
Median (IQR) Tk	25,000 (20,000-30,000)	25,000 (20,000-30,000)	0.518†

Data were expressed as frequency (Percentage) if not mentioned otherwise. IQR: Interquartile Range. *Chi-square test, †Mann-Whitney U test.

Most caesarean sections in both arms were performed as elective surgery (Table II). Repeat caesarean section occurred in 74 (53.2%) participants. The groups were comparable in terms of their parity and body mass index. The mean duration of operation was also similar in both groups (p=0.691).

Table II Clinical characteristics of the study participants

Variables	Study groups		p-value
	Single-dose (n=70)	Multiple doses (n=69)	
Indication for CS			
H/O CS	43 (61.4)	31 (44.9)	0.054*
Bad obstetric history	3 (4.3)	6 (8.7)	
Cephalopelvic disproportion	4 (5.7)	6 (8.7)	
Failed induction	3 (4.3)	2 (2.9)	
Fetal distress	9 (12.9)	13 (18.8)	
Malpresentation	7 (10.0)	9 (13.0)	
Multiple pregnancies	1 (1.4)	2 (2.9)	
Parity			
Median (IQR)	1 (0-1)	1 (0-2)	0.098†
Body mass index, kg/m^2			
Mean ±SD	22.3±2.2	21.9±2.1	0.387‡
Duration of operation, minute			
Mean ±SD	42.8±7.8	40.5±2.1	0.691‡

Data were expressed as frequency (Percentage) if not mentioned otherwise. CS: Caesarean Section, IQR: Interquartile Range, SD: Standard Deviation. *Chi-square test, †Mann-Whitney U test. Student's t-test

Postoperative febrile morbidity was the most frequent complication observed in the study without any statistical difference between groups (p=0.341). Overall, there was no statistically significant difference in the proportion of post-operative wound infection between the two groups (p=0.62). The median duration of hospital stay was three days in both groups (Table III).

Table III Outcomes of antibiotic use among the study participants

Variables	Study groups		p-value
	Single-dose (n=70)	Multiple doses (n=69)	
Postoperative complications			
Postoperative febrile morbidity	5 (7.1)	2 (2.9)	.341**
Wound erythema	3 (4.3)	1 (1.4)	0.620**
Wound discharge	3 (4.3)	2 (2.9)	1.0**
Wound gap	3 (4.3)	1 (1.4)	0.620**
Wound infection	3 (4.3)	1 (1.4)	0.620**
Duration of hospital stay			
Median (IQR) Days	3 (3-3)	3 (3-3)	0.819

Data were expressed as frequency (Percentage) if not mentioned otherwise. IQR: Interquartile Range, **Fischer exact test, †Mann-Whitney U test.

Discussion

This study was a randomized clinical trial in which a single dose of cefazolin (1g) given after cord clamping was compared with cefazolin (1g) 12 hourly for 24h and then cefixime 200mg tablets twice daily for six days of prophylactic antibiotics for women undergoing caesarean section (Either electively or due to an emergency). The single- and multiple-dose study groups were similar in demographics and operative characteristics, with no significant differences. There were no significant differences in the rates of postoperative infections (Wound infections and febrile morbidity) between the study groups. Our findings suggested that a single dose of cefazolin can sufficiently prevent maternal infection after caesarean delivery. The conclusions of this study are consistent with the evidence-based recommended single-dose regimen.[15] They should help to allay obstetricians' fears in resource-limited settings.[9,10]

The overall incidence of postoperative febrile morbidity was 5.0%, with no difference between the arms. This was the most common of the three infectious morbidity outcomes measured. This overall incidence of 5% was lower compared with the study by Igwemadu et al who reported a febrile morbidity rate of 11.8% in the short-term prophylaxis group and 11.1% in the long-term prophylaxis group (p=.822).[16]

The overall incidence of wound infection was 2.9% (3.1% in the single-dose arm and 1.4% in the multiple-dose arm). This is like the findings of a 4.5% and 1.9% overall wound infection rate in a similar study done in Nigeria and Uganda, respectively, comparing short-term versus long-term antibiotic prophylaxis for caesarean section.[17,18] However, other studies reported a comparatively higher rate of wound infection (>7%).[16,19] The lower wound infection rate could be related to environmental factors because infection control protocols differ across facilities.

Hospital stay was the same in both groups, meaning that single-dose versus multiple doses of antibiotic does not affect the hospital stay and is related to the number of days required for wound healing. This has also been confirmed by Shaheen et al.[20] They reported no significant difference in the incidence of postoperative infection and mean duration of hospital stay when comparing single-dose antibiotics versus multiple-dose antibiotics.[20]

Limitation

The limitations of the present study include the inability to blind the study participants and obstetric caregivers. Moreover, we could not record the clinical signs and symptoms that may have occurred at home after discharge till two weeks post-caesarean delivery.

Conclusion

The present study confirms that multiple doses of antibiotics are unnecessary for preventing maternal infection after caesarean delivery. We have shown that single-dose cefazolin is as effective as multiple-dose antibiotic prophylaxis in preventing post-caesarean section infectious morbidity.

Recommendation

Multicentric research with larger sample sizes in low-resource settings comparing single- with multiple-dose regimens is necessary to help validate or disprove the present study findings for clinical recommendations.

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Contrbution of authors

NS-Conception, data collection, data analysis, drafting & final approval.

NB-Design, interpretation of data, critical revision & final approval.

MA-Data collection, drafting & final approval.

SA-Data analysis, critical revision & final approval.

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Disclosure

All the authors declared no competing interest.

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