International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Agarwal K et al. Int J Reprod Contracept Obstet Gynecol. 2023 Apr;12(4):1028-1032
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20230807

Original Research Article

Single dose versus multiple doses of antibiotics in women undergoing caesarean section: a randomized non-inferiority trial

Krishna Agarwal*, Hansveen Kaur Lamba

Department of Obstetrics and Gynaecology, Maulana Azad Medical College, New Delhi, India

Received: 08 February 2023
Accepted: 03 March 2023

***Correspondence:**
Dr. Krishna Agarwal,
E-mail: hansa.lamba226@gmail.com

ABSTRACT

Background: The study aimed to compare the rates of surgical site infection in women undergoing caesarean section, given either a single dose of antibiotic 30-60 minutes before giving skin incision or multiple doses. There is enough evidence available from high-income countries supporting a single dose of prophylactic antibiotic. However, there is scanty data from middle- and low-income countries.
Methods: An open-ended randomized trial was undertaken on 400 women undergoing caesarean section. Women in the intervention group were given one dose of intravenous cefazolin before skin incision. Women in the comparison group were given intravenous ceftriaxone before skin incision, and intravenous ceftriaxone plus metronidazole for forty-eight hours after caesarean.
Results: There was no significant difference between the single and multiple-dose regimen of antibiotic prophylaxis in caesarean sections when compared for postoperative surgical site infections. Secondary outcome variables, that is, side-effects of antibiotics were significantly more in the multiple-dose group.
Conclusions: A single-dose regimen for antibiotic prophylaxis is as effective as a multiple-dose regimen, in low-risk women undergoing caesarean section, both elective and emergency.

Keywords: Antibiotics, Prophylaxis, Surgical site infection, Caesarean section

INTRODUCTION

Caesarean delivery constitutes a very important risk factor for infection in the postpartum period, and higher rates of post-operative infection have been observed after caesarean delivery in comparison to other surgical procedures.[2] Prophylactic antibiotics are aimed at achieving peak bioavailability of drug at the time of incision, as it is this time when maximum microbial contamination is likely to occur.[3]

International guidelines are in place regarding prophylactic use of antibiotics for prevention of surgical site infection in caesarean section. They recommend the use of single dose of first generation cephalosporin to be given 30-60 minutes before skin incision.[2-6] According to WHO recommendation on prophylactic antibiotics for women undergoing caesarean section, a single dose of first generation cephalosporin or penicillin should be used in preference to other classes of antibiotics.[7] WHO also emphasizes on the importance of using a single dose regimen, 30- 60 minutes before skin incision, and a higher dose or second dose can be given depending on clinical factors like high BMI, prolonged surgery or massive blood loss, as risk of developing post- caesarean infection is increased.[7] National guidelines also uphold the use of single dose of intravenous cefazolin before skin incision.[8-9] Despite this, use of multiple doses of antibiotics is still rampant in clinical practice in India which may be partly due to lack of evidence from Indian setting, and also due to suboptimal asepsis in our hospitals. Till date, there are few studies from Indian setting which evaluate the outcomes of single dose of antibiotic for caesarean section. Therefore, this randomized controlled trial was planned to

generate local evidence to know whether single-dose cephalosporin is as effective in preventing surgical site infection after caesarean section as the multiple-dose regimen.

METHODS

The current study is an open-ended randomized trial with 2 parallel treatment groups. The patients were recruited at Lok Nayak Hospital, a tertiary care teaching hospital in Delhi. All women with term pregnancy (37 to 41 completed weeks) undergoing elective or emergency caesarean section were enrolled in the study. Women with clinical evidence of infection - fever or leucocytosis; already receiving or scheduled to receive antibiotic therapy for some other reason; moderate anemia (Hb at enrolment); known HIV positivity; women with heart disease needing antibiotic prophylaxis for prevention of SABE; second stage caesarean section; rupture of membranes (>24 hours); women with penicillin allergy; and BMI >30 kg/m^2 were excluded from the study.

Pregnant women admitted in maternity wards and labor room at Lok Nayak Hospital were assessed, and those who were found to be eligible based on inclusion and exclusion criteria were recruited in the study. Women in the intervention group were given one dose of 1-gram injection cefazolin intravenously within 30 to 60 minutes before skin incision. An additional dose was given after 4 hours of initial dose in case of surgery lasting >1 hour, blood loss >1500 ml, or rupture of membranes. Complete asepsis was practiced by all the staff involved. Hand scrubbing was done for 5 minutes and skin preparation was done with chlorhexidine and povidone-iodine. Women in the comparison group were given antibiotic prophylaxis and care according to the existing practices, that is injection ceftriaxone 1gm IV BD and Injection metronidazole 500 mg IV TDS for 3 days. If evidence of puerperal pyrexia (temperature of 100.4°F on 2 occasions 4 hours apart after 48hrs of surgery) was present, the patient was started on multiple drug regimen. Approval for the study was taken from the institutional research ethics committee. The participants were fully informed about the study objectives and procedure, and written informed consent was taken.

Temperature charting was done 4-hourly for all patients postoperatively. Routine postoperative investigations like CBC, urine routine, and urine culture (on day 3) were sent. Patients were daily assessed for breast engorgement and on the 3rd postoperative day for stitch line. If puerperal fever was recorded, fever investigations were sent and therapeutic antibiotics were started accordingly. If the mother and baby were healthy, they were discharged on the 4th postoperative day. The suture removal was done on the 10th postoperative day. Adverse events and side effects of antibiotics were noted in the case report form. A pre-designed case report form was prepared in which all data was recorded. Data was entered in the MS Excel sheet and analyzed using statistical software SPSS version 25. The continuous data was expressed as mean±SD. The categorical data was expressed in percentage. Continuous data was checked for normal distribution and when found normally distributed, the two groups were compared using unpaired t-test. In the case of non-normally distributed continuous data, it was compared using the Mann-Whitney U test. For categorical data, the Chi-square test was used and in case the number was less than 5, then Fisher's exact test was used. The level of significance was taken as a p value of <0.05.

RESULTS

A total of 400 subjects were recruited for the study, 200 in the study arm, and 200 in the comparison arm. The mean age, literacy, occupation, and BMI of the participants was comparable in both groups. However, the mean number of PV examinations done and absent membranes were significantly higher in the comparison group. There was no significant difference between the two groups about the type of caesarean section, that is elective vs. emergency, number of caesareans, amount of blood loss, and time taken (Table 1).

Table 1: Demographic profile, labor, and operative details of the participants.

Parameters	Study group (N=200) Frequency (%)	Comparison group (N=200) Frequency (%)	P value
Age (years) (mean±SD)	27.02±4.52	26.53±4.36	
<30	140 (70.0)	152 (76.0)	0.224
≥30	60 (30.0)	48 (24.0)	
BMI*			
Underweight	49 (24.5)	44 (22.0)	0.838
Normal	144 (72.0)	149 (74.5)	
Overweight	7 (3.5)	7 (3.5)	
No. of per-vaginal examinations per patient	1.14±1.11	1.41±1.18	0.022
Membrane status (Absent)	60 (30.0)	79 (39.5)	0.046
Type of Surgery			0.286
Elective	70 (35.0)	60 (30.0)	

Continued.

Parameters	Study group (N=200) Frequency (%)	Comparison group (N=200) Frequency (%)	P value
Emergency	130 (65.0)	140 (70.0)	
Caesarean Section (CS)			
1st CS	109 (54.5)	114 (57.0)	0.851
Previous 1 CS	71 (35.5)	66 (33.0)	
Previous 2 CS	19 (9.5)	20 (10.0)	
Previous 3 CS	1 (0.5)	0 (0.0)	
Incision-to-closure time (hours)			
<1	137 (68.5)	150 (75.0)	0.370
1-1.5	60 (30.0)	47 (23.5)	
>1.5	3 (1.5)	3 (1.5)	
Blood Loss (ml)			
<500	117 (58.5)	135 (67.5)	0.199
500 ml to 1L	81 (40.5)	63 (31.5)	
>1L	2 (1.0)	2 (1.0)	

Table 2: Primary outcomes.

Parameters	Study group (N=200) Frequency (%)	Comparison group (N=200) Frequency (%)	P value
Fever			
Absent	194 (97.0)	194 (97.0)	0.592
Low grade	3 (1.5)	1 (0.5)	
High grade	3 (1.5)	5 (2.5)	
Uterine tenderness	0	0	1.000
Wound Discharge			
Absent	195 (97.5)	186 (93.0)	0.083
Serous	4 (2.0)	12 (6.0)	
Purulent	1 (0.5)	2 (1.0)	
Lochia			
Healthy	200 (100.0)	200 (100.0)	1.000
Foul smelling	0	0	
Surgical Site Infection			
None	198 (99.0)	194 (97.0)	0.284
Superficial	2 (1.0)	6 (3.0)	
Deep	0	0	

The primary outcome variables were comparable between the two groups (Table 2), as there was no significant difference in terms of fever, uterine tenderness, wound discharge, lochia, and surgical site infection (SSI). The comparison group had significant side- effects of not feeling well, nausea, and taste changes (Table 3).

Table 3: Secondary outcomes.

Parameters	Study group (N=200) Frequency (%)	Comparison group (N=200) Frequency (%)	P value
Side effects of antibiotics	2 (1.0)	17 (8.5)	<0.001
Not feeling well	0	17 (8.5)	<0.001
Nausea	2 (1.0)	15 (7.5)	<0.003
Vomiting	0	3 (1.5)	0.246
Diarrhoea	0	1 (0.5)	0.999
Headache	1 (0.5)	5 (2.5)	0.217
Taste changes	0	7 (3.5)	0.022
Thrombophlebitis	1 (0.5)	0 (0.0)	1.000
Re-suturing of the caesarean section abdominal wound	1 (0.5)	1 (0.5)	1.000

Additionally, those who developed SSI had a higher prevalence of risk factors like anemia, higher incision to closure time (>1 hour), and longer duration of catheterization (Table 4).

The primary outcome variables were comparable between the two groups (Table 2), as there was no significant difference in terms of fever, uterine tenderness, wound discharge, lochia, and surgical site infection (SSI). The comparison group had significant side- effects of not feeling well, nausea, and taste changes (Table 3). Additionally, those who developed SSI had a higher prevalence of risk factors like anemia, higher incision to closure time (>1 hour), and longer duration of catheterization (Table 4).

Table 4: Risk factors among participants with SSI vs. without SSI.

Risk Factor	No SSI group (N=392)	SSI group (N=8)	P value
Anemia			
Absent	287 (73.2)	3 (37.5)	0.039
Mild	105 (26.8)	5 (62.5)	
No. of PVs (mean±SD)	1.27±1.15	1.62±1.19	0.388
Labour			
Not in labor	163 (41.6)	4 (50.0)	0.758
Latent Phase	223 (56.9)	4 (50.0)	
Membrane Status (Absent)	137 (65.1)	6 (75.0)	0.719
Type of Surgery			
Elective	128 (32.7)	2 (25.0)	1.000
Emergency	264 (67.3)	6 (75.0)	
Blood Loss (ml)			
<500	248 (63.3)	4 (50.0)	0.511
500 ml to 1L	140 (35.7)	4 (50.0)	
>1L	4 (1.0)	0 (0.0)	
Incision-to-closure time (hours)			
<1	285 (72.7)	2 (25.0)	0.012
1-1.5	101 (25.8)	6 (75.0)	
>1.5	6 (1.5)	0 (0.0)	
Duration of urinary catheterization (hours)			
12	265 (67.6)	2 (25.0)	0.005
24	84 (21.4)	6 (75.0)	
>24	43 (11.0)	0 (0.0)	

DISCUSSION

This study was conducted to find out whether a single-dose antibiotic regimen is as effective as multiple-dose regimen in the prevention of surgical site infection, and found that in a low-risk pregnancy, there was no significant difference between the two when compared for postoperative surgical site infections, provided pre-existing infections (like urinary and respiratory tract infection) and factors predisposing to infections (like diabetes mellitus, obesity, moderate to severe anemia and prolonged rupture of membranes) were ruled out. We could find very few studies in the Indian settings, which have observed the outcomes of single dose antibiotic regimen for infection prevention in caesarean section. Jyothi et al conducted a randomized controlled trial in 200 women in which a single dose of antibiotic was given in both arms.[10] One arm included only first generation cephalosporin, and second arm included both cephalosporin + azithromycin.

The overall incidence of SSI in their study was 9%, but was higher (15%) in the only cefazolin group compared to the present study (1%). The present study has also revealed that the single-dose regimen has the benefit of more patient compliance, fewer side- effects, and less cost. Shakya et al, Pore et al and Prathima et al have similarly observed that there was no difference in infectious morbidity in the single and multiple-dose groups for antibiotic prophylaxis in women undergoing caesarean section.[10-13]

Our study reiterates that a single dose of Cefazolin given pre-operatively, 30-60 minutes before incision, is an effective antibiotic regimen for prophylaxis in caesarean section surgery, as maximum chances of contamination are at the time of incision. There is no added advantage of multiple doses of antibiotics given post-operatively. In our study, outcomes like nausea and taste changes were significantly higher in the comparison group, compared to the study group. Other side effects like vomiting, diarrhea, and headache were comparable in both groups. Shakya et al, Prathima et al and Jyothi et al reported no antibiotic-

related side-effects in their studies. However, Pore et al reported minor adverse drug effects such as nausea, headache, and dizziness which were comparable in both groups.[10-13] The strength of our study was that it included both elective and emergency caesarean sections, in laboring and non-laboring patients. Also, patients were followed for a long term (30 days post-operatively). Additionally, our study has looked at the association of SSI with various parameters and analyzed what were the risk factors for SSI, which only one other similar study has done.[10]

Limitations

The limitation of current study was that only low-risk women were included in this study.

CONCLUSION

The single-dose regimen for antibiotic prophylaxis in a caesarean section is as efficacious as multiple drug regimen in preventing SSI. At the same time, it has fewer side effects, is well tolerable, cost-effective, and has less risk of developing drug resistance. So, it should be preferred over multiple-dose regimen, even in low income countries like ours, in low-risk women undergoing caesarean section, both elective and emergency.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Surgical Site Infection. Available at: https://www.cdc.gov/hai/ssi/ssi.html. Accessed on 6 February 2020.
2. Committee on Practice Bulletins-Obstetrics. Use of Prophylactic Antibiotics in Labor and Delivery. Obstet Gynecol. 2018;132:e103-19.
3. Van Schalkwyk J, Van Eyk N. No. 247-Antibiotic prophylaxis in obstetric procedures. J Obstet Gynaecol Can. 2017;39:e293-9.
4. SR Bailey, N Field, CL Townsend, AJ Rodger, P Brocklehurst. Antibiotic prophylaxis for women undergoing caesarean section and infant health. BJOG. 2016;123:875-6.
5. Temming C, Eppes F, Srinivas G, Colditz M. Evidence-based bundles and cesarean delivery surgical site infections: a systematic review and meta-analysis. Obstet Gynecol. 2017;130:735-46.
6. Prophylactic antibiotics in obstetrics and gynaecology. Available at: https://ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women's Health/Statement and guidelines/Clinical - General/Prophylactic-antibiotics-in-obstetrics-and-gynaecology-(C-Gen-17)-Review-July-2016.pdf?ext=.pdf. Accessed on 6 February 2020.
7. WHO recommendation on prophylactic antibiotics for women undergoing caesarean section. Available at: https://www.who.com. Accessed on 6 February 2020.
8. National Guidelines. Available at: https://www.mohfw.gov.in/pdf/National%20Guidelines%20for%20IPC%20in%20HCF%20-%20final%281%29.pdf. Accessed on 11 December 2022.
9. Treatment Guidelines for Antimicrobial Use in Common Syndromes. Available at: https://main.icmr.nic.in/sites/default/files/guidelines/Treatment_Guidelines_2019_Final.pdf. Accessed on 11 December 2022.
10. Jyothi MS, Kalra JK, Arora A, Patil A, Suri V, Jain V, Shafiq N, Saini SS, Gautam V. Randomized controlled trial of cefazolin monotherapy versus cefazolin plus azithromycin single dose prophylaxis for cesarean deliveries: A developing country's perspective. J Family Med Prim Care. 2019;8:3015-21.
11. Shakya A, Sharma J. Comparison of single versus multiple doses of antibiotic prophylaxis in reducing post-elective Caesarean section infectious morbidity. Kathmandu Univ Med J. 2010;8:179-84.
12. Pore SM, Sardesai SP, Tapare VS, Kulkarni MV, Malhotra AP, Chavan CS. Single-dose cefazolin plus metronidazole versus existing multi-dose regimen for prophylaxis in caesarean section. Indian J Pharmacol. 2012;44(2):279-80.
13. Prathima, Savitha, Tejeswini, Anitha. Comparative study of single-dose versus multiple doses of antibiotic prophylaxis in caesarean delivery. Int J Reprod Contracept Obstet Gynecol. 2017;6:215-8.

Cite this article as: Agarwal K, Lamba HK. Single dose versus multiple doses of antibiotics in women undergoing caesarean section: a randomized non-inferiority trial. Int J Reprod Contracept Obstet Gynecol 2023;12:1028-32.