

# Short term antibiotic prophylaxis for emergency cesarean delivery : Is there a difference?

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## Abstract

**Objective :** To evaluate the efficacy of amoxicillin-clavulanic acid when given as a two dose versus the more traditional triple dose regimen for cesarean section prophylaxis. **Methods :** We conducted a prospective study of 122 women undergoing emergency cesarean section. All patients received 2.4 g of amoxicillin-clavulanic acid at the time of cord clamping intravenously. Subsequent doses of 1.2 g were administered 6 hours apart after the initial dose. **Results :** Patient characteristics and risk factors for infection were comparable for the two groups. Analysis of results demonstrated no significant differences in infective morbidity (6.5% versus 8.1%) between the two and triple dose groups respectively. **Conclusion :** The results of the present study suggest that two doses of amoxicillin-clavulanic acid is equally effective as triple dose therapy in reducing post cesarean section endometritis. This implies that two dose regimen would decrease the cost to the patient while maintaining very acceptable infection rates.

## INTRODUCTION

The incidence of cesarean section has risen steadily over the past two decades. Morbidity associated with this operative procedure is therefore of increasing concern. The frequency of infection varies from 5% to 85% with a mean incidence of 35% to 40% in most studies<sub>1</sub>. The most common complication associated with cesarean delivery is endometritis. In general, the highest incidence of infection occurs in indigent women having cesarean delivery after extended duration of labor and ruptured membranes. A number of well designed studies have documented the efficacy of prophylactic antibiotics in reducing the rates of postpartum endometritis and wound infection in patient who have undergone emergency cesarean delivery<sub>2</sub>. Hofmeyr et al<sub>2</sub> have clearly stated that further placebo controlled trials in emergency cesarean section are not ethically justified.

The fact that prophylactic antibiotics reduce endometritis by two-thirds to three-quarters justifies a policy of administering antibiotics to women undergoing nonelective cesarean section<sub>3,4</sub>. Nevertheless, there is no consensus on which antibiotic to use. The regimen chosen depends on the pathogens usually associated with postoperative infection and the antimicrobial susceptibility patterns in the local hospital. Bergstrom et al<sub>5</sub> reported that a combination of gentamicin and metronidazole was effective for prevention

of infection before emergency cesarean section. However, Hopkins et al<sub>3</sub> concluded that both ampicillin and first generation cephalosporins represent good choices for prophylaxis in women undergoing cesarean section. There does not appear to be added benefit in utilizing a more broad spectrum agent or a combination regimen. Amoxicillin is a frequently used antibiotic in our set-up and may not be the most appropriate choice for prophylaxis due to increasing incidence of resistant *Escherichia coli*. So the next best agent was amoxicillin-clavulanic acid ( AMX-CL ) which has a side-effect profile similar to amoxicillin, at the same time has a broader spectrum that includes anaerobes and  $\beta$  lactamase producing strains.

The objective of antimicrobial prophylaxis is to achieve sufficient antibiotic tissue concentration before possible bacterial wound contamination. So, it is recommended to administer antibiotics intravenously before the skin incision. One of the few exceptions to this 'rule' has been in the case of cesarean section prophylaxis; prophylactic antibiotics have usually been withheld until after the umbilical cord was clamped. The rationale has been that administering antibiotics to the mother before delivery will result in placental transfer to the fetus and subsequent masking of infections in the neonate. Support for this approach can be found in the work of Thigpen et al<sub>6</sub> who found no significant

differences in maternal infectious morbidity whether antibiotics were given before skin incision or at cord clamping. So it would seem prudent to delay prophylactic antibiotic administration until after delivery.

Of all obstetric procedures cesarean section after prolonged labor with ruptured membranes is associated with the largest bacterial inoculum. Thus this may be the one procedure for which a single dose of prophylaxis is not as effective as two or three dose prophylaxis<sup>7</sup>. Current information<sup>8</sup> suggests that additional doses of an antibiotic for prophylaxis should be given at intervals of two times the half life of the antibiotic to maintain adequate levels of the antimicrobial throughout the surgical procedure. Hence, the subsequent doses of the amoxicillin-clavulanic acid were administered after an interval of 6 hours. The optimal duration of administration is still controversial with tendencies persisting toward extended antibiotic coverage instead of coverage within 24 h of bacterial contamination. This study was designed to compare the efficacy of two doses of amoxicillin-clavulonic acid with those of a three-dose regimen in preventing postoperative infection in women undergoing emergency cesarean section.

## **METHODS**

This prospective study was conducted between March 2005 and August 2006 in the department of obstetrics and gynecology, Kasturba hospital Manipal. All patients were considered at high risk for development of postoperative infectious morbidity because they were in labor or had ruptured membranes. Patients with clinical signs of chorioamnionitis, placenta previa, fibroid or known hypersensitivity to penicillin were excluded from this trial. After informed consent was obtained, patients were randomly allocated by the resident in charge of the labor room to receive either two or three doses of amoxicillin-clavulanic acid, The anesthetist administered 2.4 g of amoxicillin-clavulanic acid to all women at the time of cord clamping intravenously. Patient assigned for two doses protocol, received second dose of 1.2 g six hours after the initial dose of AMX-CL. Patients in the three dose group received two additional doses of 1.2 g six and 12 hours postoperatively. In both groups bladder catheter was removed after 24h. Wound care followed a standard scheme in both groups, the occlusive dressing applied in the theater being removed after 48 h.

Each patient was examined daily and postoperative infectious morbidity was noted from the day of the operation

up to the day of the discharge from the hospital. Oral temperature of  $\geq 100.4^{\circ}\text{F}$  on two occasions at least 6 hours apart was carefully evaluated for the cause of febrile morbidity Endometritis was defined as fever with concomitant uterine tenderness and foul smelling lochia. Wound infection was defined as an abnormal looking wound surrounded by cellulitis and/or draining purulent material. Urinary tract infection was documented if a patient complained of burning micturition with a positive urine culture of  $\geq 10^5$  bacteria per mL. Laboratory monitoring tests included complete blood count, urine analysis and cervical swab for aerobic and anaerobic culture. Follow-up examination at six weeks was carried out to look for late infectious morbidity.

The protocol was accepted by the institutional ethics committee. The sample size required was 97 in each treatment arm. This figure was based on the incidence of endometritis in a previous study by Hawrylyshyn, to give a power of 80% at the 5% significance level. Differences in continuous variables were analysed with independent sample t test for normally distributed data and the Mann-Whitney U test for skewed data. Differences in discrete variables were analysed by chi-square test and the fisher exact test as appropriate.  $P < 0.05$  was considered statistically significant.

## **RESULTS**

A total of 122 women were enrolled in the study. Sixty one women were randomized to two dose protocol and 61 women received three doses of amoxicillin-clavulanic acid. There were no significant differences between the treatment groups with respect to maternal characteristics and intrapartum risk factors for infectious morbidity (Table1).

**Figure 1**

Table 1: Preoperative profile of patients

	Two doses group n=61	Three doses group n=61	P value
Age (years)	26.7 ± 4	27.2 ± 4.2	0.48
Body mass index(Kg/m <sup>2</sup> )	24.7 ± 3.6	24.6 ± 3.7	0.84
Parity			
Primigravida	38	38	
multigravida	23	23	
Gestational age (weeks)	38.3 ± 2.2	37.6 ± 2.3	0.09
Duration of labour (h)	8.9 ± 5.4	8 ± 5.4	0.33
Duration of rupture of membranes ( range h )	2-16	3-29	
Number of vaginal examination	3.5 ± 1.8	3.5 ± 1.6	1.0

Operative indications are listed in table 2. Various intraoperative risk factors for postoperative infectious morbidity were evaluated (Table 3).

**Figure 2**

Table 2: Indications for cesarean delivery

Indications	Two dose	Triple dose
Fetal distress	22	18
Cephalopelvic disproportion	11	12
Failure to progress	10	9
Previous cesarean section	11	7
Breech Presentation	7	8
Others	0	7

**Figure 3**

Table 3: Operative risk factors for infectious complications

	Two dose	Triple dose	P value
Operating Time(h)	1.05 ± 0.2	1.1 ± 0.2	0.26
Surgeon			
Consultant	40	38	1.71
Resident	21	23	
Intraoperative blood loss ( ml)	542.6 ± 215	514 ± 198	0.46
Dense adhesions	9	9	

The frequency of infectious morbidity in the two groups are shown in Table 4. An analysis of the results of the two antibiotic regimens did not demonstrate any statistically significant difference in postoperative infective morbidity. Endometritis was successfully treated with gentamicin and metronidazole for 5-7 days. In the patients with urinary tract infection, urine cultures showed Klebsiella and Pseudomonas and they were treated according to sensitivity tests. The two cases of wound infection were treated according to culture and sensitivity tests. No patient developed a pelvic abscess and there were no episodes of pelvic thrombophlebitis. The duration of hospitalization was the same in the two groups of patients, with a mean stay of 6.9 days for the double dose group and 6.7 days for the triple dose group. Three women in the triple dose regimen developed diarrhea. The newborns did not show any complication related to the antibiotics used.

**Figure 4**

Table 4: Comparison of postoperative infectious morbidity by treatment group

	Two dose n=61(%)	Triple dose n=61 (%)	P value
Febrile morbidity	1(1.6)	2(3.2)	1.0
Endometritis	0	1(1.6)	1.0
Wound infection	1(1.6)	1(1.6)	1.0
Urinary tract infection	2(3.2)	1(1.6)	1.0
Total	4(6.5)	5(8.1)	1.0

## DISCUSSION

The value of prophylactic antibiotics in reducing endometritis after cesarean section is well documented.

However, for how long antibiotics should be given is still controversial. One of the major issues is the choice of antibiotic to be used for prophylaxis. In postcesarean infection, the most common pathogens are group B Streptococci, anaerobic Streptococci, Escherichia coli, Staphylococcus aureus and Bacteroides. All these organisms are sensitive to amoxicillin-clavulanic acid. Many of the earlier studies<sup>410</sup> which used multiple antibiotic agents such as penicillin with gentamicin or metronidazole with gentamicin again would not be considered as prophylaxis by today's standards. Rather, a single antibiotic agent is preferable as this will minimize the chance of adverse drug reaction. It is evident that many of the earliest dosages consisting of 3 to 5 days of antibiotic administration<sup>11</sup> would today no longer be considered prophylactic. Most recent studies<sup>912131415</sup> advocating short course prophylaxis have restricted to two or three doses of antibiotics within the first 24 hours following operation. This view was supported in the present study. Each hospital needs to formulate its own antibiotic protocol by clinical trials and the results of such trial should be the basis for future therapy. Keeping this in mind and the indigent population our institution caters to, two or three doses of broad spectrum amoxicillin-clavulanic acid was considered.

Success of antibiotic prophylaxis depends on the appropriate dosing of the antibiotic. By increasing the initial dose to 2.4 g, it reduces the size of the bacterial inoculum introduced into the uterus. Most patients included in this study have one or the other risk factors for surgical site infections like prolonged labour, prolonged rupture of membranes, frequent vaginal examinations and also systemic illness like anemia, obesity and diabetes. In the present study, we did not note a difference between the two groups in rates of endometritis, wound infection, or other infectious morbidity. Our results agree with a previous study by Chittacharoen et al.<sup>16</sup> From an economic point of view, two doses of prophylaxis has the advantage of being cheaper than three doses. Also, two dose regimen carries a smaller risk of superinfection by resistant organisms. However, there was a limitation in the present study. The sample size could not be met due to wide variations in the use of antibiotics within our institution.

As a result of the above findings in the present study, we suggest that two doses of amoxicillin-clavulanic acid might be one of the best choices as a prophylactic drug in cesarean

section. A triple dose prophylactic regimen appeared to offer no added benefit over a double dose.

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