

Infectious Diseases in Obstetrics and Gynecology 6:220–223 (1998)
© 1998 Wiley-Liss, Inc.

Incidence of Postpartum Endomyometritis Following Single-Dose Antibiotic Prophylaxis With Either Ampicillin/Sulbactam, Cefazolin, or Cefotetan in High-Risk Cesarean Section Patients

N. Noyes,^{1*} A.S. Berkeley,¹ K. Freedman,² and W. Ledger²

¹The New York University Medical Center, New York, NY

²The New York Hospital-Cornell Medical Center, New York, NY

ABSTRACT

Objective: To assess the efficacy of single-dose antibiotic prophylaxis against postpartum endomyometritis in high-risk cesarean section patients.

Design: Patients were administered one of three single-dose antibiotic regimens following umbilical cord clamping after cesarean section delivery.

Setting: Prospective randomized trial at a university-based hospital.

Patients: The study evaluated 293 consenting women undergoing cesarean section who had either experienced labor for a duration of ≥ 6 hr or rupture of amniotic membranes.

Main outcome measures: Development of postpartum endomyometritis.

Results: The incidence of postpartum endomyometritis was 7/95 (7.4%) following the ampicillin/sulbactam regimen, 14/98 (14.3%) after the cefazolin regimen, and 11/99 (11.1%) after the cefotetan regimen. There was no significant difference in postpartum infection among the three study arms. In addition, the incidence of endomyometritis in the three single-dose study arms was not higher than previously noted in studies where three doses of antibiotic were administered.

Conclusion: Single-dose antibiotic prophylaxis should replace the standard triple-dose therapy for uninfected women undergoing cesarean section who are at risk for postoperative endomyometritis. Ampicillin/sulbactam, cefazolin, and cefotetan are all reasonable antibiotic choices for single-dose therapy. *Infect. Dis. Obstet. Gynecol.* 6:220–223, 1998. © 1998 Wiley-Liss, Inc.

KEY WORDS

antibiotic prophylaxis; cesarean section; obstetrics

The current incidence of birth by cesarean section in the United States is greater than 20%. The postoperative infection rate after cesarean section ranges from 10% to 90%, and both the incidence and severity of infection is known to be higher in patients undergoing operative vs. vaginal delivery.^{1,2} The need for antibiotic prophylaxis during high-risk cesarean deliveries has been firmly established by multiple investigators who have demonstrated a significant reduction in post-

operative endomyometritis with such therapy.^{3–5} In a trial of three-dose intravenous antibiotic prophylaxis and antibiotic lavage at New York Hospital, the incidence of postoperative endomyometritis was significantly reduced from 32% to 12% in patients undergoing cesarean section in labor.⁸ Multiple-dose prophylaxis was the previous standard of care at New York Hospital in patients undergoing cesarean section following rupture of membranes (ROM) or labor. At the time of the

*Correspondence to: Dr. Nicole Noyes, Director, Reproductive Surgery, The New York University Medical Center, New York, NY 10016.

present study, the use of single-dose therapy after umbilical cord clamping at other institutions had been shown to have efficacy equal to three-dose regimens for prophylaxis against infection.^{6,7} The current study was undertaken to evaluate a single-dose prophylactic antibiotic regimen for operative deliveries.

SUBJECTS AND METHODS

From July 1988 to November 1990, 756 gravid women admitted to The New York Hospital in labor or having had ROM for 6 hours were enrolled in a prospective randomized trial to evaluate the efficacy of single-dose antibiotic prophylaxis with one of three antibiotic agents. Written consent was obtained on admission to the hospital. If the patient underwent cesarean section, she was randomized to receive intravenously either 1.5 g of ampicillin/sulbactam (A/S) (Unasyn®, Pfizer, New York, NY), 1 g of the first-generation cephalosporin cefazolin (Ansef®, Smithkline Beecham, Pittsburgh, PA), or 1 g of the second-generation cephalosporin cefotetan (Cefotan®, Zeneca, Wilmington, DE) after umbilical cord clamping.

Criteria for the study included being in labor and/or having ROM for at least 6 hours, as these were considered risk factors for the development of endomyometritis. Exclusion criteria were as follows: <18 years of age, known allergy to penicillin or cephalosporin antibiotics, antibiotic therapy within 72 hours prior to hospital admission, history of group B β -streptococcal infection, prophylactic antibiotic therapy for medical indications, prior use of steroid therapy for underlying medical illness or enhancement of fetal lung maturity, or clinical evidence of chorioamnionitis at the time of cesarean section. Other than complete blood count (CBC) and evaluation of a voided urine sample for protein and sugar, no other laboratory or microbiologic evaluations were performed preoperatively. Postoperative lochia cultures were obtained if the patient had febrile morbidity or symptoms suggestive of infection. Febrile morbidity was diagnosed if the patient had an oral temperature above 39°C on two occasions 6 hours apart more than 24 hours following the operative delivery. Endomyometritis was diagnosed if febrile morbidity was associated with foul-smelling lochia or uterine tenderness or if no other sources of infection were found on clinical or laboratory examination.

The incidence of endomyometritis was evaluated as it related to the following variables: the particular antibiotic administered, the service assignment of the patient (ward vs. private), race, number of hours of labor, number of hours of ROM, whether oxytocin was used, number of vaginal examinations performed, whether the cesarean was done for an emergent indication (e.g., fetal distress or vaginal bleeding), the type of anesthesia administered, length of surgery, and whether the patient experienced postoperative anemia (i.e., hematocrit <28%). The Student *t*-test and chi-square analysis were used, and differences were considered significant at $P < 0.05$.

RESULTS

Of the 756 patients who consented to participate on admission, 300 (39.6%) ultimately underwent cesarean section. One hundred of these patients were randomized to receive A/S, 100 to cefazolin, and 100 to cefotetan. Five patients from the A/S group, two from the cefazolin group, and one from the cefotetan group were considered unevaluable, as they did not meet the protocol criteria. The reasons were as follows: two patients inadvertently received the prophylaxis for vaginal delivery rather than cesarean section, two patients had positive group B β -streptococcal cultures and had simultaneously received intravenous ampicillin prophylaxis, two patients had elevated temperatures at the time of cesarean section, and two patients inadvertently received two prophylactic doses of cefoxitin in the early postoperative period. Thus, evaluable patients included 95 who received A/S, 98 who received cefazolin, and 99 who received cefotetan.

Epidemiologic and clinical parameters are given in Tables 1 and 2. The ratio of Caucasian to non-Caucasian patients was 1.2:1, and the ratio of private to ward service assignment was 1.9:1. The percentage of patients who received oxytocin was 52.7%. Regional anesthesia was administered to 91.4%, and the remainder received general anesthesia. There were no statistically significant differences in the preoperative parameters among the three study arms. Indications for cesarean section in all patients, in order of highest frequency, were as follows: failure to progress/cephalopelvic disproportion, fetal distress, malpresentation, previous cesarean section, multiple gestation, or other indications, such as placenta previa, active herpes sim-

TABLE 1. Epidemiologic and clinical parameters of study group^a

Age (year)	31.2
Weight (lb)	160.5
Hematocrit (%)	
Preoperative	36.0
Postoperative	32.7
Estimated gestational age (wk)	38.6
Ruptured membranes (hr)	7.3
Labor (hr)	12.7
Sterile vaginal exams (n)	4.6
Surgical time (min)	54.1
Length of stay (day)	5.2

^aValues are expressed as means unless otherwise indicated. No significant difference was noted within the three treatment arms.

TABLE 2. Patient distribution (n = 292)

Race	Non-Caucasian	Caucasian
	132	160
Service assignment	Ward	Private
	101	191
Labor augmentation	Oxytocin augmentation	No oxytocin
	154	138
Anesthesia	Regional	General
	267	25

plex infection, and severe preeclampsia. The indications were evenly distributed among the antibiotic groups. All patients experienced labor and/or ROM of at least 6 hours' duration.

The incidence of postpartum endomyometritis was 7/95 (7.4%) in the A/S group, 14/98 (14.3%) in the cefazolin group, and 11/100 (11.0%) in the cefotetan group (Table 3). These differences were not statistically different, with *P* values ranging from 0.19 to 0.63. The incidence of endomyometritis in the treatment groups was markedly lower than the 32% rate previously observed at The New York Hospital in patients who had not received antibiotic prophylaxis for cesarean section.⁸ There were no life-threatening postoperative complications and no increased lengths of hospital stay in the patients with endomyometritis. Three patients experienced transient untoward effects. A single A/S-treated patient reported mild leg pain of uncertain etiology that lasted 2 days. She was observed and recovered spontaneously. Of the cefotetan-treated patients, there were two adverse reactions. One patient had mild chest pain on the left side felt to be musculoskeletal in nature. This pain resolved with conservative management. The other patient developed a pruritic rash that re-

TABLE 3. Incidence of endomyometritis following prophylaxis with ampicillin/sulbactam, cefazolin, or cefotetan

Study arm	n	Incidence of	Side
		postpartum endomyometritis	effects
Ampicillin/sulbactam	95	7 (7.36)	1
Cefazolin	98	14 (14.26)	0
Cefotetan	99	11 (11.1)	2

solved following two doses of diphenhydramine hydrochloride. No adverse reactions were reported in the cefazolin group.

Clinical epidemiologic parameters in all study patients were examined in an attempt to establish contributing factors to endomyometritis (Table 4). Non-Caucasian patients and those on the ward service were 2.1 times more likely to develop endomyometritis. Fifteen percent of the non-Caucasian group and 16.8% of the ward-service group developed endomyometritis, compared with 7% of Caucasian patients and 7.8% of the private-service patients (*P* = 0.04 and 0.03, respectively).

A patient undergoing cesarean section under general anesthesia at The New York Hospital was three times as likely to develop endomyometritis as one receiving regional anesthesia. Twenty-eight percent of patients who had general anesthesia developed endometrial infection, compared with 9.3% of the patients undergoing regional anesthesia (*P* = 0.01). Surgery lasting 1 hour or more was associated with a 2.7-fold increased risk of developing endomyometritis over procedures performed in less than 1 hour (18.7% vs. 7.0%, respectively; *P* = 0.007). Postoperative anemia, defined as a hematocrit < 28%, increased the risk of postoperative endometrial infection threefold, with an incidence of 25.7% if the hematocrit was less than 28% vs. 8.9% if the hematocrit was ≥28% (*P* = 0.01). A preoperative weight of ≥200 lb was associated with a 2.5-fold increased risk of postoperative endomyometritis, compared with a preoperative weight < 200 lb (*P* = 0.02). Factors not found to be associated with an increased incidence of endomyometritis included labor longer than 12 hours, ROM longer than 8 hours, more than six sterile vaginal exams, use of oxytocin, or emergent indication for cesarean section (*P* = 0.53 to 0.98).

TABLE 4. Incidence of endomyometritis by factor

Race	Non-Caucasian	Caucasian	P
	15%	7%	0.004
Service assignment	Ward	Private	
	16.8%	7.8%	0.03
Anesthesia	General	Regional	
	28%	9.3%	.01
Surgery duration	>1 hour	≤1 hour	
	18%	7%	0.007
Postoperative hematocrit	<28%	≥28%	
	25.7%	8.9%	0.006

DISCUSSION

Single-dose antibiotic prophylaxis resulted in a low incidence of postpartum endomyometritis when used in high-risk patients undergoing cesarean section. No statistically significant difference in infection rate was noted regardless of whether patients received A/S (1.5 g), the first-generation cephalosporin cefazolin (1 g), or the second-generation cephalosporin cefotetan (1 g). The power of this study is such that approximately 550 additional subjects would be needed to verify that there was no difference in infection rate between the groups. The *P* values observed when comparing the incidence of endomyometritis in the three study arms ranged from 0.19–0.630, which did not suggest a trend toward differences in infection rates among the groups.

Univariate analysis implicated several clinical epidemiologic factors as predictors of endomyometritis. Risk factors associated with an increased incidence of postoperative endomyometritis included non-Caucasian ethnicity, ward-service assignment, obesity, use of general anesthesia, prolonged operating time, and the presence of postoperative anemia. Factors found not to be associated with an increased incidence of endomyometritis included prolonged labor, prolonged rupture of fetal membranes, a high number of recorded vaginal examinations, the use of oxytocin, and an emergent indication for surgery. Prior studies have implicated prolonged ROM, many vaginal exams, and protracted duration of labor in postpartum uterine infection. The mean values for these three parameters in this study were 7.3 hours, 4.6 exams, and 12.7 hours respectively. Perhaps there were not enough patients with excessive values when evaluating these risk factors to see a significant influence.

The findings of the present study as well as others^{9–11} suggest that the modified penicillin A/S may be an effective prophylactic antibiotic for decreasing the incidence of postoperative endomyometritis in women undergoing high-risk cesarean sections. This agent and first- and second-generation cephalosporins administered as a single dose appear to represent suitable alternative therapies for prophylaxis against postpartum endomyometritis.

REFERENCES

- Sweet RL, Ledger WJ: Puerperal infections morbidity. *Am J Obstet Gynecol* 117:1093–1100, 1973.
- Gassner CG, Ledger WJ: The relationship of hospital-acquired maternal infection to invasive intrapartum monitoring techniques. *Am J Obstet Gynecol* 126:33–37, 1976.
- Wong R, Gee CL, Ledger WJ: Prophylactic use of cefazolin in monitored obstetric patients undergoing cesarean section. *Obstet Gynecol* 51:407–411, 1978.
- Young R, Platt L, Ledger WJ: Prophylactic cefoxitin in cesarean section. *Surg Gynecol Obstet* 157:11–14, 1983.
- Benigno BB, Ford LC, Lawrence WD, et al.: A double-blind, controlled comparison of piperacillin and cefoxitin in the prevention of post-operative infection in patients undergoing cesarean section. *Surg Gynecol Obstet* 162:1–7, 1986.
- McGregor JA, French JI, Mekowski E: Single dose cefotetan versus multi-dose cefoxitin for prophylaxis in cesarean section in high risk patients. *Am J Obstet Gynecol* 154:955–960, 1986.
- Duff P, Robertson AW, Read JA: Single dose cefazolin vs cefonicid for antibiotic prophylaxis in cesarean delivery. *Obstet Gynecol* 70:718–721, 1987.
- Berkeley AS, Hirsch JC, Freedman KS, et al.: Cefotaxime for cesarean section prophylaxis in labor. Intravenous administration vs lavage. *J Reprod Med* 35:214–218, 1990.
- McGregor JA, Crombleholme WR, Newton E, et al.: Randomized comparison of ampicillin-sulbactam to cefoxitin and doxycycline or clindamycin and gentamicin in the treatment of pelvic inflammatory disease or endometriosis. *Obstet Gynecol* 83:998–1004, 1994.
- Hemsell DL, Wendel GD, Hemsell PG, et al.: Inpatient treatment for uncomplicated and complicated acute pelvic inflammatory disease: ampicillin/sulbactam versus cefoxitin. *Infect Dis Obstet Gynecol* 1:123–129, 1993.
- Lewis DF, Fontenot MT, Brooks GG, et al.: Latency period after preterm premature rupture of membranes: a comparison of ampicillin with and without sulbactam. *Obstet Gynecol* 86:392–395, 1995.



Hindawi
Submit your manuscripts at
<http://www.hindawi.com>

