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Prophylactic antibiotic prescription for cesarean section

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Abstract

Objectives. To assess the use of prophylactic antibiotics for cesarean section, and to identify factors associated with a doctor's intraoperative prescription.

Design. A hospital-based, cross-sectional study.

Study participants. All 967 medical records of women undergoing cesarean section from January 1998 to February 1999 in a university hospital, Southern Thailand.

Main measures. Independent variables consisted of patient and doctor factors. The outcome variable was whether any antibiotics were given intraoperatively. Multivariate logistic regression with random effects was used to identify factors associated with the doctor's prescription.

Results. Prophylactic antibiotics were prescribed in 82% of all patients. One hundred and eighty-eight patients (21%) received antibiotics postoperatively. Of the patients receiving intraoperative antibiotics after cord clamping, 8% received only a single dose and 53% received an additional postoperative prescription. The most commonly used antibiotic was ampicillin. Intraoperative prescription was significantly associated with longer duration of ruptured membranes, higher number of vaginal examinations and doctors' age. Doctors aged 30–39 years had three and seven times the likelihood of prescribing intraoperative antibiotics compared with their younger and older colleagues, respectively.

Conclusions. Administration of single-dose prescriptions was still an uncommon practice. Prophylaxis was given more commonly to patients with well known risks for infection, and was given by doctors aged 30–39 years.

Keywords: antibiotic prescription, cesarean section, prophylactic antibiotics

A systematic review in the Cochrane Library concluded that antibiotic prophylaxis in all cases of cesarean section significantly reduced the incidence of puerperal infection [1]. Time of drug administration was different from other general surgeries because of the fetus. The intraoperative administration of a drug shortly after cord clamping is considered to be as effective as administering the drug preoperatively. The recommended duration of prescribed antibiotics in many trials has been reduced from ≥ 5 days to 3 days, then to 24 hours, then to three doses and finally to a single dose [2–4]. A second review of the Cochrane Library concluded that a single dose of ampicillin or first-generation cephalosporins has similar efficacy in reducing puerperal infection. In addition, the benefits are not different from broad-spectrum cephalosporins [4].

Despite such well established evidence, there have been very few studies on how doctors prescribe antibiotic prophylaxis to patients who have had cesarean section [5,6]. One survey study investigated the guidelines for patient selection and drug regimens in an obstetric department in Denmark [5]. Another study evaluated the change of antibiotic prophylaxis in cesarean section through an educational program [6]. Neither study focussed on the actual practice or predictor analysis for prophylactic antibiotic prescription. Documented guidelines regarding antibiotic prophylaxis for cesarean section have never been established in our department. Therefore, this study aimed to assess prophylactic antibiotic prescription with regard to usage, time of administration, type of antibiotics, and number of doses, and to identify factors associated with intraoperative antibiotic prescription.

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Methods

This study was undertaken in a university hospital in Southern Thailand. Setting a confidence interval (CI) of 95%, the estimated prevalence of single-dose antibiotic prophylaxis in cesarean section from a pilot study of 10% and an acceptable error of 2%, at least 865 patients undergoing cesarean section were required to estimate the prevalence of single-dose antibiotic prescription. Therefore, all medical records of patients who underwent cesarean sections from January 1998 to February 1999 were reviewed retrospectively. Patients with a history of penicillin allergy or any evidence of infection before the cesarean sections were excluded. These were because the doctor's decision for giving antibiotic prophylaxis may be constrained by a history of penicillin allergy in some cases of elective cesarean sections, and women with evidence of infection before their cesarean sections were given antibiotic treatment for specific underlying infections.

The patterns of prophylactic antibiotic prescriptions were classified as no antibiotics, intraoperative antibiotics only, postoperative antibiotics only, and combined intra- and postoperative antibiotics. Prophylactic antibiotics are defined as antibiotics given to prevent infections [7]; therefore, women having puerperal morbidity classified as the evidence of febrile morbidity in this study were excluded to rule out the therapeutic treatment. Puerperal morbidity was defined as temperature $\geq 38°C$ occurring on any two of the first 10 postpartum days, exclusive of the first 24 hours, taken by mouth using a standard technique at least four times daily [8].

In the analysis for predictors of intraoperative antibiotic prescription, the dependent variable was modeled as prescribing (1)/not prescribing (0) intraoperative antibiotics. The potential predictor variables consisted of both patient and doctor variables. Patient variables included age, parity, gestational age at delivery, body mass index (BMI), type of service (non-private versus private), duration of labor, duration of ruptured membranes, number of vaginal examinations, and indication for cesarean section (elective versus non-elective). Elective cesarean section was defined as cesarean sections performed before the presence of labor and/or ruptured membranes. Doctor variables comprised gender, age, and years after residency training. The doctors who performed the cesarean sections were either residents or faculty members who decided on the use of prophylactic antibiotic prescription.

The association between the independent and dependent variables was evaluated by univariate analysis using chi-square test. Multivariate logistic regression with random effects was employed for identification of factors associated with the doctor's intraoperative prescription because the observed patients were nested in an individual doctor; therefore, models with random effects were taken into account. All patient and doctor variables were initially included in the full multiple logistic regression model. The exploratory significant variables were defined by the likelihood-ratio test with a probability value of 0.2. The significant variables for intraoperative prophylactic prescription were concluded in the final model with a *P*-value of 0.05. Missing data in this study were handled as one stratum of the variable for analysis. Any significant variables with missing data were tested for a significance of stratum of known data.

Table 1 Patient characteristics

Characteristics	*n* (%)
Age[1] (years)	
<25	108 (12.3)
25–29	255 (29.0)
30–34	305 (34.7)
≥35	211 (24.0)
Antenatal care[2]	
No	9 (1.0)
Yes	870 (99.0)
Gestational age[3] (years)	
<34	17 (1.9)
34–36	47 (5.4)
≥37	815 (92.7)
Most common indications for cesarean section	
Previous cesarean section	328 (37.3)
Cephalopelvic disproportion	249 (28.3)
Fetal distress	102 (11.6)
Breech presentation	67 (7.6)
Placenta previa	33 (3.7)
Premature ruptured membranes with failed induction	26 (3.0)
Pregnancy induced hypertension	12 (1.3)
Twins pregnancy	11 (1.2)
Failed induction	9 (1.0)
Transverse lie	6 (0.7)

[1]Mean ± standard deviation (SD), 30.7 ± 5.3 years.
[2]Mean of number of antenatal care ± SD, 9.2 ± 3.2.
[3]Mean ± SD, 38.4 ± 1.7 weeks.

Results

There were 967 cesarean deliveries in this period, and 923 patients were eligible according to the inclusion and exclusion criteria. Forty-four patients were excluded, 21 for a history of penicillin allergy, 13 for antibiotic use within the previous 7 days, four for fever (>37.8°C), one for chorioamnionitis (fever, uterine tenderness, maternal and fetal tachycardia), and five for combined fever and antibiotic use within the previous 7 days. Medical records were available for 879 (95%) patients. Table 1 shows patient characteristics. The obstetric complications were the five most common indications for cesarean section: previous cesarean section, cephalopelvic disproportion, fetal distress, breech presentation, and placenta previa.

Eleven of 12 patients with gestational diabetes (92%) received one to four doses of prophylactic antibiotics. One hundred and fifty-eight patients (18%) did not receive any

antibiotics. Among patients who received prophylactic antibiotics, 188 patients (21%) received only postoperative antibiotics while 533 patients (61%) received intraoperative antibiotics after cord clamping (8% for single dose only and 53% for additional postoperative prophylactic antibiotics). Ninety-four percent of patients who were prescribed intravenous postoperative antibiotics received them within the first postoperative day. After excluding the cases with puerperal morbidity, subsequent oral antibiotics were still prescribed in 55% of patients. The most common intraoperative prophylactic antibiotic was 2 grams of ampicillin (99.2%).

Thirty-one doctors who managed the eligible patients consisted of 15 residents and 16 faculty members. All doctors prescribed prophylactic antibiotics in at least some patients undergoing cesarean section. The predictor and outcome variables are shown in Tables 2 and 3. Prophylactic intraoperative antibiotic prescription was more common in nulliparous patients, in patients with a high body mass index (BMI), longer duration of labor or ruptured membranes, and higher number of vaginal examinations, and in those undergoing emergency cesarean section. Senior doctors prescribed prophylactic antibiotics less frequently than younger ones. Ten percent of the patients had missing data on BMI because of no record of height or weight on the day of surgery.

Table 4 demonstrates the procedures for developing the logistic model with random effects using probability values of the likelihood-ratio test. In the full model analysis, missing data on BMI (10%) in this study were handled as one stratum of the variable. The data showed that known values of BMI were not significant predictors, but missing values of BMI were independently associated with an increased probability of intraoperative antibiotic prescription [adjusted odds-ratio (OR) 1.8, 95% CI 1.1–3.0]. In-depth exploration of missing BMI data indicated that the patients in this group were not related to other independent factors for intraoperative prescription, but were more likely to be private patients and to be patients of one doctor who often prescribed intraoperative antibiotics. When that doctor was excluded from the model, the status of BMI as known or missing was no longer a significant predictor.

In the final model of multiple logistic regression analysis, the factors significantly associated with the prescription of intraoperative antibiotic prophylaxis were duration of ruptured membranes, number of vaginal examinations, and age of doctor (Table 5). The presence of ruptured membranes was a highly significant factor associated with intraoperative prophylactic antibiotic prescription. There was no significant random-effects variance among doctors for prescribing intraoperative prophylactic antibiotics ($P = 0.09$).

Among 671 patients who did not develop febrile morbidity or other postoperative infections, 429 patients (64%) received one to three doses of perioperative antibiotics, and 242 patients (36%) received more than three doses and/or oral prophylactic antibiotics. Only 'years after residency training' was a significant predictor for giving less or more than three doses of perioperative antibiotics. Doctors who completed their residency training >5 years ago gave more than three doses of perioperative antibiotics ($P = 0.03$; OR 1.8; 95% CI 1.0–3.1), but those who completed their residency training 1–5 years ago gave that regimen less (OR 0.6; 95% CI 0.2–1.2) when compared with residents.

Table 2 Patient variables and outcome variable

Patient variables	Intraoperative antibiotic prescription	
	No, *n* (%) (*n* = 346)	Yes, *n* (%) (*n* = 533)
Parity[1]		
Nulliparity	112 (25.6)	325 (74.4)
Multiparity	234 (52.9)	208 (47.1)
Gestational age (weeks)		
<37	30 (46.9)	34 (53.1)
≥37	316 (38.8)	499 (61.2)
Body mass index[1]		
<24	64 (45.7)	76 (54.3)
25–29	167 (37.4)	280 (62.6)
≥30	75 (39.5)	115 (60.5)
Unknown	40 (39.2)	62 (60.8)
Type of service		
Non-private	133 (39.5)	204 (60.5)
Private	213 (39.3)	329 (60.7)
Duration of labor (hours)[1]		
0	202 (56.1)	158 (43.9)
1–6	58 (30.7)	131 (69.3)
7–12	60 (29.4)	144 (70.6)
>12	26 (20.6)	100 (79.4)
Duration of ruptured membranes (hours)[1]		
0	273 (53.1)	241 (46.9)
1–6	43 (21.9)	153 (78.1)
7–12	17 (14.7)	99 (85.3)
>12	13 (24.5)	40 (75.5)
Number of vaginal examinations[1]		
0	210 (56.4)	162 (43.6)
1–5	126 (29.5)	301 (70.5)
≥6	10 (12.5)	70 (87.5)
Indication of cesarean section[1]		
Elective	194 (56.4)	150 (43.6)
Non-elective	152 (28.4)	383 (71.6)

[1]Significant association between independent and dependent variables (*P* value <0.05).

Discussion

Prophylactic antibiotics were prescribed in cases of cesarean section in our study hospital with a proclivity of 2 grams of intraoperative ampicillin prescription. The proportion of patients receiving a single dose of antibiotics after cord clamping as suggested by the systematic review was very

Table 3 Doctor variables and outcome variable

Doctor variables	Intraoperative antibiotic prescription	
	No, *n* (%) (*n* = 346)	Yes, *n* (%) (*n* = 533)
Age (years)[1]		
<30	156 (38.8)	246 (61.2)
30–39	47 (17.7)	218 (82.3)
≥40	143 (67.4)	69 (32.6)
Gender[1]		
Male	232 (37.0)	395 (63.0)
Female	114 (45.2)	138 (54.8)
Years after residency training[1]		
0	128 (39.0)	200 (61.0)
1–5	44 (31.4)	96 (68.6)
≥6	174 (42.3)	237 (57.7)

[1]Significant association between independent and dependent variables (*P* value <0.05).

Table 5 Final model of patient and doctor factors for the prescription of intraoperative antibiotic prophylaxis from multiple logistic regression with random effects

Factors	OR	95% CI
Duration of ruptured membranes (hours)		
0	1	–
1–6	2.9	1.8–4.8
7–12	4.1	2.0–8.2
>12	2.5	1.1–5.5
Number of vaginal examinations		
0	1	–
1–5	1.5	1.0–2.4
≥6	3.2	1.3–7.9
Age of doctor (years)		
<30	1	–
30–39	3.0	1.7–5.5
≥40	0.4	0.2–0.9
Random-effects variance[1]	*P* = 0.09	

OR, odds ratio; 95% CI, 95% confidence interval.
[1]*P*-value of random-effects variance.

low, whereas a combination of intraoperative and additional postoperative prescription was common. Almost all patients who were prescribed postoperatively received intravenous antibiotics within the first postoperative day, and about half subsequently received oral antibiotics. Prescription of antibiotic prophylaxis was influenced by a 'high risk' status of the patient, but not on a universal basis as directed by the evidence of its efficacy.

Prophylactic antibiotics were most commonly used for patients who had undergone cesarean section; however, there was a wide variation in the time of administration, type of antibiotic, number of doses, and indications for prescription. In this study, most patients were prescribed antibiotics for prophylaxis after cord clamping, but some patients were prescribed postoperatively. A questionnaire survey from an obstetric clinics in Denmark found that 44% of prophylactic antibiotics were administered after cord clamping and 27% were applied before skin incision [5]. Evidence showed that antibiotics given after cord clamping did not give less protection than those given before the procedure [9]. In addition, early administration resulted in masking neonatal

Table 4 Model of multiple logistic regression with random effects for all patient and doctor factors using the significance of likelihood-ratio test

Variables	*P* value of likelihood-ratio test		
	Initial model[1]	Intermediate model[2]	Final model[2]
Age of patient	0.44	–	–
Parity	0.18	0.08	–
Gestational age	0.26	–	–
BMI	0.02	0.02 (0.08)[3]	–
Type of service	0.46	–	–
Duration of labor	0.38	–	–
Duration of ruptured membranes	<0.01	<0.01	<0.01
Number of vaginal examinations	0.13	0.03	0.01
Indication of cesarean section	0.31	–	–
Gender of doctor	0.77	–	–
Age of doctor	0.02	<0.01	<0.01
Years after residency training	0.90	–	–

[1]Probability value for inclusion in the model is 0.2 by the likelihood-ratio test.
[2]Test of the significant variables for including in the model (*P* value <0.05).
[3]*P* value for the likelihood-ratio test of all stratum of BMI is 0.02, but that of the known stratum of BMI is 0.08.

infections or increasing the cost for neonatal septic work up, thus it should be avoided [10]. Since 1978, most published trials have administered antibiotics after cord clamping [4].

Prescribed antibiotics varied among ampicillin, cefazolin, cefuroxime or cefoxitin in the observational study on post-cesarean infection after antibiotic prophylaxis [11,12]. The summary of a Swedish–Norwegian Consensus Conference for antibiotic prophylaxis in surgery recommended that second-generation cephalosporins as an intravenous single dose be used for all emergency and some elective cesarean sections [7]. A systematic review also recently concluded that a single dose of ampicillin or first-generation cephalosporins has been established to be as efficacious as the other extended broad-spectrum antibiotics [4]. Serum levels of free individual drug above the minimal inhibitory concentration are needed in antibiotic applications [13,14]. In addition, the degree of colonization and drug resistance of organisms causing antibiotic failure need to be considered in each area. Fortunately, healthy pregnant women undergoing cesarean section are unlikely to be colonized with drug-resistant organisms from the community prior to surgery [15]. Thus, high-spectrum antibiotics should not be required and this cost can be reduced, especially in developing countries. The most commonly used antibiotic in this study was ampicillin, which is cheaper and of lower spectrum than cephalosporins.

A single dose of prophylactic antibiotics should be sufficient if given intraoperatively after cord clamping. Additional antibiotics given prior to cord clamping or after (e.g. for 24-hour postpartum or longer) did not increase the protection [4]. Yet in our study and other previous studies [5,6,11, 12,16], these additional dosages were often administered, although most antibiotics were not prescribed beyond 24 hours. The question of why nearly half of the patients who received postoperative prophylactic antibiotics were prescribed subsequent oral antibiotics regardless of any post-cesarean infections in this study was unanswered and needs further study. The cases of post-cesarean infection were excluded for calculation of prophylactic oral antibiotics in order to reduce the bias of oral antibiotics for infectious treatment.

Administration of prophylactic antibiotics in this study was mostly confined to patients with a high risk for postoperative infection, as in many previous studies [5,7,8,17]. In contrast, the Cochrane Review, which collected trials to re-analyze by meta-analysis, revealed that antibiotic prophylaxis is beneficial for both elective and non-elective patients [1]. However, as our study collected data before this Cochrane Review was published, it is not surprising that prophylaxis was omitted among elective patients. One recent study examined the use of antibiotic prophylaxis in 50 consecutive cesarean sections in eight centers in five countries. There were wide variations in the time of drug administration, type of drug, and the percentage of single-dose regimen [18]. The only significant predictor among the doctor variables in our study was age of doctor. Intraoperative prophylactic prescription was more common in young faculty members, but less so in the senior faculty members when compared with residents. This may result from the fact that antibiotic prophylaxis for cesarean section was not commonly used in the past. However, when the antibiotics were given, the senior faculty members tended to use more than three doses of antibiotics and/or oral antibiotics, as in past practice. Why the middle-age group of doctors had the highest likelihood of giving antibiotics is not known. In-depth studies on behavioral aspects of the doctors should be carried out.

In the analysis of predictors for intraoperative prescription, patient and doctor variables were considered because individual doctors decided to prescribe prophylactic antibiotics with respect to not only patient factors, but also based on personal judgement. In addition, multivariate logistic regression with random effects was employed to deal with the nesting of two levels of data. However, all patients of each doctor and all doctors were studied, thus there was wide variation in the numbers of patients among individual doctors. In particular, a few doctors who had a high number of patients might predominate in the representative results. The practice of antibiotic prophylaxis for cesarean section in this university hospital had a discrepancy with evidence, especially practising long-term prophylactic regimen. Further studies to identify the doctors' reasons for the practices of prophylactic antibiotic prescription for cesarean section should be conducted so that proper intervention can be planned and successfully implemented. In addition, reliable and up-to-date evidence should be disseminated as soon as possible to all doctors to encourage the best evidence-based practice.

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