ACTA FAC MED NAISS

UDC 618.5-089.888.61:615.33

Original article

ACTA FAC MED NAISS 2008; 25 (2): 61-67

Predrag Vukomanovic,
Milan Stefanovic,
Ranko Kutlesic, Jelena Milosevic

Clinic of Gynecology
and Obstetrics
Clinical Center Nis

ANTIBIOTIC PROPHYLAXIS – SINGLE CENTER EXPERIENCE

SUMMARY

This prospective, randomized, controlled trial was performed to evaluate the effectiveness of single-dose antibiotic prophylaxis versus common five-day combination antibiotic therapy in decreasing the infectious morbidity, following elective caesarean section.

Eighty-six women undergoing elective caesarean section were randomly enrolled in the study in 2 groups, 43 patients each. There was no statistical difference in the admission variables between the two groups. Group I had single-dose cefuroxime (C) 1.5 g intravenously after umbilical cord clamping; group II had common procain-benzilpenicilin (PBP) 1.600.000 IU, and gentamycin (G) 120 mg every 12h, intramuscularly, for 5 days. Postpartum complications, including febrile morbidity, wound infection, endometritis, urinary tract infection, and transient postpartum fever were recorded during hospitalization. Wound infection was the most common complication occurring in 13.95% of women in group I and 18.61 % in group II. Five-day antibiotic therapy did not decrease febrile morbidity, wound infection, endometritis and urinary tract infection. On average, women who received cefuroxime stayed in hospital a day less than those who received PBP/G (7.6 vs. 8.7 days). Four women (9.3%) in group I and five women (11.63%) in group II had microbiological evidence of wound infection. Staphylococcus aureus was the most common pathogen (48%) isolated. The same proportions in both groups (2.3% in group I and 2.3% in group II) required the antibiotic change.

Common combined antibiotic prolonged therapy in elective caesarean section did not reduce postoperative infectious morbidity in this study. According to this, it is important to emphasize that five-day combined antibiotic use is absolutely unjustified and irrational prophylaxis modality, since the antibiotic prophylaxis lasts three days at the most. Postoperative infectious morbidity rate is not lower than other acceptable modalities of antibiotic prophylaxis.

Key words: **caesarean section, antibiotic prophylaxis, infective morbidity**

Corresponding author. Predrag Vukomanovic • Phone:+381 64 11 31 526 • E-mail: pedjav@bankerinter.net

INTRODUCTION

Caesarean section is an essential widely practised operation. Over the past 3 decades, the rate of caesarean section has increased steadily, and may reach up to 25% in some centers (1). Infectious morbidity is the most common complication following caesarean section with reported rates ranging from 18% to 83%, while it was less then 10% (2) for vaginal delivery. The use of prophylactic antibiotics reduced the incidence of endometritis by two-thirds to three-quarters, and therefore justified its routine use for all women undergoing caesarean section. While the risk of postoperative infection following caesarean section is higher for emergency deliveries than for elective ones, prophylactic antibiotics have also been shown to reduce both endometritis and wound infection following elective caesarean delivery (3). Penicillins, cephalosporins, metronidazole, and combinations of clindamycin plus gentamycin have all been studied for use in prophylaxis. There does not appear to be a clear advantage of any of these antibiotics over others (4-6). There is some evidence that the combination of penicillin plus aminoglycoside may reduce febrile morbidity to a greater extent than penicillin alone. However, the increased risk of nephrotoxicity and ototoxicity with aminoglycosides should be considered. Duration of antibiotic prophylaxis and modality of therapy (one or two antibiotics) seems to be an actual queston-controversy. Which antibiotics should be used for prophylaxis, and the best prophylactic regime have yet to be de defined. The newer antimicrobials must be compared to the old standard (procain-benzilpenicillin plus gentamycin) and their clinical applicability determined (7,8).

AIMS

The aim of this study was to compare the efficacy of single-dose cefuroxime with our 5-day-standard procain-benzilpenicillin/gentamycin treatment in preventing postoperative complications (endometritis, wound infection and other febrile morbidity) in women undergoing delivery with elective caesarean section.

MATERIAL AND METHODS

This study was carried out during 2005 and 2006 at Obstetric Department of Clinical Center Nis. Eighty-six patients who planned elective caesarean section for various reasons were enrolled in the study in 2 groups, 43 patients each. Women were excluded from the study if they had received antibiotics 2 weeks prior to the operation; if they had any visible infection or increased temperature at the time of the operation; if they were allergic to any of the antimicrobials used; or if they did not wish to participate in the study.

Patients were randomized to receive either cefuroxime as single intravenous dose of 1.5 g after umbilical cord clamping or common intramuscular 1.600.000 IU/120 mg procain-benzilpenicillin/ gentamycin (PBP/G) every 12 hours for 5 days. After giving verbal consent, a complete history of the participants was taken using a standard questionaire. A physical examination was also performed. All caesarean sections were performed by a standard technique and all postoperative care followed standard clinical practice. The following postpartum complications were recorded:

1. Postoperative febrile morbidity, defined as an axillar temperature of 38.0 ºC on 2 occasions, at least 4 hours apart, excluding the first 24 hours;

2. Postoperative infection which includes:

- endometritis (fever, uterine tenderness and abnormal lochia);
- wound infection (fever, cellulitis and exudates);
- pelvic abscess (collection of puss);
- peritonitis;

3. Other febrile morbidity, e.g. urinary tract infection, transient postpartum fever.

Once febrile morbidity was identified, patients were examined to localize the potential source of infection (tonsils, breasts, chest, abdomen and pelvis). Urine analysis (urinoculture) was done, and the white-blood cell count was determined. Wound and lochia swabs were sent for culture and sensitivity testing when it was necessary. Wound morbidity was managed by local wound toilet with hydrogen peroxide, saline irrigation and iodine-povidon solution. On discharge from hospital, women were informed to report any fever, wound dehiscence or foul smelling lochia immediately, and all women were seen at four-week postnatal visit for evidence of wound dehiscence.

The duration of hospitalization, the need for therapeutic antibiotics and all neonatal data were recorded.

Obtained results were statistically processed, using X^2-test, Student t-test and Fischer exact test, and presented in Tables. P-value <0.05 was considered significant.

RESULTS

A total of 86 women were recruited to the study; 43 were randomized to cefuroxime and 43 to PBP/G. The two groups were similar with respect to age, parity, gestational age, weight, preoperative haemoglobin values and body temperature *(Table1)*.

Table 1. Reproductive biohumoral characteristics

	Cefuroxime group n = 43				Procain-benzilpenicillin/gentamycin group n = 43			
Age (years)	28.6 ± 1.35				28.1 ± 1.44			
Parity	primipara		multipara		primipara		multipara	
	15	34.88%	28	65.12%	12	27.91%	31	72.09%
Gestational age (weeks)	38.6 ± 1.12				38.67 ± 1.15			
Body weight (kg)	78.8 ± 5.34				79.1 ± 6.17			
Preoperative HgB (g/L)	95.6 ± 7.49				95.9 ± 7.19			
Body temperature (ºC)	36.6 ± 0.12				36.7 ± 0.11			

The indications for caesarean section were similar in both groups *(Table 2)*. Women who had previous caesarean section constituted over half the women in each group.

Table 2. Indications for caesarean section

	Cefuroxime group n = 43		Procain-benzilpenicillin/gentamycin group n = 43	
Previous caesarian section	30	69.8%	32	74%
Fetal distress	4	9.3%	3	6.97%
Maternal distress	2	4.65%	3	6.97%
Malpresentation	6	13.9%	3	6.97%
Others	1	2.33%	2	4.65%

The surgical data are presented in Table 3. The type of skin incision, lenght of surgery, presence of adhesiones and silent uterine rupture, excessive blood loss and type of skin closure were not significantly different between the groups.

The postpartum morbidity and maternal outcome are shown in Tables 4 and 5. There was no significant difference between the groups regarding postoperative maternal outcome. Although there was no difference in morbidity, the women who received cefuroxime stayed in hospital a day shorter than those who received procain-benzilpenicillin/gentamycin and this was statistically significant ($p < 0.05$).

Table 3. Presented surgical data

	Cefuroxime group n = 43				Procain-benzilpenicillin/gentamycin group n = 43			
Pfanennstiel	35		81.39%		37		86.05%	
Midline	8		18.61%		6		13.95%	
Length of operation (min)	48.55 ± 8.31				51.12 ± 5.42			
Adhesiones	7		16.28%		5		11.63%	
Silent rupture of uterus	2		4.65%		1		2.33%	
Abdominal skin closure	Single suture		Dermodermal suture		Single suture		Dermodermal suture	
	26	60.46%	17	39.54%	29	67.44%	14	32.56%
Atonia	0		0%		1		2.33%	
Blood loss	1		2.33%		1		2.33%	

Table 4. Postpartum morbidity

	Cefuroxime group n = 43				Procain-benzilpenicillin/gentamycin group n = 43			
Postpartum morbidity	n = 9 (20.93%)				n = 11 (25.58%)			
	With t°		Without t°		With t°		Without t°	
	7	16.28%	2	4.65%	8	18.6%	3	6.98%
Wound infection	4	9.3%	2	4.65%	5	11.63%	3	6.98%
Cellulitis erythema	3	6.98%	0	0%	3	6.98%	0	0%
Serous / serosanguinous	0	0%	2	4.65%	1	2.32%	3	6.98%
Purulent exudata	1	2.32%	0	0%	1	2.32%	0	0%
Endometritis	1	2.32%	0	0%	1	2.32%	0	0%
Urinary infection	0	0%	0	0%	1	2.32%	0	0%
Transient postpartum fever	2	4.65%	0	0%	1	2.32%	0	0%

Table 5. Maternal outcome

	Cefuroxime group n = 43		Procain-benzilpenicillin/gentamycin group n = 43	
Resuture	2	4.64%	2	4.64%
Days in hospital*	7.6		8.7	
Microbiologically diagnosed wound infection	4	9.3%	5	11.6%
Antibiotic change	1	2.32%	1	2.32%

** p-value <0.05 – statistically significant*

Postpartum complications occured in 9 (20.93%) women given cefuroxime: 6 (13.95%) with wound infection; 1 (2.32%) with endometritis and 2 (4.65%) with transient postpartum fever. Out of 11 women (25.58%) with postpartum complications in PBP/G group, there were: 8 (18.613%) with wound infection; 1 (2.32%) with endometritis; 1 (2.32%) with urinary tract infection; and 1 (2.32%) with transient postpartal fever. Four women in group I (9.3%), and 5 in group II (11.63%) had microbiological evidence of wound infection. Staphylococus aureus was the most common pathogen occuring in 5 women (2 in group I and 3 in group II). Other isolated organisms included: group B-streptococcus (1 in group I), Pseudomonas aeroginosa (1 in group II), and Enterococcus fecalis (1 in both groups). Two women (one in each group) had endometritis. One from group I stayed in hospital for 18 days (E.colli was isolated) and the other, from group II, stayed in hospital for 26 days (Enterococcus fecalis was isolated). After the antibiotic change, the women were discharged from hospital in a healthy condition. Two women (4.64%) in both groups had wound brakedown from the 7th to 10th day of hospitalization and after therapeutic antibiotics, so wound toilet resuture was performed.

Febrile morbidity occured in 7 women (16.28%) given cefuroxime: 4 (9.3%) had fever with wound infection, 1 (2.32%) had endometritis, and 2 (4.65%) had no cause for pyrexia. Out of 8 women (18.6%) who had fever in the PBP/G group, 5 (11.63%) had fever with wound infection, 1 (2.32%) had endometritis, 1 (2.32%) had urinary tract infection, and 1 (2.32%) had transient postpartum fever. Two women in group I (4.65%) and 3 women in group II (6.98%) had postpartum morbidity without fever. Wound infection was the most common postpartum complication in both groups, occuring in 13.95% in group I and in 18.61 % in group II. The frequency of wound cellulitis, serous exudate and the presence of pus were similar in both groups. Microbiologically proved wound infections appeared in 4 (9.3%) and 5 (11.63%) cases.

In 3 women with transient postpartum fever (2 (4.65%) in group I and 1 (2.32%) in group II), their first spike in temperature in all cases was recorded within the first 24 hour and their temperatures returned to normal within 48 hours. They did not

receive therapeutic antibiotics and were all discharged in a good condition.

One woman with urinary tract infection had E. coli on culture.

DISCUSSION

Although prophylactic antibiotic medications have been shown to reduce the incidence of postoperative infectious morbidity after caesarean delivery, the most effective regimens have not been established (9). The present study of the use of prophylactic antibiotics in elective caesarean section, recruited 86 women in order to compare the risk of postpartum morbidity in two different modes of antibiotics use. One of the suggested criteria for the use of prophylactic antibiotics is that there should be a high incidence of postoperative infection exceeding 15-20% in the absence of prophylaxis (10,11). Our trial compared two regimens of prophylaxis and efficacy of a single-dose cefuroxime versus 5-day-standard PBP/G treatment.

The prevalence of febrile morbidity in 34.88%, following elective caesarean section, was comparable to figures from other institutes (12,13). Fever may occur after any surgical procedure and a low grade fever following elective caesarian section may not necessarily be a marker of infection. Some investigators excluded the first 48-hour after operation in their definition of febrile morbidity. Fever with infection focus would necessitate the commencement of an empirical antibiotic regimen prior to culture results (14).

Endometritis is another indicator of postoperative caesarean section infection. In most studies, as in the present study, it is clinically diagnosed based on fever, uterine tenderness and abnormal lochia. In some studies, it is also frequently a diagnosis of exclusion, microbiological studies on amniotic fluid and endometrial scrapings (15). Culture results are not immediately available to influence the decision to administer prophylactic antibiotics at the time of surgery. Clinical risk factors which hasten the entry of cervicovaginal organisms into the amniotic fluid such as the onset of labour, prolonged rupture of the membrans and multiple vaginal examinations are more important predictors of endometritis than the presence of organisms in the amniotic fluid. The low rate of endometritis in this study, therefore, may be explained by the fact that women having elective caesarean section with intact membranes do not have a sufficiently large inoculums of cervicovaginal organisms for colonization of the endometrium (16-18).

Wound infection was the most common postpartum complication in both groups, occuring in 13.95% in group I and in 18.61 % in group II. Although prophylactic antibiotics did not reduce the wound infection rate, the women in group I stayed in the hospital for one day less. Wound infection and endometrits contributed to all cases of prolonged hospital stay for more than one week. This concurs with the reports of other authors (19). Surgical preparation of the abdomen and a lapse in surgical technique and haemostasis can influence the infected wounds. The isolation of bacteria that is not present in the genital tract, such as Staphylococcus aureus, which is found in the skin and Pseudomonas aeroginosa, which is found in the hospital environment, lends support to this iatrogenic etiology of wound infection. Collection of blood or serous fluid in wounds may be due to lack of proper haemostasis and surgical techniques. These are excellent culture media that may result in infection if contaminated. Regarding risk factors for wound infection, only an increased body mass predisposed women to a higher infection rate. However, there was no difference in wound infection rate between cefuroksime and PBP/G. Recommendation of Sanford guide for antimicrobial therapy, from 2006, suggests that optimal antimicrobial therapy with the use of Cefazolin 1-2 g or Cefoxitim 1-2 g or Cefotetan 1-2 g or cefuroxime 1-2 g intravenously follows the chord clamping (20). The majority of wound infections did not require the use of antibiotics, but were treated by local measures of wound toilet including hydrogen peroxide, saline irrigation and iodine-povidon solution (21).

This study showed that there is no prolonged two-antibiotic regimen, compared to the single-dose antibiotic regimen of wide spectre in elective caesarian section. We suggest that antibiotic prophylaxis in elective caesarian section be applied in one dose directly after umbilical cord clamping. The proper surgical handling of tissues and meticulous haemostasis are probably of greater importance than regimen of antibiotics in reducing postoperative infectious morbidity. According to this, it is important to emphasize that five-day combined antibiotic use is absolutely unjustified and irrational prophylaxis modality, since the antibiotic prophylaxis lasts three days at the most. Postoperative infective morbidity rate is not lower than other acceptable modalities of antibiotic prophylaxis (22).

REFERENCES

1. Mahomed K. A double blind randomized controlled trial on the use of prophylactic antibiotics in women undergoing elective caesarean section. Br J Obstet Gynecol 1988; 95: 689-692.

2. Bagratee JS, Modley J, Kleinschmidt I, Zawilski W. A randomised controlled trial of antibiotic prophylaxis in elective caesarean delivery. Int J Obstet Gynecol 2001; 108:143-148.

3. Litta p. Risk factors for complicating infection after caesarean sction. Clinical and experimental obstetrics and gynecology 1995; 22: 71-75.

4. Emmons SL, Krohn M, Jackson M, Eschenbach DA. Development of wound infections among women undergoing caesarean section. Obstet Gynecol 1998; 82:759-764.

5. Meyer NL, Hosier KV, Scott K, Lipscomb GH. Cefazolin versus Cefazolin plus Metronidazole prophylaxis at Caesarean Section. Soutern Medical Journal 2003; 96:992-995

6. Mandach U. A randomised controlled trial of antibiotic prophylaxis in elective caesarean delivery. Int J Obstet Gynecol 2002; 109:1423-1424.

7. Kristensen GB, Geiter EC, Mather O. Single dose cefuroxime prophylaxis in non-elective caesarean section. Acta Obstet Gynecol Scand 1990; 69:497-500.

8. Smaill F, Hofmeyer GJ. Antibiotic prophylaxis for cesarean section. Cochrane Database Syst Rev 2002; 19:75-79.

9. Swartz WH, Grolle K, Corson SL. The use of prophylactic antibiotics in caesarean section, a review of the literature. J Reproductive Med 1999; 26:595-609.

10. Tran TS, Jamulitrat S, Chongsuvivatwong V, Geater A. A risk factor for postcaesarean surgical site infection. Obstet Gynecol 2000; 95:367-371.

11. Morales M et al. Spontaneus delivery or manual removal of the placenta during caesarean section. Int J Obstet Gynecol 2004; 111:908-912.

12. Killian CA, Graffunder EM, Vinciguera TJ, Venecia RA. Risk gactors for surgical-site infections folowing caesarean section. Infect Control Hosp Epidemiol 2001; 22:613-617.

13. Mah MW, Pyper AM, Oni GA, Memish ZA. Impact of antibiotic prophylaxis on wound infection after caesarean section in a situation of expected higher risk. Am J Infect Control 2001; 29:85-88.

14. Beattie PG, Rings TR, Hunter MF, Lake Y. Risk factors for wound infections following caesarean section. Aust N Z J Obstet Gynecol 1994; 34:398-402.

15. Horan TC, Edwards JR, Culver DH, Gaynes RP. Risk factors for incisional surgical site infections after caesarean sectons; results of 5-year multicenter study. Infec Control Hosp Epidemiol 2000; 21:145.

16. Schein M. Caesarean section. A manual for doctors. World J Surg 2006;: 30:655-657.

17. Normand MC, Damato EG. Postcesarean infection. Journal of obstetric, gynecologic and neonatal nursing 2001; 30:642-648.

18. Roberts S et al. The microbiology of post-cesarean wound morbidity. Obstet Gynecol 1993; 81:383-386.

19. Henderson E, Love EJ. Incidence of hospital-acquired associated with caesarean section. J Hosp Infect 1995; 29:245-255.

20. Gilbert DN, Moellering RC, Eliopoulos GM, Sande MA. The Samford Guide to Antimicrobial Therapy 2006; 36th Edition:125-126.

21. Yip SK, Lau TR, Rogers MS. A study on prophylactic antibiotics in caesarean section- is it worthwhile? Acta Obstet Gynecol Scand 1997; 76:547-549.

22. Rizk DEE, Nsanze H, Mabrouk MH. Systemic antibiotic prophylaxis in elective caesarean delivery. Int J Gynecol Obstet 2002; 61:245-251.

ANTIBIOTSKA PROFILAKSA – ISKUSTVO JEDNOG CENTRA

Predrag Vukomanović, Milan Stefanović, Ranko Kutlešić, Jelena Milošević

Klinika za ginekologiju i akušerstvo, Klinički centar u Nišu

SAŽETAK

Ova prospektivna, randomizirana, kontrolisana studija sprovedena je u cilju evaluacije efikasnosti primene jedne profilaktičke doze antibiotika u poređenju sa uobičajenom petodnevnom kombinovanom antibiotskom terapijom u smanjenju infektivnog morbiditeta nakon elektivnog carskog reza.

U studiju je uključeno 86 žena porođenih elektivnim carskim rezom, koje su podeljene u dve grupe od po 43 žene. Nema statističke razlike u prijemnim karakteristikama između ove dve grupe. Prva grupa je primala jednu dozu cefuroksima (C) od 1,5 g intravenski nakon klemovanja pupčanika. Druga grupa je primala prokain-benzilpenicilin (PBP) u dozi 1.600.000 IJ i gentamicin (G) 120 mg intramuskularno svakih 12 sati 5 dana. Postpartalne komplikacije, uključujući febrilni morbiditet, infekciju rane, endometritis, urinarnu infekciju i prolaznu postpartalnu groznicu bile su zabeležene tokom hospitalizacije. Infekcija rane je bila najčešća komplikacija koja se javila u 13,95% žena u prvoj grupi i 18,61% u drugoj grupi. Petodnevna antibiotska terapija nije smanjila febrilni morbiditet, infekciju rane, endometritis i urinarnu infekciju. U proseku, žene koje su primale cefuroksim ostale su u bolnici 1 dan kraće u odnosu na žene iz druge grupe koje su primale PBP/G (7,6 u odnosu na 8,7 dana). Četiri žene (9,3%) u prvoj grupi i pet (11,63%) u drugoj grupi imale su mikrobiološki dokazanu infekciju rane. Staphylococcus

aureus je bio najčešće izolovani patogen (48%). Isti broj žena u obe grupe (2,3% u prvoj i 2,3% u drugoj grupi) zahtevao je promenu antibiotika.

Uobičajena produžena kombinovana antibiotska terapija kod elektivnog carskog reza ne redukuje postoperativni infektivni morbiditet u ovoj studiji. U skladu sa tim, važno je istaći da petodnevna kombinovana primena antibiotika predstavlja apsolutno neopravdan i neracionalan modalitet profilakse, budući da antibiotska proifilaksa traje najduže tri dana. Postoperativni infektivni morbiditet nije niži u odnosu na druge prihvatljive modalitete antibiotske profilakse.

Ključne reči: **carski rez, antibiotska profilaksa, infektivni morbiditet**