Original Article

Antibiotic prophylaxis for hysterectomy and cesarean section: Amoxicillin-clavulanic acid versus cefazolin

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Abstract

Objective: To compare amoxycillin-clavulanic acid with cefazolin as short term antibiotic prophylaxis in women undergoing hysterectomy and elective cesarean section. **Method:** Sixty women undergoing hysterectomy were randomly assigned either to 2.4g intravenous amoxycillin-clavulanic acid (AMX/CL) or 2g cefazolin 30 min before hysterectomy. One hundred and twenty two women delivered by elective cesarean were randomized to a single dose of either of the above antibiotics at cord clamping. Each patient was assessed daily until discharge for evidence of febrile status and the presence of infection at the operative site and urinary tract. **Results:** Infectious morbidity was found in 11% and 12.5% of hysterectomy patients in AMX/CL and cefazolin groups respectively. Ten women had post-cesarean infections (six AMXCL, four cefazolin, P=0.51) **Conclusion:** Broad spectrum amoxycillin-clavulanic acid was not superior to cefazolin in the prevention of postoperative infection when given as prophylaxis in hysterectomy and elective cesarean cases.

Key words : antibiotic prophylaxis, hysterectomy, abdominal, vaginal, cesarean delivery, elective, emergency

Introduction

Hysterectomy and cesarean section are the most commonly preformed operations among inpatients in Kasturba Hospital. The two most frequent complications of these surgeries are fever and operative site infection. Many studies¹ have been published in recent years stressing the need for antimicrobial prophylaxis in hysterectomy. Women undergoing elective cesarean section are considered low risk

population. Although serious infectious complications are uncommon in this group, a literature survey^{2,3,4} demonstrated that prophylactic antibiotics significantly reduced the risk of endometritis and wound infection.

Hysterectomy is performed through a contaminated field and it is the mixed aerobic / anaerobic bacterial flora of the lower genital tract that serves as a reservoir for most of the pathogens associated with postoperative sepsis. The use of prophylactic antibiotics in hysterectomy and cesarean section in our hospital is not standardized and is determined by the consultant in charge of the case. The most commonly used regimen is to give three doses of cefazolin intravenously. However cefazolin is not active against anaerobes which are the potential pathogens in the vaginal flora. So theoretically cefazolin due to its limited spectrum does not meet the guidelines as an ideal agent for prophylaxis. Amoxicillin and the beta-lactamase

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inhibitor clavulanic acid has been shown to have an increased spectrum of activity against a wide variety of aerobic and anaerobic bacteria. Against this background, a prospective trial was performed to compare amoxicillin-clavulanic acid (AMX/CL) with cefazolin in preventing sepsis following hysterectomy and elective cesarean cases.

Methods

Women who were scheduled to undergo hysterectomy for benign disease and elective cesarean delivery were enrolled in this trial. The cesarean was considered elective if the procedure was performed in the absence of labor and before rupture of membranes. We excluded patients who gave history of hypersensitivity to penicillin or cephalosporin; or signs of pre-existing infections and those who had received antibiotic therapy within the last seven days prior to surgery. The patients received information concerning objectives of the trial prior to surgery and written consent was obtained. The study protocol was approved by the ethical committee of the hospital.

Patients were randomly allocated to one of the two regimens: amoxycillin-clavulanic acid 2.4g (Augmentin, Glaxo Smith Kline) and Cefazolin 2g (Reflin, Ranbaxy). Study medication was given intravenously at the time of induction of anesthesia 15-

30 min before incision). In the case of extensive blood loss (>1000 ml) or a surgical duration of longer than 3 hrs, a second dose of the antibiotic was administered. The second dose was given 4 hrs after the initial dose of antibiotic. In the group of patients undergoing cesarean delivery, the medication was administered as a single dose immediately after clamping the umbilical cord. Surgery was performed by the staff gynecologists or the third year residents with faculty supervision. In women who underwent vaginal hysterectomy for prolapsed the catheter was retained for three days.

After surgery, each patient was assessed daily until they were discharged from the hospital. Two main outcome measures of this study were fever and infection. Febrile morbidity was defined as a temperature of ≥ 100.40 F recorded on at least two successive occasions 6 hrs apart, excluding the first 24 hrs after surgery. Infection of one of more sites was diagnosed by clinical symptoms and signs and /or laboratory tests. The infections included abdominal wound infection, pelvic cellulitis, vaginal cuff infection, or urinary tract infection (both symptomatic and asymptomatic) Pelvic cellulitis was diagnosed by the triad of increasing lower abdominal discomfort, temperature elevation and increasing tenderness to gentle deep lower abdominal palpation. The patients in the cesarean section group were followed up for the development of endometritis (i.e. fever, uterine tenderness and offensive lochia). All

Table 1. Characteristics of the patients in the two surgical groups

	Hysterectomy		Cesarean delivery (CD)		P
	AMX/CL	Cefazolin	P	AMX/CL	Cefazolin
Number of patients	36	24		55	67
Mean age, years(SD)	47.6(7)	43.2(4)	0.02	28.4(4)	27.1(3)
BMI kg/m2 (SD)	23.7(4)	23(2)	0.5	24.5(3)	24(3)
Associated systemic disease	6	4	0.05	5	2
Type of surgery	TAH±BSO n=24	TAH±BSO n=21		Primary CD n=32	Primary CD n=34
	VH/LAVH n=12	VH/LAVH n=3 n=12		Repeat CD n=12	Repeat CD n=12

Table 2. Risk factors for developing postoperative infection

	Hysterectomy			Cesarean section		
	AMX/CL	Cefazolin	P	AMX/CL	Cefazolin	P
Mean duration of operation, min (SD)	150.9(39)	147.2(34)	0.71	45.3(3.6)	45.5(3.3)	0.73
Mean blood loss, mL (SD)	441.1(135)	508.3(207)	0.13	567.2(165)	523.8(147)	0.22
Mean days of catheterization (SD)	1.7(0.9)	1.2(0.6)	0.02	1	1.01(0.1)	0.36

Table 3. Incidence of postoperative infections and duration of postoperative hospitalization

	Hysterectomy		P	Cesarean delivery (CD)		
	AMX/CL N=36(%)	Cefazolin N=24(%)		AMX/CL N=55(%)	Cefazolin N=67(%)	P
Mean postoperative hospital stay - days	8.6	9.5	0.27	10.6	9	0.46
Wound infection	2(5.5)	0	1	3(5.5)	2(2.9)	0.82
Pelvic cellulitis	0	1(4.2)	0.84	-	-	-
Endometritis	-	-	-	1(1.8)	1(1.5)	1
Asymptomatic bacteriuria	2(5.5)	2(8.3)	1	2(3.6)	1(1.5)	0.76
Total infections	4(11)	3(12.5)	1	6(10.9)	4(5.9)	0.51

the women were evaluated for six weeks postoperatively in order to determine any late morbidity.

Differences in continuous variables were analyzed with student-t test for normally distributed data and the Mann Whitney test for skewed data. Differences in discrete variables were analyzed by using Yates corrected Chi square test with one degree of freedom. A p value of <0.005 was considered significant.

Results:

The study group consisted of 182 patients from April 2004 to September 2005 who underwent hysterectomy

(n=60) and cesarean delivery (n=122). The characteristics of the study patients are presented in Table 1. No significant differences were found between the two treatment groups with respect to clinical characteristics except the age in women who had hysterectomy. This might be due to the fact that ten subjects with genital prolapsed were included in the AMX/CL group and were significantly older than the comparable cefazolin group. Risk factors for developing postoperative infection are presented in Table 2. In the hysterectomy group, 26 subjects received a second dose of antibiotic for massive blood loss and prolonged surgery. Both drugs were very well tolerated. One case of diarrhea was observed in the AMX/CL group and no side effects were observed with

cefazolin.

Six women (10%) developed febrile morbidity following hysterectomy. Most of these women had received packed cells for decreased hemoglobin postoperatively. None exhibited symptoms or physical findings of clinical infection, and none received additional antibiotics. Two patients (1.6%) who had undergone cesarean section developed febrile episodes and the fever was caused by congestion of the breasts. Table 3 summarizes the rates and types of infections observed in the two surgical groups. The patients who developed pelvic cellulitis were treated with parenteral antibiotics. Endometritis was reported in two patients who underwent cesarean delivery. In the AMX/CL group, the patients responded promptly to oral antibiotics. One lady who had received cefazolin developed late endometritis. She was rehospitalized and managed with combination antimicrobial therapy. None of the patients in this study developed postoperative urinary tract infection. Hospital stay was computed beginning with the day of surgery. The postoperative hospitalization was similar for both the drugs.

Discussion

Many of the studies that have supported the development of antimicrobial prophylaxis guidelines are quite old. Moreover there is a great variation in the use of antimicrobial prophylaxis by surgeons during hysterectomy. Triolo⁵ and Kocak⁶ have evaluated AMX/CL as a prophylactic antibiotic for laparotomic gynecologic surgery. They included clean procedures such as adnexectomy, where prophylactic antibiotics are not indicated⁷. So, in our study we included only abdominal and vaginal hysterectomy. A one day point prevalence study performed in our hospital (November 2003) for infectious morbidity following cesarean delivery was found to be 15%. Most of the authorities⁸ suggested that prophylactic antibiotics should be considered for all elective cesarean deliveries in which the combined incidence of endometritis and wound infection exceeds 5%. So, in this study, we decided to administer antibiotic prophylaxis for the cesarean patients.

The incidence of febrile morbidity in the hysterectomy group was 10%. This data is consistent with that reported by Chongsomchai et al⁹. Hemsell et al¹⁰ believe that febrile morbidity per se does not indicate significant infection, and hence should not be included

categorically as a type of postoperative infection. In the hysterectomy group, we found low overall percentage of postoperative infections in both the antibiotic groups. Similar data was reported by Cormio et al¹¹. Asymptomatic bacteriuria was observed frequently (5.5% of the AMX/CL group and 8% of the cefazolin treated patients).

The incidence of post-cesarean infections was low and was similar when compared with other studies^{12,13}. Post-cesarean bacteriuria may be further reduced by avoiding routine catheterization. The present study has shown that AMX/CL which has activity against all the potential pathogens was not superior to cefazolin in its ability to prevent infection in these women. If drug costs only are considered, the use of AMX/CL was more expensive.

Recently, another aspect of prophylaxis is to shorten the duration of antibiotic use. For most hysterectomies, a single dose of antibiotic is sufficient¹⁴. Current information suggests that additional dose should be given at intervals of twice the half-life of the antibiotic to maintain adequate levels throughout the procedure¹⁵. Keeping these data in mind, we administered the second dose of antibiotic 4 hours after the initial one.

In summary, this prospective study confirms that antibiotic prophylaxis had a beneficial effect on women undergoing hysterectomy and elective cesarean delivery. Both the drugs - AMX/CL and cefazolin seem equally effective.

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