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Single Dose Versus 24-Hour-Dose Intravenous Ampicillin in Prophylaxis of Febrile Morbidity in Abdominal Hysterectomy: A Randomized Controlled Trial

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ABSTRACT

Objective To compare the febrile morbidity rate after elective abdominal hysterectomy between patients given single dose vs 24-hour-dose intravenous ampicillin prophylaxis.

Study design Randomized controlled trial.

Setting Department of Obstetrics and Gynecology, Faculty of Medicine, Prince of Songkla University.

Subjects Eighty-seven patients who underwent elective abdominal hysterectomy at Songklanagarind hospital from March to December 2002.

Intervention The subjects were randomly allocated to receive either single dose or 24-hour-dose intravenous ampicillin prophylaxis.

Main outcome measures Febrile morbidity rate in the two groups.

Results The characteristics and risk factors for postoperative infection among the two groups were not statistically significantly different. There was no statistical difference in febrile morbidity between the two groups. The febrile morbidity rate was 5/43 (11.6%) and 3/44 (6.8%) in the single dose and 24-hour-dose, respectively.

Conclusion Single dose and 24-hour-dose of intravenous ampicillin prophylaxis showed no significant difference in preventing febrile morbidity after elective abdominal hysterectomy.

Key words: abdominal hysterectomy, ampicillin, prophylaxis, and febrile morbidity

Hysterectomy is the most frequently performed major operation in gynecology.[1] Although no concrete data exist regarding the yearly number of abdominal hysterectomies in Thailand, it is a commonly performed procedure. The most common complications of abdominal hysterectomies are urinary tract infection, wound infection, or vaginal cuff infection.[2-4]

Prophylactic antibiotics can significantly reduce the incidence of pelvic infections in patients undergoing either an abdominal or vaginal hysterectomy.[5,6] Antibiotic prophylaxis has been standard practice in vaginal hysterectomies for many years. Support for prophylactic antibiotics in abdominal hysterectomies has undergone a recent meta-analysis showing its benefit.[6,7] The abdominal hysterectomy is an example of a "clean contaminated procedure", where

contamination occurs at the end of the operation when the vagina is incised.[8] The bacteria commonly involved in surgical wound infection or sepsis after gynecologic surgery include enteri gram-negative, group B streptococci, enterococci, and anaerobes.[9] Antibiotics that can be used for prophylaxis before a hysterectomy are the first, second, and third generation cephalosporins and penicillins.[5,6,8-10] The efficacy of a single dose of some antibiotics has been proved comparable with multiple dose regimens.[11,12]

Ampicillin is an aminopenicillin active against such gram-negative organisms as Escherichia coli, proteus, salmonella, shigella, Haemophilus influenzae and group B streptococci.[13] Ampicillin can be used for prophylaxis before hysterectomy.[5,11] In Songklanakarind Hospital, we use ampicillin for prophylaxis in gynecologic procedures because of its low cost, broad spectrum efficacy, safety, and adequate half-life. The number of doses, However, varies with the surgeon. Due to the lack of information about the appropriate doses of ampicillin for prophylaxis before an elective abdominal hysterectomy, we conducted this randomized, controlled trial to determine a suitable dosage for prophylaxis before elective abdominal hysterectomy due to nonmalignant diseases by comparing febrile morbidity between single dose and 24-hour-dose intravenous ampicillin.

Materials and methods

All the patients who were scheduled for elective abdominal hysterectomy due to nonmalignant disease at Songklanakarind Hospital from March to December 2002 were enrolled in the study after informed consent was obtained. Exclusions for participation included patients who had serious hepatic or renal function impairment, patients who had received any antibiotic within 72 hours before surgery, patients who had known hypersensitivity to the penicillin drug group, and patients who had signs and symptoms of infection at the time of their hysterectomy. Eighty-seven patients were randomly assigned by a computer program into two groups. Patients in Group1 (single dose) received 2 gm of ampicillin intravenously 30 minutes before the operation, administered by an anesthesist. Group 2 (24-hour-dose) patients received the same initial dose as group 1, and also received 1 gm of ampicillin intravenously every 6 hours, for three additional doses. This study protocol was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University.

Routine preoperative care including, skin preparation, vaginal douche, soap enema the evening before surgery, a povidone-iodine scrub and shaving of surgical area, were performed for all patients. All the abdominal hysterectomy procedures were performed by attending staff or senior resident physicians under the direct supervision of a member of the attending staff. All of the procedures were performed with the patient under general anesthesia. The foley catheter was removed on the first postoperative morning. The women were seen twice daily during their hospitalization. Oral temperature was taken and recorded every 6 hours, and if a patient's temperature was 38°C or greater, the attending physician was called for patient evaluation and proper management. All patients were routinely re-evaluated four weeks postoperatively.

The main objective of this study was to assess the febrile morbidity rate after elective abdominal hysterectomy between patients who used single dose and 24-hour-dose intravenous ampicillin prophylaxis. Febrile morbidity was defined as a temperature of 38°C or greater, on two successive occasions 6 hours apart, excluding the first 24 hours postoperatively, taken by oral measurement with a standard technique.[12,14]

Sample size was calculated by using the expected febrile morbidity in single dose ampicillin with 33% and 24-hour-dose with 8% from the retrospective data in 68 patients (= 0.2, = 0.05). The statistical methods for analysis of data generated during this clinical trial included the Unpaired t-test and Fisher's exact test. P values less than 0.05 were considered significant.

Results

The final study group included eighty-seven patients, after 9 were excluded from the evaluation because they did not receive the antibiotic according the protocol, or the operation was cancelled. Forty-three cases (49.43%) randomly received single dose ampicillin (Group 1), while 44 in 87 cases (50.57%) received 24-hour-dose ampicillin (Group 2). The mean age in the single dose group was 46.5 ± 6.3 years and 46.0 ± 6.8 years in the 24-hour-dose group. The risk factors of postoperative pelvic infection such as body mass index (BMI), operative time, and the amount of blood loss, were demonstrated in Table 1. The age and risk factors were not significantly different, compared among both groups.

Table 1. Characteristics of patients and risk factors for postoperative infection

	Single dose (n=43)	**24-hour-dose (n=44)**	**p-value**
Age (year ± SD)	46.5 ± 6.3	46.0 ± 6.8	0.73
BMI (kg/m^2)	23.6	22.7	0.24
Operative time (min)	125.9	130.0	0.33
Blood loss (ml)	300.0	400.0	0.94

The sites of primary disease were categorized into four primary sites among 87 patients: myometrium 55 cases (63.21%), ovary 15 cases (17.2%), cervix 12 cases (13.8%), and endometrium 5 cases (5.74%), as shown in Table 2. Myometrial conditions of the uterus are the most common indication of abdominal hysterectomy: myoma uteri 50 cases (57.4%), and adenomyosis 5 cases (5.7%). There were no statistical differences in the sites of primary diseases among both study groups (the overall p value = 0.06). The abdominal hysterectomy with or without necessitating additional surgery was depended on the specific operative findings, technical difficult of the surgical procedure, and adjacent organ injury. There were not statistical different among two groups (the overall p value = 0.66). The various types of surgical procedure are reported in Table 3.

Table 2. Category of surgical indications by the sites of primary disease

	Single dose (n=43) N (%)	**24-hour-dose (n=44) N (%)**
Cervix	8(18.6%)	4(9.0%)
Endometrium	2(4.6%)	3(6.8%)
Myometrium	30(69.7%)	25(56.8%)
Ovary	3(6.9%)	12(27.2%)

Overall p-value = 0.06

Table 3. Distribution of abdominal hysterectomy with or without necessitating additional surgery

	Single dose (n=43) N(%)	24-hour-dose (n=44) N(%)
TAH only	15(34.8%)	11(25.0%)
TAH with salpingo-oophorectomy	25(58.1%)	31(70.4%)
TAH with appendectomy	2(4.6%)	1(2.2%)
TAH with repairing of urinary tract	1(2.3%)	1(2.2%)

Overall p-value = 0.66

The main outcome measure, the febrile morbidity, was determined postoperatively, according to the defined criteria. The total postoperative febrile morbidity rate was established of 8 in 87 patients (9.1%): 5 in 43 cases (11.6%) in group 1, and 3 in 44 cases (6.8%) in group 2, respectively. The statistical comparison among both groups showed no statistical difference (p value =0.44). The laboratory investigations of febrile morbidity showed the negative culture on blood and urine culture. While waiting for culture results to be available, 5 in 9 patients (55.5%) of febrile morbidity case underwent spontaneous regression, and did not required treatment. While, the vaginal cuff cellulitis was reported of 3 in 87 patients: 1 case (2.3%) in the group 1, and 2 cases (2.2%) in the group 2. All had been successfully responded to combined antibiotic therapy.

Discussion

The results of numerous prospective clinical trials, and a meta-analysis study, have shown the effectiveness of prophylactic antibiotics in decreasing the incidence of febrile morbidity following abdominal hysterectomy.[6,7,10,16,17] On the basis of these results, it is generally recommended that cephalosporins can be used to prevent postoperative fever and infection after an abdominal hysterectomy. Various penicillins (e.g. ampicillin, mezlocillin, penicillin, piperacillin) can be used for prophylaxis before a hysterectomy.[5] The choice of agent should be based on efficacy and cost.[5] Hemsell et al. proposed guidelines for antibiotic prophylaxis in obstetric and gynecologic surgery.[8] The agent selected must:

- be of low toxicity,
- have an established safety record in patients,
- not be routinely used for the treatment of serious infections,
- have a spectrum of activity that includes the microorganisms most likely to cause infection,
- reach a useful concentration in relevant tissues during the procedure,
- be administered for a short duration, and
- be administered so that it is present in surgical sites at the time of incision.

Although this study did not compare the efficacy of ampicillin and a placebo group, the total febrile morbidity rate in both prophylactic regimens was 9.19%, which was similar to the findings of previous studies in patients who received antibiotic prophylaxis before an operation.[10,16,17] Some reports also confirm ampicillin prophylaxis can be used in preventing febrile morbidity following hysterectomy.[11,18] Conversely, Chongsomchai et al. reported that there was no statistically significant difference in febrile morbidity between an ampicillin and a placebo groups.[10]

In deciding a suitable dose of antibiotic prophylaxis in hysterectomy, most reports suggest that single dose preoperative prophylaxis is as effective as a multiple dose regimen in preventing postoperative infection and morbidity.[5,6,8,12] Although in our study, the 24-hour-dose group has less febrile morbidity, the numbers were not statistically significant. In a previous large study, Benson et al. reported that no statistically significant difference was found

between a short and long course of ampicillin for preventing febrile morbidity following vaginal hysterectomy.[11] Postoperative infections occurring in the female pelvis are usually polymicrobial in etiology.[8,12] The most common infections associated with abdominal hysterectomy are urinary tract infection, wound infection, and vaginal cuff infection which is similar to our study.[2-4]

In conclusion, our study indicated that there were no significant differences between the single dose and the 24-hour-dose of ampicillin intravenously in preventing febrile morbidity after elective abdominal hysterectomy. The limitation of our study was sample size calculation. Rate of febrile morbidity from retrospective data was different from outcome of this study. So that, further study needs to be done using a large sample size and including a placebo group for additional comparison.

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