# Comparison of Short *Versus* Long Duration of Ampicillin and Gentamicin for Radical Hysterectomy

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**Abstract**

Prophylactic antibiotic therapy for radical hysterectomy is still controversial. Although the efficacy of antibiotics have been demonstrated, there remains the question of duration of administration. In this study, we retrospectively reviewed 95 patients who underwent radical hysterectomy and pelvic lymphadenectomy for cervical cancer at our institute. The management was uniform except for the duration of antibiotic administration. Group I (34 cases) had ampicillin and gentamicin for 3 days while group II (61 cases) had the same regimen for 7 days. No significant difference was found in terms of postoperative infection (2.9% in group I and 1.6% in group II) or febrile morbidity (32.4% *versus* 50.8%). Other factors such as the patients' age, body weight, preoperaive hemoglobin level, amount of blood loss and blood transfused, operative time, duration of retroperitoneal drain and duration of suprapubic cystostomy. Only operative time had a significant influence on febrile morbidity regardless of the duration of antibiotics administered. In conclusion, the antibiotic administration gave a radical hysterectomy and pelvic lymphadenectomy a very low incidence of postoperative infection. Longer duration of treatment did not appear to lessen postoperative infection nor febrile morbidity. Shorter duration of antibiotic administration needs further evaluation.

Prophylactic antibiotic in patients undergoing radical hysterectomy and pelvic lymphadenectomy has not been studied extensively. However, most gynecologic oncologists routinely utilize prophylactic antibiotic therapy in their radical hysterectomized patients(1). The most current controversy about its use in radical hysterectomy concerns the duration of treatment. In vaginal hysterectomy, earlier investigations favoured antibiotic treatment for 5-7 days. While they demonstrated a significant decrease in infectious morbidity, these regimens tended to be associated with an increase

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in resistant flora[2]. With regard to radical hysterectomy, there are very few studies concerning the optimum duration of antibiotics use.

In this study, we retrospectively compared the efficacy of 3-day with 7-day Ampicillin-Gentamicin combination in patients undergoing radical hysterectomy and pelvic lymphadenectomy.

## MATERIAL AND METHOD

Between January 1990 and December 1994, records of all patients undergoing radical hysterectomy and pelvic lymphadenectomy as a primary treatment of cervical cancer at Maharaj Nakorn Chinag Mai Hospital were evaluated. Patients enrolled in this study were those who had ampicillin and gentamicin perioperatively for 3 or 7 days. Patients having other antibiotic regimens or these two antibiotics for a different duration were excluded. Patients with preoperative infection, fever of 37.8°C or greater within 24 hours preoperatively were also excluded from the study. Accordingly 95 charts were available for this study, 34 cases received 3 days (group I) and 61 cases 7 days of antibiotics (group II).

All patients had preoperative complete and differential blood count, urine analysis, blood chemistry panel and chest X-ray. Preoperative skin and vaginal preparations included standard abdominal and perineal shave, povidone-iodine scrub of the abdomen and vaginal douch with zephiran. Preoperative mechanical bowel preparation was not performed, but the patients received castor oil the night before operation. Transurethral catheter was inserted preoperatively and removed the next day after the function of the suprapubic cystostomy was established.

All patients underwent radical hysterectomy with pelvic lymphadenectomy and suprapubic cystostomy by three gynecologic oncologists in the same manner. Low midline incision was done by scapel, then electrocautery was used for cutting and hemostasis. The abdominal cavity was then explored. A complete bilateral pelvic lymphadenectomy was carried out. Radical hysterectomy was then done, with removal of 3-4 cm of the upper part of the vagina and the parametrial tissues to the lateral pelvic wall. Chromic catgut suture was used during the pelvic operation, silk was also used for ligating vessels and bleeding point. Hemostatic clips were employed during pelvic nodes dissection. After hysterectomy, the vagina was closed with chromic catgut suture and the pelvic cavity was routinely irrigated with warm physiologic saline. Pelvic peritonization was reconstituted after bilateral retroperitoneal tube drains were placed along the pelvic sidewall, exited through the left and right lower quadrants of the anterior abdominal wall. Abdominal closure was performed with 0 chromic catgut for parietal peritoneum, 1-0 vicryl for rectus sheath, 00 plain catgut for subcutaneous fat. The skin was finally closed with subcuticular suture of vicryl 000, 0000; or 00000. Postoperatively, tube drains were connected to intermittent high pressure suction and were discontinued when drainage was less than 10-20 ml. Suprapubic cystostomy was discontinued when residual urine volume was less than 100 ml.

A combination of 1 gram ampicillin and 80 mg gentamicin was given approximately 1 hour preoperatively. Intravenous ampicillin was continued every 6 hours for the first 2 days, followed by 500 mg orally four times a day. Intramuscular gentamicin was continued every 8 hours. Both antibiotics were given for a duration of 3 (Group I) or 7 days (Group II).

Routine postoperative care was given. Febrile morbidity was defined as an oral temperature of 38.0°C or higher excluding the first 48 hours after surgery. Urinary tract infection was diagnosed when greater than $10^5$ bacterial colonies were obtained per ml of urine culture. When postoperative infections were diagnosed, the patients received appropriate antibiotics.

The medical record of each patient was reviewed for age, weight, preoperative hemoglobin level, amount of blood loss and blood transfused, operative time, duration of retroperitoneal drain, duration of suprapubic cystostomy, presence of postoperative infection and febrile morbidity. Patients's profile data in the two groups were compared using *t*-test and chi-squares statistic as appropriate and a p-value of 0.05 or less was considered significant.

## RESULTS

Ninety-five patients were enrolled in the study, 34 were in group I and 61 were in group II. The mean age of the patients was 42.1 years (range 22-66 years). Eighty-eight (92.6%) had stage Ib while 7 (7.4%) had stage IIa cervical cancer. Eighty (84.2%) of these patients had squamous cell, 11 had adenocarcinoma, 3 had adenosquamous and 1 had anaplastic carcinoma. (Table 1 and Table 2)

**Table 1. Comparison of patients' profile (mean ± SD) between the two groups.**

| | Group I 3 days antibiotics (n=34) | Group II 7 days antibiotics (n=61) |
|---|---|---|
| Age (Yr) | 41.6±9.5 | 42.3±8.6 |
| Weight (Kg) | 54.4±9.6 | 53.5±6.8 |
| Preoperative hemoglobin (g) | 12.5±1.5 | 12.9±1.4 |
| Estimated blood loss (ml) | 622.1±312.7 | 784.4±645.5 |
| Blood transfusion (U) | 0.68±1.0 | 0.83±1.6 |
| Duration of surgery (minutes) | 176.2±31.8 | 177.7±33.9 |
| Duration of tube drain (days) | 4.5±1.7 | 4.4±1.5 |
| Duration of suprapubic cystostomy (days) | 12.7±4.9 | 13.9±6.7 |

**Table 2. Comparison of tumor stage, tumor histology, postoperative infection and febrile morbidity between the two groups.**

| | Group I 3 days antibiotics (n=34) | Group II 7 days antibiotics (n=61) |
|---|---|---|
| Stage | | |
| Ib | 32 (94.1%) | 56 (91.8%) |
| IIa | 2 (5.9%) | 5 (8.2%) |
| Histology | | |
| Squamous | 28 (82.4%) | 52 (85.2%) |
| Nonsquamous | 6 (17.6%) | 9 (14.8%) |
| Adenocarcinoma | 5 | 6 |
| Adenosquamous | 1 | 2 |
| Anaplastic | - | 1 |
| Postoperative infection | 1 (2.9%) | 1 (1.6%) |
| Febrile morbidity | 11 (32.4%) | 31 (50.8%) |

There was no significant difference in patients' age, weight, preoperaive hemoglobin level, amount of blood loss and blood transfused, operative time, duration of retroperitoneal drain, duration of suprapubic cystostomy between the two groups. (Table 1)

Postoperative infections were found in only 2 cases, both had urinary tract infection with bacteria > $10^5$ colonies per ml of urine culture (*E. coli* in 1 case in group I and Acintobacter in the other case in groupII). No surgical-site related infections such as wound infection, drain-site infection or pelvic cellulitis were observed. The rates of febrile morbidity were not statistically different among the two groups (Table 2).

Analysis of the study group as a whole demonstrated that the patients' age, weight, preoperative hemoglobin, amount of blood loss, amount of blood transfused, operative time, duration of retroperitoneal drain, duration of suprapubic cystostomy had no significant influence on the rate of febrile morbidity. The only parameter that showed significant relationship with febrile morbidity was the operative time, i.e. of 28.1 per cent *vs* 52.4 per cent in those with operative time of less and more than 2 hours and forty minutes, respectively (p = 0.02).

We then reassessed the risk of febrile morbidity between group I and group II by stratifying the patients according to operative time of equal to or less than and more than 2 hours and forty minutes. We still can not demonstrate the difference in the febrile morbidity rate in both groups.

In summary, this study demonstrated that patients undergoing radical hysterectomy and pelvic lymphadenectomy who were administered perioperatively with ampicillin and gentamicin for 3 or 7 days had very low risk of postoperative infection (2.1%). Febrile morbidity was found in 44.2 per cent of all cases. Febrile morbidity rate was higher in those who had longer operative time, while longer administration of antibiotics had no influence. Whether similar regimen for shorter duration, i.e. less than 3 days would raise the rate of postoperative infection and febrile morbidity needs further studies.

## DISCUSSION

Radical hysterectomy and pelvic lymphadenectomy is an operation that carries siginificant risks of postoperative infections considering extensive retroperitoneal dissection of pelvic nodes, rectum and bladder, with increased blood loss, prolonged operative procedure and bladder catheterization. Even with this high risk of infection, the use of antibiotics in this radical procedure has not been adequately studied.

Sevin et al[1] conducted a national survey of gynecologic oncologists regarding their use of prophylactic antibiotics for radical hysterectomy. Of 111 questionaires that were answered and returned; 65 per cent used routine antibiotic prophylaxis while 19 per cent used it only occasionally and 16 per cent did not use any at all.

The role of antibiotics in patients undergoing radical hysterectomy and pelvic lymphadenectomy is still controversial. However, most studies to date have demonstrated some efficacy.

From the randomized placebo controlled studies by Sevin et al[1], radical hysterectomy patients who had 12 doses of cefoxitin perioperatively had significantly lower rate of surgical and non-surgical site related infection and lower overall morbidity. Rosenshien et al[3] also observed that a single dose of doxycycline significantly reduced infectious morbidity and pelvic cellulitis. Micha et al[4] compared three doses of mezlocillin with placebo and found that the rate of wound infection and infectious morbidity were significantly lower in the mezlocillin treated group. Hemsell et al[5] conducted a similar study comparing three doses of cefoperazone and salbactam with placebo. They observed that 10 per cent of the antibiotic treated group had postoperative infection compared to 27 per cent in the placebo group. They commented further that operative site infection rate of 27 per cent in the placebo group was high enough to warrant antibiotic prophylaxis.

Although from these placebo-controlled trials, prophylactic antibiotics had been shown to reduce the risk of infection, some reports still questioned their benefit. Marsden et al[6] from their placebo controlled trial observed that although their radical hysterectomy patients with 12 doses of cefoxitin had lower infective morbidity and surgical site related infection than those in the placebo group, these differences did not achieve statistical significance. They claimed that many factors other than the use of antibiotic prophylaxis were therefore, more or equally important in determining the incidence of infection after radical hysterectomy. They also suggested that cases of high risk patients might benefit more noticeably from the use of prophylactic antibiotics. Another retrospective study by Bendrold and Kjorstad[7] in 35 patients undergoing radical hysterectomy demonstrated no surgically related infection and only 17 per cent incidence of febrile morbidity. They concluded that radical hysterectomy in their hospital was not carrying significant risk of post-operative infection and that prophylactic antibiotic could not be routinely recommended.

Using antibiotics in radical hysterectomy is still controversial, although most studies demonstrated the efficacy of antibiotics and gynecologic oncologists preferred to use prophylactic antibiotics in their radical hysterectomy patients; there remains the question of duration of administration. In our hospital, radical hysterectomy patients received routine perioperative antibiotics, but various regimens, dosage and durations were in currrent used. The most common regimen was that of ampicillin in combination with gentamicin.

In this study, we compared the use of 3 days and 7 days of ampicillin and gentamicin in our radical hysterectomy patients and found them to be equally efficacious. These patients had a standard method of pre - postoperative preparations and similar operative procedures. Moreover, the patients in both groups had comparable profiles including patients' age, weight, preoperaive hemoglobin level, amount of blood loss and blood transfused, operative time, duration of retroperitoneal drain, duration of suprapubic cystostomy.

Most, if not all studies, repeatedly used cephalosporin as prophylactic antibiotc for radical hysterectomy, and none to our knowledge used ampicllin and gentamicin. In this study, we demonstrated that the combination of ampicillin and gentamicin, both of which are inexpensive, appeared to be as effective in the prevention of postoperative infection, and longer use of this regimen has not been shown to be more effective in terms of postoperative infection or febrile morbidity.

In the retrospective study by Orr et al[8], comparing single dose and multiple doses of cefoxitin or metronidazole, they also showed that both were equally effective. Seven et al[9] also demonstrated in their randomized double blind study that 3 and 12 doses of cefoxitin had no significant difference regarding postoperative infection or febrile morbidity. On the other hand, Biglia et al[10] demonstrated in their retrospective study that radical hysterectomy patients who received long term antibiotics (greater than 72 hours) had fewer postoperative complications and less febrile morbidity. It seems that there is still controversy about the optimum duration of postoperative antibiotic treatment in patients undergoing radical hysterectomy, although common sense would suggest that prolonged antibiotics are needed because of prolonged operative time, more tissue damage, retroperitoneal drain and prolonged catheterization of the bladder.

This study demonstrated that 3 days of postoperative antibiotics was enough for radical hysterectomy patients. Our study, however, showed an overall low risk of postoperative infection, which may be from the relatively short mean operative time of 2.9 hours compared to 3.4-5.8 hours in the other studies[1,3,4], moderate blood loss of 726 ml compared with 794-2000 ml[1,4,6,9] and the use of suprapubic cystostomy in all patients. This study also demonstrated that the only factor that had significance on febrile morbidity was the duration of surgery. This is concordant with other studies. Schapin[11] found prophylactic cefoxitin to be of no benefit in simple abdominal hysterectomy lasting longer than 3 hours and 20 minutes. This study showed that radical hysterectomy patients with operative time more than 2 hours 40 minutes had significantly more risk of infectious morbidity, however, the duration of antibiotics use had no influence on infectious morbidity whether in the high or low risk group.

In conclusion, this study suggested that attention to preoperative preparation, intraoperative technique, gentle tissue handling, shorter operative time, less blood loss and use of suprapubic cystostomy and 3 days' use of ampicillin and gentamicin are associated with low risk of postoperative infection. However, whether even shorter duration of ampicillin and gentamicin would yield the same efficacy or not needs further study.

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## REFERENCES


1. Sevin BU, Ramos R, Lichtinger M, et al. Antibiotic prevention of infectious complicating radical abdominal hysterectomy. Obstet Gynecol 1984; 64: 539-45.
2. Cartwright PS, Pittaway DE, Jones HW III, Entman SS. The use of prophylactic antibiotics in obstetrics and gynecology, a review. Obstet Gynecol Surv 1984; 39: 539.
3. Rosenshein NB, Ruth JC, Millar I, et al. A prospective radomized study of doxycycline as a prophylactic antibiotic in patients undergoing radical hysterectomy. Gynecol Oncol 1983; 15: 201-6.
4. Micha JP, Kucera PR, Burkett JP, et al. Prophylactic mezlocillin in radical hysterectomy. Obstet Gynecol 1987; 69: 251-4.
5. Hemsell DL, Bernstein S, Bawdon RE, Hemsell PG, Heard MC, Nobles BJ. Prevention of major operative site infection after radical abdominal hysterectomy and pelvic lymphadenectomy. Gynecol Oncol 1989; 35: 55-6.
6. Marsden DE, Cavanagh D, Wisniewski BJ, Roberts WS, Lyman GH. Factors affecting the incidence of infectious morbidity after radical hysterectomy. Am J Obstet Gynecol 1985; 152: 817-21.
7. Bendvold E, Kjorstad KE. Antibiotic prophylaxis for radical abdominal hysterectomy. Gynecol Oncol 1987; 28: 201-4.
8. Orr JW Jr, Sisson PF, Patsner B. Single-dose antibiotic prophylaxis for patients undergoing extended pelvic surgery for gynecologic malignancy. Am J Obstet Gynecol 1990; 162: 718-21.
9. Sevin BU, Ramos R, Gerhardt RT, guerra L, Hilsenbeck S, Averette HE. Comparative efficacy of short-term versus long-term cefoxitin prophylaxis against postoperative infection after radical hysterectomy : a prospective study. Obstet Gynecol 1991; 77: 729-34.
10. Biglia N, Giai M, Cortese P, Bottero A, Sismondi P. Postoperative infections and antibiotic prophylaxis in radical hysterectomy, retrospective study. Minerva Ginecol 1991; 43: 435-41. (abstract)
11. Shapiro M, Munoz A, Tager I, et al. Risk factors for infection at the operative site after abdominal or vaginal hysterectomy. N Engl J Med 1982; 307: 1661.


# การศึกษาเปรียบเทียบการให้แอมพิซิลลิน–เจ็นตะไมซิน 3 วัน และ 7 วันในผู้ป่วยที่ได้รับการผ่าตัดมดลูกออกทั้งหมด


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การให้ยาปฏิชีวนะร่วมด้วยในการผ่าตัด radical hysterectomy ยังมีข้อโต้แย้งกันอยู่ แม้ว่าส่วนใหญ่จะมีความเห็นว่าการให้ยาปฏิชีวนะนั้นมีประโยชน์ แต่ก็ยังไม่สามารถบอกได้ว่าควรจะให้ยาเป็นเวลานานเท่าไรจึงจะเหมาะสม การศึกษานี้ได้ศึกษาเปรียบเทียบผู้ป่วยมะเร็งปากมดลูกที่ได้รับการผ่าตัด radical hysterectomy with pelvic lymphadenectomy จำนวน 95 รายที่ได้รับการผ่าตัด และดูแลรักษา รวมทั้งให้ยาปฏิชีวนะชนิดเดียวกัน คือ Ampicillin และ Gentamicin โดยผู้ป่วยกลุ่มที่ 1 จำนวน 34 รายได้รับยาปฏิชีวนะเป็นเวลา 3 วัน ส่วนกลุ่มที่ 2 จำนวน 61 ราย ได้รับยาปฏิชีวนะนาน 7 วัน ผลการศึกษาพบว่าผู้ป่วยทั้งสองกลุ่มมีอัตราการติดเชื้อหลังผ่าตัด (2.9% *vs* 1.6%) และการมีไข้หลังผ่าตัด (febrile morbidity : 32.5% *vs* 50.8%) ไม่ต่างกัน จากการศึกษาปัจจัยต่าง ๆ ได้แก่ อายุ น้ำหนัก ระดับความเข้มข้นของเลือด จำนวนเลือดที่เสียไประหว่างการผ่าตัด การให้เลือดระหว่างผ่าตัด ระยะเวลาที่ใช้ในการผ่าตัด ระยะเวลาที่ใส่สาย drain ระยะเวลาที่ใส่สายสวนปัสสาวะ (suprapubic cystostomy) พบว่าสิ่งที่สัมพันธ์กับภาวะมีไข้หลังผ่าตัด คือ ระยะเวลาที่ใช้ในการผ่าตัดเท่านั้น โดยสรุปพบว่าผู้ป่วยที่ได้รับการผ่าตัด radical hysterectmoy และได้รับยาปฏิชีวนะจะมีอัตราการติดเชื้อต่ำ แต่การให้ยาปฏิชีวนะเป็นเวลานานไม่ได้ทำให้อัตราการติดเชื้อ หรือภาวะมีไข้หลังผ่าตัดลดลง



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