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Antibiotic prophylaxis in gynecological surgery. A literature review

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Abstract

Gynecological surgical procedures are associated with significant morbidity, and a major impact on the quality of life. The antibiotic prophylaxis should minimize the risk of postoperative infections complications, preventing in the same time the adverse effects of long-term antibiotic usage. The aim of this paper is to detail the current recommendations for antibiotic prophylaxis in gynecological surgical procedures performed by open abdominal or laparoscopic approach. We have performed a review of the English language literature from the PubMed/Medline database using the following search details: ("Antibiotic Prophylaxis"[Mesh]) AND "Gynecologic Surgical Procedures"[Mesh]. We used the similar articles function to find additional secondary resources. Antibiotic prophylaxis should not be performed in elective laparoscopic gynecological procedures without the opening of the uterus or vagina. During hysterectomy for benign or malignant disease, the first dose of antibiotic prophylaxis should be infused one hour prior to skin incision, excepting Vancomycin and Fluoroquinolone that should be started two hours before. The antibiotic should be repeated if the duration of the surgery lasts more than two half-lives of the drug or the intraoperative bleeding is greater than 1500 mL. The antibiotic prophylaxis should be discontinued within the first 24 hours after surgery. Timely administration of adequate antibiotics and a meticulous surgical technique are mandatory for effectively decreasing the risk of postoperative infectious complications. Thorough adherence to international recommendations for antibiotic prophylaxis discontinuation within 24 hours should minimize the adverse events of antibiotic usage.
Keywords: *antibiotic prophylaxis; gynecological surgery, emergency surgery; gynecological oncology*

Introduction

Gynecological surgical procedures are associated with important morbidity, a secondary major impact on quality of life, and on fertility, especially in younger patients. Surgical site infections (SSIs) represent 14% - 16% of all hospital-acquired infections, with a frequency as high as 20% for intra-abdominal procedures and up to 10% in gynecological patients[1,2]. Seven percent of patients with an open approach for gynecological cancers develop SSIs, which are associated with a significantly longer hospital stay and a more than five-fold increase in the risk of reintervention[3]. The antibiotic prophylaxis should minimize the rate of postoperative infectious complications, while preventing the adverse effects of long-term antibiotic usage, such as *Clostridium difficile* infection, the development of multidrug-resistant bacteria, and decrease intervention-related costs. The aim of the antibiotic prophylaxis is to prevent SSIs by decreasing the bacteria burden at the surgical situs during surgery[4]. An evaluation of the use of antibiotic prophylaxis in 34,133 Medicare patients with a major surgical procedure revealed that only 55.7% had an antimicrobial dose administered within one hour before incision, and that in only 40.7% of cases were the antibiotics discontinued within 24 hours[1]. However, despite the major healthcare impact worldwide there is no general consensus for antibiotic prophylaxis, and local hospital protocols may differ from national recommendations[5].

The aim of this article is to detail the current recommendations for antibiotic prophylaxis in gynecological emergencies and oncological surgical procedures.

Methods

We have performed a review of the English language literature from PubMed/Medline database using the following search details: "Antibiotic Prophylaxis"[Mesh] and "Gynecologic Surgical Procedures"[Mesh]. We used similar articles function to find additional secondary resources.

Results

Moment of antibiotic prophylaxis administration

According to the current evidence the first dose of antibiotic should be completely administered one hour before the skin incision[6]. Due to their longer infusion time, the administration of Fluoroquinolone and Vancomycin should start two hours before the surgical incision[6]. Steinberg et al. studied the correlation of timing for antimicrobial prophylaxis and the risk of SSIs, and showed that the risk increased incrementally as the time between antibiotic infusion and incision increased[7]. After excluding antibiotics with a longer infusion time, they found that when the antibiotic was administered within 30 minutes before surgery the infectious risk was 1.6%, compared to 2.4% when the administration fit within the 31-60 minutes (OR =

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1.74, 95%CI = 0.98-3.04). The intraoperative redosing was effective only when the preoperative dose was adequately given and the surgery lasted more than four hours (OR=3.08, 95%CI = 0.74- 12.9)[7]. Weber et al. showed that administration of Cefuroxime 59 to 30 minutes before incision decreases the risk of SSIs[8]. The SSI rate was higher when antibiotics were administered less than 30 minutes (OR = 1.95, 95%CI = 1.4-2.8, p<0.001) or 120-60 minutes (OR = 1.74, 95%CI 1.0 – 2.9, p = 0.035) before incision[8]. During surgery the antibiotic administration should be repeated if the increases over two half-lives of the drug or the intraoperative bleeding is greater than 1500 mL[9].

Time to discontinue

The antibiotics prophylaxis should not be continued after the surgical procedure ends, and in particular patients when a repeated dose is administered in the postoperative period, the discontinuation should be in less than 24 hours[10,11].

Choosing the appropriate antibiotic

Compared to the preferred regimen (see Table I) the SSIs are more frequent after beta-lactam alternatives (OR = 1.7, 95% CI = 1.27 – 2.07), or the nonstandard antibiotics (OR = 2.95% CI = 1.31-3.1)[12].

Laparoscopic gynecological procedures

Laparoscopic gynecological procedures can be classified as clean or clean-contaminated, depending on the opening or not of the uterus or vagina[13]. For elective gynecological laparoscopic surgical procedures, excepting hysterectomy, no antibiotic prophylaxis is necessary[5,9,14]. Contrary to this evidence, an evaluation of the pattern of practice between gynecologists in 2011 revealed that 54.1% of them still used antibiotic prophylaxis for laparoscopic procedures[15]. Kocak et al. randomly allocated 200 women to 2 g of first generation cephalosporin and 250 women to no treatment as antibiotic prophylaxis in gynecological laparoscopy[16]. They found no difference in the prevalence of postoperative infection or in the mean hospital stay[16]. Cormio et al. compared the efficacy of Amoxicillin-Clavulanic acid (164 patients) and Cefazolin (172 patients) in laparoscopic gynecological procedures[17]. No sign of infectious at the surgical site, urinary or respiratory tract infectious or death due to sepsis were observed in either groups[17]. A more recent study, from 2010, compared Cefazolin (2 g, 30 minutes before surgery -150 patients) with no antibiotic prophylaxis (150 patients) in elective laparoscopic gynecological procedures[18]. No postoperative infection was diagnosed in either groups. The overall rate of fever was 1.3% and 2% in antibiotic and no antibiotic groups, respectively. The authors concluded that infection complications in laparoscopic gynecological procedures are negligible, with no difference made by antibiotic prophylaxis[18] (Tables 1 and 2).

Abdominal and laparoscopic hysterectomy

Strict adherence to clinical guidelines for perioperative management of patients with hysterectomy may halve the rate of postoperative infections (from 4% to 2%), as proved by the study of 13,425 cases from Danish Hysterectomy Database[19]. Most commonly involved pathogens in postoperative gynecological infections come from the lower genital or gastrointestinal tract and include enteric Gram-negative bacilli, enterococci, and anaerobes[20].

Table 1 Antibiotic prophylaxis regimen options for hysterectomies[9,12]

Regimen	Drug used
Recommended regimen	Cefazolin: 2 g iv (3 g for patients over 120 kg), redosing after 4 hours Cefoxitin: 2 g iv, redosing after 2 hours Cefotetan: 2 g iv, redosing after 6 hours Ampicillin - Sulbactam: 3 g iv, redosing after 2 hours
Alternative regimen 1	Clindamycin (900 mg iv, redosing after 6 hours) OR Vancomycin (15 mg/kg iv, no redosing) AND Gentamicin (5 mg/kg iv, no redosing) OR Aztreonam (2 g iv, redosing after 4 hours) OR Fluoroquinolone (Ciprofloxicin 400 mg iv, no redosing, OR Levofloxacin 500 mg iv, no redosing, OR Moxifloxacin 400 mg iv, no redosing)
Alternative regimen 2	Metronidazole (500 mg iv, no redosing) PLUS Gentamicin (5 mg/kg iv, no redosing) OR Fluoroquinolone (Ciprofloxicin 400 mg iv, no redosing, OR Levofloxacin 500 mg iv, no redosing, OR Moxifloxacin 400 mg iv, no redosing)

Table 2 Risk factors for surgical site infections

Patients related factors	Uncontrolled diabetes [21] Smoking Steroid use Prolonged hospital stay *Staphylococcus aureus* carriers [22] Bacterial vaginosis [23]
Preoperative in-hospital measures	For hair removal - clippers are associated with fewer SSIs than razors [24]
Intraoperative measures	Excellent surgical technique (e.g. appropriate hemostasis, gentle handling of tissue)

Mahdi et al. analyzed the predictors of SSIs in hysterectomy for benign diseases[25]. Of 28,366 patients 3% (758) developed SSIs, more frequent after open surgery (4% versus 2%, p<0.001). Predictors of SSIs in open surgery were diabetes, smoking, respiratory comorbidities, obesity, ASA class equal or greater than three, perioperative blood transfusion and operative time longer than 180 minutes. In the laparoscopic group, predictors of SSIs were perioperative blood transfusion, operative time longer than 180 minutes, serum creatinine ≥2 mg/dL, platelets ≥350,000/mL[25]. A meta-analysis of 23 studies addressing hysterectomy in very obese and morbidly obese patients showed that open approach is associated with a significant higher wound infection rate (risk ratio of 4.36, 95% CI 2.79-6.8)[26]. Roy et al. published the results of 210,916 hysterectomies registered in the Premier Perspectives Database of 600 hospitals in the United States[27]. 55% of hysterectomies were by open approach, which was associated with a higher rate of SSIs. Patients with a SSIs had a three- to five-greater length of hospital stay, two-fold greater costs, and three-fold greater risk of hospital readmission[27]. A study coming from Mayo Clinic showed a 9.9% SSIs rate among 1369 patients with endometrial cancer[28]. Predictors for superficial incisional SSIs were obesity, ASA score over two, smoking, laparotomy and intraoperative transfusion. Predictors for organ/space SSIs were older age, smoking, vascular disease, prior methicillin-resistant Staphylococcus aureus infection, greater estimated blood loss, and lymphadenectomy or bowel resection[28]. An analysis of the National Surgical Quality Improvement Program Database of American College of Surgeons reveled that transfusion was associated with an increased rate of SSIs (OR = 1.8, 95%CI = 1.39-2.35), even after adjusting for preoperative anemia and case magnitude[29]. Mikamo et al. evaluated in a multicenter randomized Japanese study the effects of single versus four doses of a second-generation cephalosporin (Flomoxef) in abdominal extended hysterectomy[30]. The incidence of organ space SSIs were higher in the single-dose group even after multivariate analysis (7.14% versus 1.36%, p<0.05), with no differences regarding incisional SSIs. The authors concluded that, based on pharmacokinetics-pharmacodynamics (2-3 hours half-time), multiple doses of Flomoxef are necessary[30,31]. Brummer et al. evaluated the benefits of adding Metronidazole to Cefuroxime as antibiotic prophylaxis during hysterectomy on a cohort of 5,279 women from 53 hospitals from Finland[32]. The authors concluded that Cefuroxime was effective, whereas Metronidazole appeared to be ineffective, with no additional risk-reduction when added to Cefuroxime. Cefuroxime had a protective effect on total infection, with an adjusted odds ratio of 0.29 (95% CI =0.22-0.39). The absence of Cefuroxime (Cefuroxime versus Cefuroxime + metronidazole) was associated with an increase in overall infections (abdominal hysterectomy, OR = 3.63, 95% CI = 1.99-6.65; laparoscopic hysterectomy, OR = 3.53, 95%CI = 1.74-7.18), febrile events (abdominal hysterectomy, OR = 2.86, 95% CI = 1.09-7.46; laparoscopic hysterectomy, OR = 13.19, 95% CI = 3.36-47.49), and wound infections in abdominal hysterectomy (OR = 6.88, 95% CI = 1.09-7.49)[32].

A review of the adherence to guidelines for surgical antibiotic prophylaxis, published in 2015, showed the following: an inappropriate indication for prophylaxis ranging from 2.3%-100%, a correct time for antibiotic administration ranging from 12.73%-100%, an adequate discontinuation in 5.8%-91.4%, and an adequate antibiotic prophylaxis in 0.3%-84.5%[33].

Conclusions

Timely administration of adequate antibiotics and a meticulous surgical technique are mandatory for effectively decreasing postoperative infectious complications. Thorough adherence to international recommendations for antibiotic prophylaxis discontinuation within 24 hours should minimize the adverse events of antibiotic usage. ■

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