Antibiotic Prophylaxis in Gynaecologic Procedures

Abstract

Objective: To review the evidence and provide recommendations on antibiotic prophylaxis for gynaecologic procedures.

Outcomes: Outcomes evaluated include need and effectiveness of antibiotics to prevent infections in gynaecologic procedures.

Evidence: Medline and The Cochrane Library were searched for articles published between January 1978 and January 2011 on the topic of antibiotic prophylaxis in gynaecologic procedures. Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies. Searches were updated on a regular basis and incorporated in the guideline to June 2011. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The quality of evidence obtained was rated using the criteria described in the Report of the Canadian Task Force on Preventative Health Care (Table 1).

Benefits, harms, and costs: Guideline implementation should result in a reduction of cost and related harm of administering antibiotics when not required and a reduction of infection and related morbidities when antibiotics have demonstrated a proven benefit.

Recommendations

1. All women undergoing an abdominal or vaginal hysterectomy should receive antibiotic prophylaxis. (I-A)

2. All women undergoing laparoscopic hysterectomy or laparoscopically assisted vaginal hysterectomy should receive prophylactic antibiotics. (III-B)

3. The choice of antibiotic for hysterectomy should be a single dose of a first-generation cephalosporin. If patients are allergic to cephalosporin, then clindamycin, erythromycin, or metronidazole should be used. (I-A)

4. Prophylactic antibiotics should be administered 15 to 60 minutes prior to skin incision. No additional doses are recommended. (I-A)

5. If an open abdominal procedure is lengthy (e.g., > 3 hours), or if the estimated blood loss is > 1500 mL, an additional dose of the prophylactic antibiotic may be given 3 to 4 hours after the initial dose. (III-C)
6. Antibiotic prophylaxis is not recommended for laparoscopic procedures that involve no direct access from the abdominal cavity to the uterine cavity or vagina. (I-E)

7. All women undergoing surgery for pelvic organ prolapse and/or stress urinary incontinence should receive a single dose of first-generation cephalosporin. (III-B)

8. Antibiotic prophylaxis is not recommended for hysteroscopic surgery. (II-2D)

9. All women undergoing an induced (therapeutic) surgical abortion should receive prophylactic antibiotics to reduce the risk of post-abortal infection. (I-A)

10. Prophylactic antibiotics are not suggested to reduce infectious morbidity following surgery for a missed or incomplete abortion. (I-E)

11. Antibiotic prophylaxis is not recommended for insertion of an intrauterine device. (I-E) However, health care professionals could consider screening for sexually transmitted infections in high-risk populations. (III-C)

12. There is insufficient evidence to support the use of antibiotic prophylaxis for an endometrial biopsy. (III-L)

13. The best method to prevent infection after hysterosalpingography is unknown. Women with dilated tubes found at the time of hysterosalpingography are at highest risk, and prophylactic antibiotics (e.g., doxycycline) should be given. (II-3B)

14. Antibiotic prophylaxis is not recommended for urodynamic studies in women at low risk, unless the incidence of urinary tract infection post-urodynamics is > 10%. (I-E)

15. In patients with morbid obesity (BMI > 35 kg/m²), doubling the antibiotic dose may be considered. (III-B)

16. Administration of antibiotics solely to prevent endocarditis is not recommended for patients who undergo a genitourinary procedure. (III-E)

INTRODUCTION

Infectious complications following gynaecologic surgical procedures are a significant source of morbidity and potential mortality. They include urinary tract infection, endometritis, wound infection, vaginal cuff cellulitis, perineal infection, and sepsis, which lead to prolonged hospital stays and increased health care costs. Much work has been done to study the effect of prophylactic antibiotics in reducing infectious morbidity. A plethora of antibiotic types, dosing schedules, and routes of administration have been investigated. There is evidence to support the use of prophylactic antibiotics for a number of procedures in gynaecology. Unfortunately, few comparative trials have been conducted, leaving the clinician with uncertainty as to which regimen is superior.

ABBREVIATIONS

| BV | bacterial vaginosis |
| HSG | hysterosalpingography |
| PID | pelvic inflammatory disease |
| STI | sexually transmitted infection |
| UTI | urinary tract infection |

The presence of antibiotic resistant organisms is a reality in Canadian health care facilities. These organisms include methicillin resistant Staphylococcus aureus, vancomycin resistant Enterococcus, and extended-spectrum beta-lactamase-producing organisms.

Both morbidity and mortality are increased in infections involving these organisms, as they may be more virulent and are more difficult to treat because therapeutic options are limited. Antibiotic resistance development results mainly from the inappropriate use of antibiotics. Incomplete courses of antibiotic therapies and the unnecessary use of broader spectrum regimens play a role. Adherence to treatment and prophylaxis guidelines likely assists in reducing infection and antibiotic resistance. Physician adherence to antibiotic prophylaxis guidelines is variable and frequently at odds with published guidelines.

In addition to antibiotic prophylaxis, all factors that affect infectious risk reduction in our specialty must be reviewed. Sterile surgical fields must be ensured, and ongoing quality assessment of sterilization technique, air ventilation, and postoperative wound care are needed. Consistent infection control surveillance and reporting of infectious complications track ability to minimize these morbidities and possibly to identify clusters of infection and the emergence of antibiotic resistant organisms. This will dictate changes to operative routines to respond to evolving microbial diversity that seems inevitable.

PRINCIPLES OF ANTIBIOTIC PROPHYLAXIS

The purpose of antibiotic prophylaxis in surgical procedures is not to sterilize tissues but to reduce the colonization pressure of microorganisms introduced at the time of operation to a level that the patient’s immune system is able to overcome. Prophylaxis does not prevent infection caused by postoperative contamination. Prophylactic antibiotic use differs from treatment with antibiotics in that the former is intended to prevent infection, whereas the latter is intended to resolve an established infection, typically requiring a longer course of therapy. Prophylaxis is intended for elective procedures in which the incision will be closed in the operating room.

Before an agent can be considered for use as a prophylactic, there must be evidence that it reduces postoperative infection. It must also be safe and inexpensive, and it must be effective against organisms likely to be encountered in the surgical procedure. The agent must be administered in a way that ensures that serum and tissue levels are adequate before an incision is made and that therapeutic levels of the agent can be maintained in serum and tissue.
During surgery and for a few hours (at most) after the incision is closed. Wound infections—surgical site infections—in the form of cellulitis, abscess, or dehiscence can occur following laparotomy. Pelvic infections, such as an abscess or infected hematoma, are a risk with any surgical procedure that enters the abdominal cavity. Cuff cellulitis is a specific risk for hysterectomy. Endometritis can result from Caesarean section or surgical abortion. Urinary tract infections can occur as a result of any procedure that involves catheterization of the bladder.

A 1999 guideline published by the United States Centers for Disease Control and Prevention lists the specific and stringent criteria that must be met for diagnosis of a surgical site infection. Accurate surveillance for surgical site infection monitoring requires follow-up for 30 days postoperatively, and the trend towards early discharge from hospital makes surveillance a challenge. It is estimated that up to 84% of surgical site infections occur following discharge from hospital.

If prophylactic antibiotics are to be given, they should be administered shortly before or at bacterial inoculation. This should be done 15 to 60 minutes before skin incision. The majority of studies suggest that a single dose is effective but that for lengthy procedures (> 3 hours) the dose should be repeated at intervals 1 or 2 times the half-life of the drug. It has also been suggested that with large blood loss (> 1500 mL), a second dose should be given.

**SURGICAL PROCEDURES**

**Vaginal Hysterectomy**

A hysterectomy is considered a “class II or clean-contaminated” wound (Table 2). The method of hysterectomy may modify the inherent risk of postoperative infection. A Cochrane review suggested that vaginal hysterectomy results in fewer unspecified infections or febrile episodes (OR 0.42; 95% CI 0.21 to 0.83) than abdominal hysterectomy.

There is no meta-analysis or systematic review regarding antibiotic prophylaxis for vaginal hysterectomy. A review by Duff and Park included 20 studies, the majority of which were prospective randomized trials (18/20) and many of which were double-blinded (13/20). Without prophylaxis, the incidence of febrile morbidity averaged 40% to 50% but was reduced to 5% to 20% with prophylactic antibiotics. The type, dose, and duration of antibiotics used were highly variable, but a first-generation cephalosporin was used in the majority of studies.

A randomized trial comparing amoxicillin-clavulanic acid with cefazolin (n = 178) showed no difference in infection rates. Another trial comparing use of cefuroxime, metronidazole, or both showed an increased morbidity when metronidazole was added.

Treating bacterial vaginosis with metronidazole rectally for at least 4 days prior to vaginal hysterectomy appears to reduce the incidence of vaginal cuff infection (n = 59; 0% vs. 27%) but may be impractical given the possibility of surgery
cancellation. It is also difficult to comment on the cost-benefit of screening all women for BV prior to surgery.

**Abdominal Hysterectomy**

There are 3 meta-analyses exploring the efficacy of antibiotic prophylaxis for abdominal hysterectomy. The most recent, by Tanos and Rojansky in 1994, compared 17 trials (n = 2752) that used single dose or up to 24 hours of intramuscular or intravenous cephalosporins. There was a significant reduction in the incidence of infection in the treatment groups (OR = 0.35; 95% CI 0.3 to 0.4). Febrile morbidity was prevented by first-generation cephalosporins but not by some second- and third-generation choices. The authors concluded that a single dose of a first- or second-generation cephalosporin was efficacious and cost-effective. Mittendorf et al. (1993) meta-analyzed 25 RCTs (n = 3604) with varying antibiotic choice, duration, and routes of administration. They found that serious infections were less common in the treatment groups (9% vs. 21.1%, P = 0.001). Among those who received cefazolin or metronidazole, 11.4% and 6.3% respectively had serious postoperative infections. Lastly, Wtewaal-Evelaar (1990) examined 17 RCTs, the majority of which (14 of 17) used first- or second-generation cephalosporins. Infections were significantly reduced in the treatment groups (P < 0.001).

A randomized trial with women undergoing a gynaecologic procedure via laparotomy (which included abdominal hysterectomy) comparing amoxicillin-clavulanic acid with cefazolin (n = 511) showed no difference in infection rates. A randomized trial (n = 321) comparing placebo, ampicillin, and cefazolin, demonstrated significant superiority of cefazolin to reduce postoperative infection. A randomized study comparing a single dose versus 24-hour regimen of cefuroxime plus metronidazole, showed no difference.

**Laparoscopic Hysterectomy**

A Cochrane review showed that laparoscopic hysterectomy (laparoscopically assisted vaginal hysterectomy or laparoscopic subtotal hysterectomy) results in fewer wound or abdominal wall infections (OR 0.32; 95% CI 0.12 to 0.85) and fewer unspecified infections or febrile episodes (OR 0.65; 95% CI 0.49 to 0.87) than abdominal hysterectomy. There was no difference in any infections between laparoscopic hysterectomy and vaginal hysterectomy.

There are no trials assessing the use of prophylactic antibiotics for any types of laparoscopic hysterectomy. Given that this is a clean-contaminated procedure with a rate of postoperative infections similar to that of vaginal hysterectomy, it would seem reasonable to treat these patients in a similar fashion. A single dose of cefazolin was determined to be as effective as multiple doses in a study of 310 women who underwent laparoscopically assisted vaginal hysterectomy.

**Laparoscopy not Entering the Uterus and/or Vagina**

These procedures are considered clean (Table 2), as the genital tract is not entered. A randomized non-blinded trial of 450 women undergoing laparoscopy for various indications (not hysterectomy), found no difference in infection rates between those who received a single dose of cefazolin and those who did not.

**Recommendations**

1. All women undergoing an abdominal or vaginal hysterectomy should receive antibiotic prophylaxis. (I-A)
2. All women undergoing laparoscopic hysterectomy or laparoscopically assisted vaginal hysterectomy should receive prophylactic antibiotics. (III-B)
3. The choice of antibiotic for hysterectomy should be a single dose of a first-generation cephalosporin. If patients are allergic to cephalosporin, then clindamycin, erythromycin, or metronidazole should be used. (I-A)

4. Prophylactic antibiotics should be administered 15 to 60 minutes prior to skin incision. No additional doses are recommended. (I-A)

5. If an open abdominal procedure is lengthy (e.g., > 3 hours), or if the estimated blood loss is > 1500 mL, an additional dose of the prophylactic antibiotic may be given 3 to 4 hours after the initial dose. (II-3C)

6. Antibiotic prophylaxis is not recommended for laparoscopic procedures that involve no direct access from the abdominal cavity to the uterine cavity or vagina. (I-E)

Surgery for Pelvic Organ Prolapse and/or Stress Urinary Incontinence

A randomized double-bind, placebo-controlled trial enrolled 449 patients to receive nitrofurantoin monohydrate monocrystals or placebo preoperatively. Procedures included surgery for pelvic organ prolapse and/or stress incontinence with suprapubic catheterization. Positive urine cultures were significantly reduced (46% vs. 61%), as was symptomatic urinary tract infection (7.2% vs. 19.8%). There are no studies assessing prophylactic antibiotics prior to these surgeries without use of a suprapubic catheter. There are also no studies regarding isolated sub-urethral sling procedures (e.g., transvaginal or transobturator tapes), but given the very poor outcomes associated with mesh infection, administration of a single preoperative dose of a first-generation cephalosporin is common practice.

Recommendation

7. All women undergoing surgery for pelvic organ prolapse and/or stress urinary incontinence should receive a single dose of first-generation cephalosporin. (III-B)

Hysteroscopic Surgery

A Cochrane review of prophylactic antibiotics for transcervical intrauterine procedures did not identify any randomized trials that met their criteria. A pseudorandomized study that used centre-specific antibiotic prophylaxis analyzed 631 infertile women who underwent office hysteroscopy. Two hundred sixty-six women received amoxicillin-clavulanate and doxycycline 2 hours pre-procedure. There was no difference in post-procedural infection (1 in the antibiotic group). A randomized trial of amoxicillin and clavulanate versus placebo for hysteroscopic ablation (n = 116) found a significant difference in the occurrence of bacteremia (16% vs. 2%); however, the authors comment that the majority of organisms were of dubious clinical significance and that contamination could not be excluded in 7 of 10 cases. No significant difference was found for women treated for presumed infection (14.4% vs. 9%), but no objective measures were used. A case series of 568 women suggests that the infection risk is low (< 1%). There are no studies addressing prophylactic antibiotics in the setting of hysteroscopic myomectomy.

Recommendation

8. Antibiotic prophylaxis is not recommended for hysteroscopic surgery. (II-2D)

Induced (Therapeutic) Abortion

A meta-analysis that included 12 randomized clinical trials, demonstrated that prophylactic antibiotics significantly reduced post-abortal infection (at < 16 weeks), compared with placebo. The relative risk of upper genital tract infection following surgical abortion was 0.58 (95% CI 0.47 to 0.71) with antibiotics. The benefit was seen in women considered to be at high risk and in those at low risk for infection; thus, the authors conclude that universal prophylaxis should be given and that no more placebo-controlled trials should be performed. The most appropriate antibiotic regimen, however, is yet to be determined, as no comparative or superiority trials have been conducted. The largest trial to date (n = 1074), which had the most statistically significant reduction in postoperative infection rates (RR 0.12; 95% CI 0.08 to 0.38), used doxycycline 100 mg orally before the procedure followed by 200 mg after the procedure. Other regimens that have been effective in a randomized trial include metronidazole 400 mg orally 1 hour before the procedure and then repeated 4 and 8 hours after the procedure (RR 0.19; 95% CI 0.10 to 0.83) and doxycycline 400 mg orally 10 to 12 hours before the procedure (RR 0.47; 95% CI 0.22 to 0.73). A cost-effectiveness study looking at universal screening for sexually transmitted infections versus prophylactic azithromycin (1 g) showed that prophylactic treatment provided a significant cost savings. Disadvantages of not screening include the lack of case identification and the inability to complete therapy or conduct contact tracing. Some authors have questioned whether the presence of BV influences the rate of postoperative infection after induced abortion. In a double-blind placebo-controlled trial, treatment using 2% vaginal clindamycin for at least 3 days preoperatively did not decrease the risk of postoperative infection in patients with or without documented BV. The only statistically significant difference was seen when the authors combined the women who had intermediate BV.
flora with those who had BV (RR = 4.2 in untreated group; 95% CI 1.2 to 15.9). Another randomized blinded trial found that giving a single 2 g metronidazole suppository preoperatively to women who had confirmed bacterial vaginosis did not make a significant difference (RR = 0.53; P = 0.055). Screening and treating for bacterial vaginosis prior to surgery also may be impractical, and the cost-effectiveness is not known.

**Recommendation**

9. All women undergoing an induced (therapeutic) surgical abortion should receive prophylactic antibiotics to reduce the risk of post-abortion infection. (I-A)

**Missed or Incomplete Abortion**

There are two randomized placebo-controlled trials that assess the effectiveness of prophylactic antibiotics to reduce infectious morbidity following uterine evacuation for incomplete abortion. One trial involving 240 women used a preoperative intravenous dose of doxycycline or placebo. Chlamydia and gonorrhea rates were low (3% to 6%) in this population. No difference in postoperative infectious morbidity rates occurred up to 2 weeks post-procedure. A second study of 300 women investigated the use of 200 mg oral doxycycline at 30 to 60 minutes pre-procedure. Again, no significant difference between groups was found. A 2007 Cochrane Review on this topic concluded there is not enough evidence to recommend routine antibiotic prophylaxis for incomplete abortion at the time of evacuation of the uterus.

**Recommendation**

10. Prophylactic antibiotics are not suggested to reduce infectious morbidity following surgery for a missed or incomplete abortion. (I-E) However, health care professionals could consider screening for sexually transmitted infections in high-risk populations. (III-C)

**OFFICE PROCEDURES**

**Intrauterine Device Insertion**

Various authors have demonstrated that the risk of IUD-related infection is limited to the first few weeks to months after insertion. It is therefore likely related to contamination of the endometrial cavity at the time of insertion, rather than the IUD or strings themselves. A 1999 Cochrane Review that included 4 randomized control trials found no difference in the occurrence of PID after IUD insertion in patients who were given prophylactic doxycycline or azithromycin and in those given placebo (OR 0.89; 95% CI 0.53 to 1.51). Use of these antibiotics also did not affect whether the IUD was removed within 90 days of insertion (OR 1.05; 95% CI 0.68 to 1.63). However, if the patient is considered at high risk for sexually transmitted infections, it would be reasonable to consider screening before IUD placement.

**Recommendation**

11. Antibiotic prophylaxis is not recommended for insertion of an intrauterine device. (I-E) However, there are no studies that assess the use of prophylactic antibiotics given before an endometrial biopsy procedure, and this is not considered standard of care.

**Endometrial Biopsy**

There are no studies that assess the use of prophylactic antibiotics given before an endometrial biopsy procedure.

**Recommendation**

12. There is insufficient evidence to support the use of antibiotic prophylaxis for an endometrial biopsy. (III-L)

**Hysterosalpingography**

There are many options for preventing infection that may occur as a result of HSG:

1. Universal screening for STIs could be carried out, and patients treated as necessary.

2. Only patients at high risk (determined by history) could be screened.

3. All patients could receive prophylactic antibiotics.

4. Antibiotics could be given to patients at high risk (determined by history and/or as indicated by the presence of tubal obstruction at the time of HSG). Many of the patients may already have had screening performed as part of an infertility work-up. If infection is found, treatment should follow the Canadian Guidelines for STIs. There are no prospective studies that investigate any of these options. A retrospective study found that among 278 women who did not receive antibiotics, the incidence of PID after HSG was 1.4% (4/278), and all 4 patients had dilated tubes; 31 other patients with dilated tubes did not develop infection. A second group of patients (n = 326) received a single dose of oral doxycycline before HSG; no patient (including 56 who had dilated tubes) developed PID. This study suggests that the incidence of PID with normal tubes is very low, regardless of prophylactic antibiotics (0/398) and that the highest-risk group of women with dilated tubes at the time of HSG did benefit from prophylactic doxycycline.
Recommendation

13. The best method to prevent infection after hysterosalpingography is unknown. Women with dilated tubes found at the time of hysterosalpingography are at highest risk, and prophylactic antibiotics (e.g., doxycycline) should be given. (II-3B)

URODYNAMIC STUDIES

A systematic review in 2008 included 8 RCTs, with 995 patients, most of whom were women. The prophylactic antibiotics differed in type, dose, and duration and were compared with either placebo or no treatment. The authors noted that most of the trials had poor methodology. They concluded that there was a 40% reduction in the risk of bacteriuria (OR 0.39; 95% CI 0.24 to 0.61), correlating to a number needed to treat of 13. This study assessed only the occurrence of bacteriuria and not that of symptomatic UTI; therefore, the clinical significance is unknown. It has been estimated that only 8% of women develop a symptomatic UTI within 1 week of a diagnosis of asymptomatic bacteriuria. On the basis of the results of a decision-analysis that incorporated reasonable estimates of benefits and adverse events from the published literature, the authors concluded that prophylactic antibiotics after urodynamics in women at low risk should be administered only when the background rate of UTIs after urodynamics without prophylaxis is higher than 10%.45

Recommendation

14. Antibiotic prophylaxis is not recommended for urodynamic studies in women at low risk, unless the incidence of urinary tract infection post-urodynamics is > 10%. (I-E)

DOSAGE OF ANTIBIOTIC PROPHYLAXIS IN OBESE PATIENTS

Increased BMI is associated with higher rates of surgical infectious complications. Expert opinion recommends twice the normal dose of prophylaxis for morbidly obese patients (BMI > 35 kg/m²). However, controlled trials assessing the required dosage for antibiotic prophylaxis based on patient BMI have not been assessed in our specialty, and future research is needed.

Recommendation

15. In patients with morbid obesity (BMI > 35 kg/m²), doubling the antibiotic dose may be considered. (II-B)

RECOMMENDATIONS FOR PENICILLIN/CEPHALOSPORIN ALLERGY

Penicillin allergy is self-reported by up to 10% of patients, yet only 10% of those who report themselves as allergic are allergic when skin testing is performed. True anaphylactic response to penicillin is rare, occurring in 1 to 4 per 10,000 administrations. Allergic reaction to a cephalosporin occurs at rates of 0.17% to 8.4% in those with a penicillin allergy. Alternative prophylactic antibiotics for those deemed truly penicillin allergic include clindamycin 600 mg IV and erythromycin 500 mg IV.

PREVENTION OF INFECTIVE ENDOCARDITIS

The American Heart Association guideline published in 2007 found no evidence that genitourinary procedures cause infectious endocarditis or that administration of antibiotics prevents infectious endocarditis following such procedures. The American Heart Association therefore does not recommend prophylactic antibiotics for patients undergoing genitourinary procedures; this is a change from
the 1997 American Heart Association guideline. The 2007 guideline identifies 4 conditions that are at highest risk of adverse outcome (Table 3). For patients with the conditions listed in Table 3 who have an established gastrointestinal or genitourinary infection, or for those who receive antibiotic therapy for another reason (e.g., to prevent wound infection), it may be reasonable that the antibiotic used also be active against enterococci (ampicillin, piperacillin, or vancomycin). The guidelines also suggest that it may be reasonable for patients at high risk of infectious endocarditis who have a known enterococcal urinary tract infection or colonization to receive antibiotic treatment prior to any urinary tract manipulation. A review of this recommendation change has recently been published.55

**Recommendation**

16. Administration of antibiotics solely to prevent endocarditis is not recommended for patients who undergo a genitourinary procedure. (III-E)

**SUMMARY**

For a number of procedures in gynaecology, the use of prophylactic antibiotics has been shown to reduce infectious morbidity in a safe and cost-effective manner (Table 4). There remain a number of procedures for which the utility of prophylactic antibiotics is either unclear or not studied. Appropriate antibiotics used at the correct dose and time and with the appropriate frequency will reduce infectious postoperative complications and minimize the development of antibiotic resistant organisms.

**REFERENCES**


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