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Preoperative Antibiotic Prophylaxis

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Indications

Preoperative antibiotic prophylaxis is defined as the administration of antibiotics before surgery to help prevent surgical site infections. The use of antibiotic prophylaxis is just one of many actions taken to help reduce the rate of surgical site infections. Other preoperative actions include basic infection control strategies, instrument sterilization, and a patient's skin preparation (e.g., methicillin-resistant *Staphylococcus aureus* [MRSA] decolonization, appropriate hair removal, skin antiseptic). A patient's overall medical condition and perioperative and postoperative management are also important factors in the prevention of surgical site infections.

The most common organisms implicated as surgical site infection pathogens are dependent upon the type of wound that is involved in surgery. Wound types can be classified as clean, clean-contaminated, contaminated, or dirty/infected according to the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN). Clean wounds are not infected, without inflammation, primarily closed, and do not include the organ systems that are outlined in a clean-contaminated wound. Clean-contaminated wounds involve the respiratory, alimentary, genital, and urinary tract as long as the tract is entered without unusual contamination. Contaminated wounds include open, fresh accidental wounds including those with non-purulent inflammation. Contaminated wounds also include procedures with major breaks in sterile technique or gross spillage from the gastrointestinal tract. Dirty or infected wounds are old traumatic wounds with devitalized tissue or involve existing clinical infection or perforated viscera. During clean procedures, skin flora such as coagulase-negative *staphylococci* (e.g., *Staphylococcus epidermidis*) or *Staphylococcus aureus* are predominant pathogens in surgical site infections. In clean-contaminated procedures, the most commonly found organisms causing surgical site infections are skin flora, gram-negative rods, and *Enterococci*.

In general, the preoperative antibiotic selection is based on the site of infection and most likely pathogens for the type of wound. The goal when determining the best antibiotic is to have the narrowest spectrum of activity while still ensuring the most common organisms are targeted. Additionally, preoperative antibiotics are chosen based on cost, safety, ease of administration, pharmacokinetic profile, bacteriocidal activity, and hospital resistance patterns. By addressing all of these factors during antibiotic selection, surgical site infections are minimized while still maintaining appropriate antimicrobial stewardship practices. When addressing antibiotic surgical prophylaxis in the adult population compared with the pediatric population, many of the same antibiotics utilized in the adult population are also used in pediatrics (e.g., first-generation and second-generation cephalosporins, vancomycin).

Cefazolin is used most often for surgical prophylaxis except in cases such as significant beta-lactam allergy, known MRSA colonization, or surgical sites with probable organisms that are not covered by cefazolin alone (e.g., appendectomy, colorectal). In patients requiring only cefazolin for preoperative surgical prophylaxis, clindamycin or

vancomycin are often used as alternatives in those with significant beta-lactam allergies. In the case of MRSA colonization, vancomycin is the alternative unless additional antibiotics are required for possible gram-negative or anaerobic organisms. For patients requiring additional microbe coverage (e.g., colorectal), multiple options may be considered including cefazolin plus metronidazole, cefoxitin, or ertapenem. Additional antibiotics are options based on specific surgical sites in addition to hospital-specific and patient-specific antibiotic resistance.

Mechanism of Action

Multiple antibiotic classes are recommended for use in preoperative antibiotic prophylaxis. The antibiotics utilized are bactericidal instead of bacteriostatic. This means that any of the targeted organisms are killed instead of just preventing the multiplication of further growth. It should be noted that certain antibiotics can exhibit bacteriostatic or bactericidal properties depending on the bacterial sensitivity and antibiotic concentration. For example, Clindamycin is bacteriostatic at lower doses, but at higher doses, it can exhibit bactericidal properties. In most surgeries, the intent is to ensure the bactericidal concentration has been reached in the blood and tissues before incision.

Administration

The majority of preoperative prophylactic antibiotics are administered intravenously (IV). The initial timing of administration, redosing if applicable, duration of prophylactic therapy, and dosing in obese patients are important components in the prevention of surgical site infections as well as antimicrobial stewardship. Avoiding unnecessary use of antibiotics helps diminish the occurrence of adverse effects and antibiotic resistance development. Most antibiotics should be given within 60 minutes of a surgical incision. Exceptions include vancomycin and levofloxacin, which require administration within 120 minutes of the procedural incision due to longer administration times. If a patient is already receiving an antibiotic for another infection before surgery, and it is appropriate for surgical prophylaxis, an extra dose of the antibiotic can be administered within 60 minutes of the incision. If a patient is already receiving vancomycin and has renal failure, cefazolin should be considered before surgery instead of an extra dose of vancomycin.

Redosing antibiotics is an important factor due to the half-life of the particular antibiotic used. Factors such as renal dysfunction and extensive burns may impact the half-life of an antibiotic. Based on the antibiotics mentioned above, cefazolin and cefoxitin would have to be administered more than once depending on the length of the procedure. A perioperative dose of cefazolin should be administered again at four hours after the initial preoperative dose while cefoxitin should be administered again two hours later. Redosing antibiotics due to significant blood loss or dilution during surgery are other considerations being studied at this time.

Unless there is a known infection, prophylactic antibiotics should be discontinued within 24 hours. Experts disagree if the duration of therapy should be extended to 48 hours in cardiothoracic surgery. Two meta-analyses compared 24 hours versus 48 hours as the cut-off in cardiac surgeries and found a significant decrease in surgical site infections with the extended duration, particularly in sternal infections. The most recent guidelines from the CDC state that additional prophylactic antibiotics should not be administered after the surgical incision is closed in clean and clean-contaminated procedures. This recommendation applies to patients with or without a drain after the surgical site is closed, although there could be procedure-specific exceptions.

The three antibiotics used in adult surgical prophylaxis where weight-based dosing is recommended are cefazolin, vancomycin, and gentamicin. For patients receiving cefazolin, 2 g is the current recommended dose except for patients weighing greater than or equal to 120 kg, who should receive 3 g. There is some literature stating cefazolin 2 g should be sufficient for a patient at any adult weight. Vancomycin is dosed at 15 mg/kg, and gentamicin is dosed 5 mg/kg. Other commonly used prophylactic antibiotics in adults are dosed as the following: clindamycin 900 mg, cefoxitin 2 g, and ertapenem 1 g. All prophylactic antibiotics for pediatrics are dosed based on milligram per kilogram

body weight. Examples of pediatric dosages include the following: cefazolin 30mg/kg and vancomycin 15 mg/kg. Pediatric surgical prophylaxis dosages should not exceed the usual adult dose.

Adverse Effects

Limiting the duration of all antibiotics is important since any antimicrobial usage can alter hospital and patient bacterial flora, which can potentially lead to colonization, resistance, or *Clostridium difficile*.

Contraindications

Beta-lactam antibiotics, including cephalosporins, are commonly used for surgical prophylaxis, so it is important to identify when these antibiotics are contraindicated. If a patient has an immunoglobulin (IgE) mediated (i.e., type 1) allergy to penicillin, then penicillins, cephalosporins, and carbapenems should not be administered. A type 1 reaction would be considered anaphylaxis, urticaria, or bronchospasm that occurs 30 to 60 minutes following administration of the antibiotic. Cephalosporins and carbapenems are considered safe in patients who have not had a type-1 reaction or exfoliative dermatitis (e.g., Stevens-Johnson syndrome and toxic epidermal necrolysis). Obtaining a thorough allergy history from each patient is vital to ensure if the allergy stated by the patient is a real and significant allergy that would impact usual preoperative surgical prophylaxis.

Monitoring

Surgical site infections may occur for a variety of reasons including, but not limited to, incorrect antibiotic usage. When considering antibiotic prophylaxis practices, the correct antibiotic, dosage, timing of initial dose, and timing of any applicable redosing are major factors to review to ensure best practices are always followed. If an institution recommends a specific antibiotic in surgery when additional antibiotics are options, monitoring should take place to ensure no surgical site infections are occurring due to increasing local resistance. One example could be that growing clindamycin resistance has translated to increased surgical site infections in those receiving clindamycin due to a penicillin allergy. That information could lead an institution to switch to vancomycin instead of clindamycin in that patient population. Antibiotic selection should also be reviewed to avoid the use of antibiotics that might result in new or worsening resistance patterns identified on the antibiogram. An institution may choose to use cefoxitin instead of ertapenem in colorectal surgeries to avoid excessive usage of the carbapenem class when applicable, especially if the institution has an escalating number of carbapenem-resistant organisms.

Toxicity

No apparent toxicities are known with the recommended doses. This is partially due to the limited duration of antibiotic exposure in surgical prophylaxis.

Questions

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