REVIEW ARTICLE

Antibiotic prophylaxis for surgical site infection: Need of time

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ABSTRACT

Surgical site infection is one of the most common hospital acquired infection. Antibiotics are given prior to surgery to reduce the burden of infection. Antibiotic of right choice at right dose and given at right time achieve the right concentration in the tissue to reduce the microbes responsible for surgical site infection. It should be economical, have narrow spectrum and have minimal adverse effects. The initial antimicrobial dose should be based on the patient's body weight or body mass index. The antimicrobial should be safe for the patient and economical for the hospital. Antimicrobial prophylaxis is not recommended for most clean procedures in patients without additional postoperative infection risk factors. Apart from wound infection, surgical site infections are also related to the pre-operative preparation of patients by nursing staff. It also depends on the aseptic precautions taken by the surgeon and nursing staff while operating and also on the surgical technique and procedure followed like equipment preparation, duration of surgery and patient preparation. Surgical Prophylaxis should be used in a manner that is supported by evidence of effectiveness, minimize the effect of antibiotics on the patient's normal bacterial flora and cause minimal change to the patient's host defenses.

Key words: *Antibiotic prophylaxis, Drug resistance, Surgical site infection*

Surgical site infections (SSIs) are the second most common component of nosocomial infections. [1] Surgical prophylaxis is important to prevent surgical site infections by using an antimicrobial agent that is safe, cost-effective, and has a spectrum of activity that covers the most common pathogens for surgical procedures. Surgical prophylaxis is given to achieve appropriate serum and tissue concentrations of the antimicrobial agent prior to the time of incision and throughout the duration of the surgical procedure.

Surgical prophylactic antibiotic treatment is defined as the use of antibiotics before, during, or after a diagnostic and therapeutic procedure to prevent infectious complications. [2] On the other hand, therapeutic antibiotic treatment is defined as the use of antibiotics that reduce the growth or reproduction of bacteria, including eradication therapy. [3] This term is used to describe antimicrobial therapy prescribed to clear infection by an organism or to clear an organism that is colonizing a patient but is not causing infection.

Patients who develop SSIs are up to 60% more likely to spend time in an ICU, five times more likely to be re-admitted to the hospital, and two times more likely to die than are patients without SSI. [4] Health care costs are substantially increased for patients who develop SSIs. [5] SSI is one of the most common healthcare associated infections, with one UK study in 2001 showing the consequences to be an additional hospital stay of 6.5 days at a cost of INR 3,27,846 per patient. [6]

Surgical prophylaxis has become the standard care for contaminated surgery and clean contaminated surgery and for surgery involving insertion of artificial devices. Inappropriate use of antibiotics for surgical prophylaxis increases cost and also favouring the emergence of resistant bacteria. Surgical antimicrobial prophylaxis can alter individual and institutional bacterial picture that leads to changes in colonization rates and increased bacterial resistance. [7] Longer duration of prophylaxis or uses of multiple antimicrobial agents are the risk factors for development of C. difficile-associated colitis. [8,9]

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Principles and goals for surgical antibiotic prophylaxis

Antimicrobial agent for surgical prophylaxis should, (1) prevent surgical site infections, (2) reduce the cost and duration of treatment,[10] (3) prevent adverse effects, and (4) have no adverse consequences on the microbial flora of the patient or the hospital. [11]

To achieve these goals, an antimicrobial agent should be, (1) active against the bacterial flora most likely to contaminate the surgical site, (2) narrow spectrum antibiotic and avoid antibiotics used for serious sepsis, (3) less expensive, (4) given in an appropriate dosage and time, (5) administered for a short duration, and (6) have minimal adverse effects. [12]

Indications for surgical prophylaxis

Operations can be categorized into four classes (Table 1) according to their potential risk for infectious complications. The system is classified as follows:

Table 1: Classification of Wounds [13]

Class	Definition
Clean	Operations in which no inflammation is encountered and the respiratory, alimentary or genitor-urinary tracts are not entered. There is no break in aseptic operating theatre.
Clean-contaminated	Operations in which the respiratory, alimentary or genitor-urinary tracts are entered but without significant spillage.
Contaminated	Operations where acute inflammation (without pus) is encountered, or where there is visible contamination of the wound. Examples include, gross spillage from a hollow viscus during the operation or compound/open injuries operated within four hours.
Dirty	Operations in the presence of pus, where there is a previously perforated hollow viscus, or compound/open injuries more than four hours old.

This guideline applies to all elective operations in the clean, clean-contaminated, contaminated or dirty categories. Recommendations for prophylaxis of emergency surgery are limited to clean operations and clean-contaminated operations. As well as for antibiotic therapy for emergency operations with contaminated or dirty wounds, it is the standard therapy should be used rather than surgical prophylaxis.

Risk and benefits of surgical prophylaxis

Obese female patients above 60-years of age are more prone to surgical site infections. Patients with a history of underlying diseases like diabetes, congestive heart failure, liver failure, renal failure, hospitalization for more than 72 hours, immunosuppressant patient. Patient at increased risk of hypersensitivity reaction should avoid beta-lactams as prophylaxis.

Surgery related factors also put patient on high risk for surgical site infection. Mostly, it depends on the type of procedure, site of surgery, emergency surgery. If the duration is more than 60-120 min, any history of previous surgery, the timing of antibiotic administration, placement of foreign body like hip/knee replacement, heart valve insertion, shunt insertion and also associated conditions related to surgery like hypotension, hypoxia, dehydration, hypothermia. [14]

Surgical site infections are also related with the patient preparation like shaving the operating site, preparation of operating site like draping the patient. Surgeon and nursing preparation like hand washing, skin antiseptics and gloving are also important. It also depends on the surgical technique and procedure followed like equipment preparation, duration of surgery and patient preparation.

Surgical site infection also depends on the intra-operative procedure like magnitude of tissue trauma and devitalization, blood loss, hematoma, wound classification, potential bacterial contamination, presence of drains, packs, drapes, ischemia and wound leakage.

Choice of antibiotics

The antimicrobial agent should have activity against the most common surgical-site pathogens. The most predominant organisms causing surgical infections are *S. aureus* and coagulase-negative *staphylococci* (Eg: *Staphylococcus epidermidis*) belonging to skin flora. [15] In clean-contaminated procedures, the predominant organisms include gram-negative rods and enterococci in addition to skin flora. Agents that are FDA-approved for use in surgical antimicrobial prophylaxis include intravenous cephalosporins like cefazolin, cefuroxime, cefoxitin or cefotetan, oral tinidazole (if anaerobic infection is likely), intravenous gentamicin, intravenous or rectal metronidazole (if anaerobic infection is likely), intravenous flucloxacillin (if methicillin-susceptible staphylococcal infection is likely) and intravenous vancomycin (if methicillin-resistant staphylococcal infection is likely). [16] Alternatives to cephalosporins with beta-lactam allergy, there are vancomycin and clindamycin. [17] On the basis of local antimicrobial resistance patterns and institutional incidence of infections caused by organisms such as *Clostridium difficile* and *Staphylococcus epidermidis*, vancomycin and clindamycin are appropriate alternatives to beta-lactams. [18] (Table 2)

In surgical patients, there is a wide range of organisms which has the probability of causing infection but SSI is usually caused due to a small number of common pathogens. Antibiotics should be used only for those organisms that are expected in the operative site. The antibiotics chosen must be disease-specific and should have antimicrobial susceptibility. The antibiotic should be used on the basis of its resistance in the hospital and drug costs. Narrow spectrum antibiotic which are less expensive should be the first choice for prophylaxis during surgery.

Hypersensitivity to penicillin should also be considered while using as surgical prophylaxis as it may have clinically-disastrous results. Another issue is over-diagnosis of an allergy, resulting in failure to use a beta-lactam when it would have been suitable.

Selection and dosing

A single standard therapeutic dose of antibiotic is sufficient for prophylaxis under most circumstances. The drug dosing should be weight-based. As obese persons are at increased risk for surgical site infection therefore the pharmacokinetics of drugs may be altered in obese patients. [20] (Table 3)

Timing and route of antibiotic administration

Antibiotic takes an approximate time to reach an effective concentration in the tissue that reflects its pharmacokinetic profile and the route of administration. [21] Antibiotic prophylaxis for surgery is given within one hour before incision except for fluoroquinolone or vancomycin, which are given within two hours prior to surgical incision. The timing of dosing is important as most beta-lactam have short half-lives hence it should be given within one hour prior to incision.

Stone et al. demonstrated the lowest SSI rates among patients undergoing gastro-intestinal, biliary, and colon operations when antimicrobials were administered within 1 hour before incision (mostly 15-60 minutes). [22] Whenever a proximal tourniquet is applied, the entire dose of antibiotic should be administered before the tourniquet is inflated.

On the other hand, if the antibiotic prophylaxis is administered too late or too early then the efficacy of the antibiotic is reduced and that may increase the risk of SSIs. [23] Prophylaxis given three hours after the start of the operation significantly reduces its effectiveness. [24] Additional doses are strongly recommended during intra-operative procedures of longer duration where time required is approximating two times the half-life of the drug. This corresponds with redosing antimicrobials at a frequency of one interval shorter than usual. (Table 3)

Intravenous route are most commonly used than intramuscular as peak tissue level can be achieved by this route. Other routes like oral or rectal antibiotics are given earlier to achieve tissue concentration. They must be given 2-4 hours before the incision. Tropical antibiotics are not recommended except for ophthalmic or burn surgeries. On the other hand, administration of fluoroquinolones by oral route achieves comparable serum and tissue levels to antibiotic prophylaxis via the IV route. [25]

Table 2: Recommendations for commonly surgical antimicrobial prophylaxis [19]

Type of procedure	Recommended agents	Alternative agents in patients with beta-lactam allergy
Cardiac (coronary artery bypass)	Cefazolin, Cefuroxime	Clindamycin, Vancomycin
Cardiac device insertion procedures (Eg: pacemaker implantation)	Cefazolin, Cefuroxime	Clindamycin, Vancomycin
Gastro-duodenal procedures involving entry into lumen of gastro-intestinal tract (bariatric, pancreatico-duodenectomy)	Cefazolin	Clindamycin or Vancomycin Aminoglycoside or Aztreonam or Fluoroquinolone
Biliary tract open procedure	Cefazolin, Cefoxitin, Cefotetan, Ceftriaxone, Ampicillin-Sulbactam	Clindamycin or Vancomycin + Aminoglycoside or Aztreonam or Fluoroquinolone Metronidazole + Aminoglycoside or Fluoroquinolone
Laparoscopic procedure (elective, low-risk)	None	None
Laparoscopic procedure (elective, high-risk)	Cefazolin, Cefoxitin, Cefotetan, Ceftriaxone, Ampicillin-Sulbactam	Clindamycin or Vancomycin + Aminoglycoside or Aztreonam or Fluoroquinolone Metronidazole + Aminoglycoside or Fluoroquinolone
Appendectomy for uncomplicated appendicitis	Cefoxitin, Cefotetan, Cefazolin + Metronidazole	Clindamycin + Aminoglycoside or Aztreonam or Fluoroquinolone Metronidazole + Aminoglycoside or Fluoroquinolone
Small intestine obstruction	Cefazolin+ Metronidazole, Cefoxitin, Cefotetan	Metronidazole + Aminoglycoside or Fluoroquinolone
Hernia repair (hernioplasty and herniorrhaphy)	Cefazolin	Clindamycin, Vancomycin
Colo-rectal	Cefazolin + Metronidazole, Cefoxitin, Cefotetan, Ampicillin-Sulbactam, Ceftriaxone + Metronidazole, Ertapenem	Clindamycin + Aminoglycoside or Aztreonam or Fluoroquinolone, Metronidazole + Aminoglycoside or Fluoroquinolone
Cesarean delivery	Cefazolin	Clindamycin + Aminoglycoside
Hysterectomy (vaginal or abdominal)	Cefazolin, Cefotetan, Cefoxitin, Ampicillin-Sulbactam	Clindamycin or Vancomycin + Aminoglycoside or Aztreonam or Fluoroquinolone Metronidazole + Aminoglycoside or Fluoroquinolone
Orthopedic surgeries Implantation of internal fixation devices (Eg: nails, screws, plates, wires)	Cefazolin	Clindamycin, Vancomycin
Plastic surgery (clean with risk factors or clean-contaminated)	Cefazolin, Ampicillin-Sulbactam	Clindamycin, Vancomycin
Neurosurgery (elective craniotomy and cerebrospinal fluid-shunting procedures)	Cefazolin	Clindamycin, Vancomycin

Table 3: Dosing and timing of commonly used antibiotic agents used for surgical prophylaxis

Antimicrobial	Standard dose	Weight-based dose recommendation	Recommended redosing interval, hour
Cefazolin	1-2 gm IV	20-30 mg/Kg If <80 Kg, use 1 gm If >80 Kg, use 2 gm	2-5
Cefuroxime	1.5 gm IV	50 mg/Kg	3-4
Cefamandole	1 gm IV	50 mg/Kg	3-4
Cefotetan	1-2 gm IV	20-40 mg/kg	3-6
Clindamycin	600-900 mg IV	If <10 Kg, use at least 37.5 mg If >10 Kg, use 3-6 mg/Kg	3-6
Gentamicin	1.5 mg/Kg IV	…[a]	3-6
Metronidazole	0.5-1 gm IV	15 mg/Kg initial dose (adult) 7.5 mg/Kg on subsequent doses	6-8
Vancomycin	1 gm IV	10-15 mg/Kg (adult)	6-12

*[a] If the patient's body weight is 130% higher than their ideal body weight (IBW), the dosing weight (DW) can be determined as follows: DW = IBW + [0.4 * (total body weight - IBW)]*

Duration of antibiotic administration

Antibiotics prophylaxis beyond wound closure is unnecessary as it leads to emergence of resistant bacteria strains. [26] It is unlikely that further benefit is attained by additional doses of antibiotic beyond wound closure and post-operative prophylaxis is not recommended. A single standard dose of antibiotic is sufficient for prophylaxis for most clean surgeries. Duration of antibiotic prophylaxis for surgery must be discontinued within 24 hours of the procedure. If prophylaxis is extended beyond the duration of surgery, antibiotics should be discontinued within 24 hours unless otherwise specified. *American Society of Health-System Pharmacists* (ASHP) recommends continuing prophylaxis for up to 72 hours for cardiac surgeries. [27] An additional intra-operative dose of antibiotic is recommended for surgeries longer than four hours when using an antibiotic with short half-life like cefuroxime, cefazolin etc.

Limitations of additional agents

The main purpose of antimicrobial prophylaxis is to prevent infection due to organisms most likely to be encountered for that type of operation. A single antimicrobial is sufficient for most of the surgeries to prevent surgical site infection. On the other hand, there may be cases which are contaminated and dirty (Eg: in cases of co-existing infection) for which additional coverage is necessary. In clean procedures, it is better to treat the source of infection before the elective surgery. [28]

Non-pharmacological methods of preventing infection

Infection rates are better controlled if intra-operative temperature is maintained and adequate oxygen administration with aggressive fluid resuscitation are maintained. [29, 30] Aggressive peri-operative control of blood sugar with intravenous insulin for patients undergoing cardiac operations reduces surgical site infection rates. [31] Appropriate surgical technique with minimal soft tissue dissection along with lesser operative time helps in preventing the surgical site infections.

CONCLUSION

Surgical antibiotic prophylaxis is an effective management for reducing post-operative infection provided that the antibiotic is given at the correct time, cover the organism that are likely to be encountered during particular surgery and given for appropriate duration. The selection of antimicrobial prophylaxis should be narrow spectrum that is not use in sepsis to avoid selection of resistance bacteria. It should have the least impact on the normal bacterial flora of the patient and the microbiologic ecology of the institution or hospital.

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