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ANTIBIOTIC PROPHYLAXIS TO PREVENT SURGICAL SITE INFECTIONS: A REVIEW

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Abstract:

In the majority of SSI cases, the pathogen source is the native flora of the patient's skin, mucous membranes, or hollow viscera. When skin is incised, underlying tissue is exposed to overlying endogenous flora.[9] Most typically, aerobic gram-positive cocci such as Staphylococcus *serve as the contaminant, with resistant pathogens such as methicillin-resistant* S aureus *(MRSA). Entry into hollow viscera exposes surrounding tissue to gram-negative bacilli such as* Escherichia coli, *gram-positive organisms such as enterococcus, and, occasionally, anaerobes such as* Bacillus fragilis. *Yeast species and viral pathogens also pose a risk.*

Other sources of SSI pathogens are from distance focus such as in patients with prosthesis or implant place during the surgery, surgical personnel, operating environment, surgical tools, instruments, and materials brought to the field during an operation.

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INTRODUCTION:

Wound infections are the commonest hospital-acquired infections in surgical patients.[1]

They result in increased antibiotic usage, increased costs and prolonged hospitalisation. Surgical site infection is defined as an infection occurs within 30 days after the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation and infection involves deep soft tissue (e.g. fascia, muscle) of the incision and/or the infection appears to be related to the operation and infection involves any part of the anatomy other than the incision that was opened or manipulated during an operation (e.g. organs and spaces).[2] The global estimates of SSI have varied from 0.5% to 15%, studies in India have consistently shown higher rates ranging from 23% to 38%.[3]

These infections are caused by exogenous (from the environment of the operating theatre or the surgical ward) and endogenous microorganisms (from the patients' own skin or opened viscus) which enter the operative wound during surgery. The risk factors for postoperative infections are abdominal surgeries, prosthetic surgeries (bone or soft tissue), duration of surgery is more than 2 hours, surgery on contaminated or dirty wounds. The likelihood of infection depends on bacterial count present at the site of wound at the time when surgery is over.[4] Surgical prophylaxis means prevention of infection at the site of surgery that includes, infection at site of incision and infection of deeper tissues handled during surgery.

The original surgical antibiotic prophylaxis experiments were performed 40 years ago in pigs. The results concluded that 'the most effective period for prophylaxis begins the moment bacteria gain access to the tissues and is over in three hours'.[5]

Since then there have been many studies in animal models and in humans undergoing surgery. This has resulted in the principles of antibiotic prophylaxis becoming an accepted part of surgical practice.[6] Approximately 30-50% of antibiotic use in hospital practice is now for surgical prophylaxis. However, between 30% and 90% of this prophylaxis is inappropriate. Most commonly, the antibiotic is either given at the wrong time or continued for too long.[7] Controversy remains as to duration of prophylaxis and also as to which specific surgical procedures should receive prophylaxis.[8]

The purpose of surgical prophylaxis is to reduce the incidence of SSI with minimal alteration of normal microbial flora of the host and minimal adverse effects.

Microbiology:

In the majority of SSI cases, the pathogen source is the native flora of the patient's skin, mucous membranes, or hollow viscera. When skin is incised, underlying tissue is exposed to overlying endogenous flora.[9] Most typically, aerobic gram-positive cocci such as Staphylococcus serve as the contaminant, with resistant pathogens such as methicillin-resistant S aureus (MRSA).[10,11] Entry into hollow viscera exposes surrounding tissue to gram-negative bacilli such as Escherichia coli, gram-positive organisms such as enterococcus, and, occasionally, anaerobes such as Bacillus fragilis. Yeast species and viral pathogens also pose a risk.[12]

Other sources of SSI pathogens are from distance focus such as in patients with prosthesis or implant place during the surgery, surgical personnel, operating environment, surgical tools, instruments, and materials brought to the field during an operation.

Antimicrobial Prophylaxis:

The aim of prophylaxis is to prevent infection with least possible adverse effect of drug including minimal reduction in normal flora. The prophylactic regimen in patients undergoing surgery should include an agent effective against the most likely infecting organisms, but need not eradicate every potential pathogen. The choice of antibiotic should be based on the local antibiogram. The antibiotics utilized are bactericidal instead of bacteriostatic. The abusive use of antibiotics may lead to the development of superbugs, and bacteria can develop acquired resistance to antibiotics that they have encountered. Many powerful superbugs develop with the continual abuse of powerful new antibiotics.[13]

Important points for surgical antimicrobial prophylaxis administration:[14] The prophylactic agent chosen should have activity against the most common surgical wound pathogens

- Prophylaxis is unnecessary if the patient is already receiving antibiotics that cover the likely pathogens
- Patients receiving therapeutic antimicrobials for a remote infection before surgery to ensure adequate serum and tissue levels of antimicrobials with activity against likely pathogens for the duration of the operation

- Intravenous administration is ideal because it produces reliable and predictable serum and tissue concentrations
- Administration of first dose of antimicrobial should be done within 60 min before surgical incision
- Vancomycin and fluoroquinolones should be administered 120 min before surgery as they require prolonged infusion times
- In caesarean sections, the antimicrobials should be administered pre-incision or after cord clamping. This should be done as close to the incision as practically possible
- Antimicrobial-specific pharmacokinetic and pharmacodynamic properties and patient factors must be considered when selecting a dose
- Intraoperative re-dosing is needed if the duration of the procedure exceeds 2 half-lives of the drug or if there is excessive blood loss during the procedure (i.e., >1500 ml)
- Post-operative antimicrobial administration is not necessary for most procedures. Duration of antimicrobial prophylaxis should be <24 h (within 48 h for cardiothoracic surgery) for surgical procedures.

Do not apply antimicrobial agents (ie, ointments, solutions, or powders) to the surgical incision for the prevention of SSI. Application of autologous platelet-rich plasma is not necessary for the prevention of SSI. Consider the use of triclosan-coated sutures for the prevention of SSI.[15]

Route and timing of antibiotic administration:

Prophylactic antibiotics are usually given intravenously as a bolus on induction of anaesthesia to ensure adequate tissue concentrations at the time of surgical incision. This timing of dosing is particularly important for most beta-lactams which have relatively short half-lives. Vancomycin has to be infused over one hour so it must be started earlier so the infusion finishes just before induction.

Intramuscular antibiotics are given at the time of pre-medication so that peak tissue levels are achieved at the most critical time, the time of surgical incision.
Oral or rectal antibiotics need to be given earlier to ensure adequate tissue concentrations during surgery. Metronidazole suppositories are commonly used in bowel surgery and must be given 2-4 hours before it begins. Topical antibiotics are not recommended, with the exceptions of ophthalmic or burns surgery.[16]

Duration of antibiotic administration: If the operation lasts four hours or less, one antibiotic dose is usually sufficient. In prolonged surgery of greater than four hours, further antibiotic doses may be required to maintain the concentration, particularly if the antibiotic has a short half-life. Post- operative administration of the AMA, especially after 4 hours of wound closure is recommended only in case of contaminated and dirty surgery, in which case it may be given for upto 5 days.[17]

Indications for surgical antibiotic prophylaxis:[18]

AMAs are used in the following circumstances:

A. Clean elective surgery:

1. Single dose prophylaxis for staph. aureus in uncomplicated case of hernia or breast surgery. Prophylaxis should be given for surgeries in which a prosthesis is inserted into the bone or soft tissue. Even clean surgery needs to be covered by AMA in diabetics, corticosteroid recipients and other immunocompromised patients or neutropenic patients, infants, elderly.

B. **Clean contaminated and contaminated operations**: All of them need appropriate prophylaxis.

C. **Contaminated dirty wounds:** which may be due to any injury or road side accidents – need appropriate prophylactic AMAs.

Antimicrobial agents:[19]

Commonly used antimicrobials drugs for surgical prophylaxis	
Oral (single dose given 1 hour before procedure)	
Amoxicillin 2 g (50mg/kg)	
Cephalexin 2 g (50mg/kg)	
Cefadroxil 2 g (50mg/kg)	
Clindamycin 600 mg (20mg/kg)	For patients allergic to penicillin
Azithromycin 500mg (15 mg/kg)	
Clarithromycin 500mg (15 mg/kg)	
Parenteral (single injection) just before procedure:	
Ampicillin 2 g (50mg/kg) i.m./i.v.	
Cefazolin 1g (25mg/kg) i.v.	
Vancomycin 1g (20mg/kg) i.v. (in MRSA prevalent areas and/or penicillin allergic patients)	
Clindamycin 600 mg (20mg/kg) i.v. (for penicillin allergic patients)	
Cefuroxime 1.5 g (30 mg/kg) i.v + Metronidazole 0.5 g (10mg/kg) i.v	for Gut and
Gentamicin 160 mg g (3mg/kg) i.v + Metronidazole 0.5 g (10mg/kg) i.v	biliary surgery

Dirty Contaminated dirty wounds: The antimicrobial regimens generally administered for 5 days in case of contaminated dirty wounds are: [19]

1.	Cefazolin 1g i.v. 8 hourly + Vancomycin 1g i.v. 12 hourly
2.	Cefoxitin 1g i.v. 6 hourly / Ceftizoxime 1g i.v. 12 hourly
3.	Clindamycin 0.6 g i.v. 8 hourly + Gentamicin 80mg i.v. 8 hourly
4.	Ampicillin 2 g i.v. 6 hourly / Vancomycin 1g i.v. 12 hourly + Gentamicin 80mg i.v. 8 hourly + Metronidazole 0.5 g i.v. 8 hourly
5.	Amoxicillin 1g + Clavulanate 0.2 g i.v. 12 hourly All given for 5 days

Narrower spectrum first-generation cephalosporins (ie, cefazolin) are common antibiotics utilised for Surgical antibiotic prophylaxis. Cephalosporins are widely used due to their spectrum of activity (on commensal skin flora, and some Gram negative bacteria), favourable safety profile, and extensive experience in SAP.[20] Additional coverage for Gram negative bacteria and anaerobes is occasionally utilised, often with aminoglycosides (gentamicin) for Gram negative bacteria and nitroimidazole agents (eg metronidazole or tinidazole) for anaerobes.[16]

Cephazolin is not used for surgical sites in which the most probable organisms are not covered by cefazolin alone eg. colorectal surgery and gynaecological surgery where appropriate antibiotic for anaerobic bacteria and enterobacteriaceae is required such as metronidazole, ceftizoxime, cefotetan in addition to cefazolin. Agents such as erythromycin or metronidazole plus neomycin can be used orally. Parenterally, Cefotetan or Cefoxitin or ceftizoxime is used.

Standard antibiotic prophylaxis is often hindered by the presence of β-lactam allergy, whereby immediate hypersensitivity to penicillins or cephalosporins necessitates use of alternate classes of antibiotics such as lincosamides (clindamycin, lincomycin) or glycopeptides (vancomycin, teicoplanin) for Gram-positive coverage.[21]

In patients requiring only cefazolin for preoperative surgical prophylaxis, clindamycin or vancomycin are often used as alternatives for those with significant allergies to the medication. Most patients with a beta-lactam allergy are able to tolerate cefazolin. In the case of MRSA colonization, or select patients at high-risk for MRSA, vancomycin is the alternative unless additional antibiotics are required for possible gram-negative or anaerobic organisms.[22] Additional antibiotics are options based on specific surgical sites in addition to hospital-specific and patient-specific antibiotic resistance.[20]

Table 1: **Recommendations for Surgical Antimicrobial prophylaxis -** [23]

Procedure	**Recommended Agents**	Alternative agents in patients with beta lactam allergy
Head and Neck		
Clean	None	None
Clean with placement of prosthesis (excludes tympanostomy tubes)	Cefazolin, cefuroxime	Clindamycin
Clean-contaminated cancer surgery	Cefazolin + metronidazole, cefuroxime + metronidazole, ampicillin–sulbactam	Clindamycin
Other clean-contaminated procedures with the exception of tonsillectomy and functional endoscopic sinus procedures	Cefazolin + metronidazole, cefuroxime + metronidazole, ampicillin–sulbactam	Clindamycin
Neurosurgery		
Elective craniotomy and cerebrospinal fluid-shunting procedures	Cefazolin	Clindamycin, vancomycin
Implantation of intrathecal pumps	Cefazolin	Clindamycin,vancomycin
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
Ophthalmic	Ophthalmic Topical neomycin–polymyxin B–gramicidin or fourth-generation topical fluoroquinolones (gatifloxacin or moxifloxacin) given as 1 drop every 5–15 min for 5 doseso Addition of cefazolin 100 mg by subconjunctival injection or intracameral cefazolin 1–2.5 mg or cefuroxime 1 mg at the end of procedure is optional	None
Orthopedic		
Clean operations involving hand, knee, or foot and not involving implantation of foreign materials	None	None
Spinal procedures with and without instrumentation	Cefazolin	Clindamycin, Vancomycin
Hip fracture repair	Cefazolin	Clindamycin, Vancomycin
Cardiac		
Coronary artery bypass	Cefazolin, cefuroxime	Clindamycin, vancomycin
Cardiac device insertion procedures (e.g. pacemaker implantation)	Cefazolin / Cefuroxime	Clindamycin, vancomycin
Ventricular assist devices	Cefazolin, ampicillin -sulbactam	Clindamycin, vancomycin
Thoracic		
Noncardiac procedures including lobectomy,	Cefazolin, ampicillin -sulbactam	Clindamycin, vancomycin

pneumonectomy, lung resection and thoracotomy		
Video- assisted thoracoscopic surgery	Cefazolin, ampicillin -sulbactam	Clindamycin, vancomycin
Gastroduodenale		
Procedures involving entry into lumen of gastrointestinal tract (bariatric, pancreaticoduodenectomy)	Cefazolin	Clindamycin or Vancomycin + aminoglycoside or aztreonam or Fluroquinolone
Procedures without entry into lumen of gastrointestinal tract (antireflux, highly selective vagotomy) for high risk patients	Cefazolin	Clindamycin or Vancomycin + aminoglycoside or aztreonam or Fluroquinolone
Biliary tract		
Open procedure	Cefazolin, cefoxitin, cefotetan, ceftriaxone, ampicillin -sulbactam	Clindamycin or Vancomycin + aminoglycoside or aztreonam or Fluroquinolone Metronidazole + aminoglycoside or Fluroquinolone
Laparoscopic procedure		
Elective, low risk	None	None
Elective, high risk	Cefazolin, cefoxitin, cefotetan, ceftriaxone, ampicillin -sulbactam	Clindamycin or Vancomycin + aminoglycoside or aztreonam or Fluroquinolone Metronidazole + aminoglycoside or Fluroquinolone
Appendectomy for uncomplicated appendicitis	Cefoxitin, cefotetan, cefazolin+ Metronidazole	Clindamycin or Vancomycin + aminoglycoside or aztreonam or Fluroquinolone Metronidazole + aminoglycoside or Fluroquinolone
Small intestine		
Nonobstructed	Cefazolin	Clindamycin + aminoglycoside or aztreonam or fluoroquinolone
Obstructed	Cefazolin + metronidazole, cefoxitin, cefotetan	Metronidazole + aminoglycoside or fluoroquinolone
Hernia repair (hernioplasty and herniorrhaphy)	Cefazolin	Clindamycin, vancomycin
Colorectal	Cefazolin + metronidazole, cefoxitin, cefotetan, ampicillin–sulbactam, ceftriaxone + metronidazole, ertapenem	Clindamycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or Fluroquinolone
Implantation of internal fixation devices (e.g., nails, screws, plates, wires)	Cefazolin	Clindamycin, Vancomycin
Total joint replacement	Cefazolin	Clindamycin, Vancomycin
Urologic		

Lower tract instrumentation with risk factors for infection (includes transrectal prostate biopsy)	Fluroquinolone, trimethoprim–sulfamethoxazole, cefazolin	Aminoglycoside with or without clindamycin
Clean without entry into urinary tract	Cefazolin (the addition of a single dose of an aminoglycoside may be recommended for placement of prosthetic material [e.g., penile prosthesis])	Clindamycin, Vancomycin
Clean with entry into urinary tract	Cefazolin (the addition of a single dose of an aminoglycoside may be recommended for placement of prosthetic material [e.g., penile prosthesis])	Fluoroquinolone, aminoglycoside with or without clindamycin
Clean-contaminated	Cefazolin + metronidazole, cefoxitin	Fluoroquinolone, aminoglycoside + metronidazole or clindamycin
Plastic surgery	Cefazolin	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone

Table 2 Antibiotic dosing: [24]

Drug	Standard dose	Weight based dose	Duration for bolus injection (infusion)
Cefazolin	<80 kg 1 g >80 kg 2g	20–30 mg/kg /dose	3-5 min (20- 60 min)
Cefuroxime	1.5 g	50 mg/kg	3-5 min (20- 60 min)
Metronidazole	0.5 – 1 g	15 mg/kg initial dose (7.5 mg/kg subsequent doses)	30- 60 min

PROS and CONS of Antibiotic prophylaxis for SSI:

Some studies in recent past have suggested that Antibiotic prophylaxis (AP) is not required for clean surgeries. For clean contaminated surgeries, just one dose of pre-operative AP is effective in preventing SSI.[25] The advantages of a single-dose regimen include less chance of emergence of resistance, less chance for allergies or toxicity, and less cost.

A Review of literature for some studies about antibiotic prophylaxis in SSI, however showed that prescribing patterns was not based on World Health Organization criteria for rational use of drugs and not evidence based.[26] In another study, Bharath M, et all. 2020, use of prophylactic antibiotics strictly as per the recommendation of SIGN 104 guidelines did not lead to increased SSI as compared to the patients in whom these were routinely used, leading to drastic reduction in antibiotic usage 32.76%.[27]

However, most physicians reported routinely prescribing antibiotics either preoperatively or postoperatively despite agreeing that there is not enough evidence to support their use. The clinicians need to appreciate that prophylactic antibiotics are only an adjunct to good surgical technique and therefore cannot replace it.[28]

There is no universal agreement on the choice of antibiotic for prophylactic use. Though cefazolin has been commonly used for antibiotic prophylaxis, but many studies have shown use of various other antibiotics and their effectiveness. Many studies need to be done to confirm the above findings.[29]

Future Research:

Additional research is needed in several areas related to surgical antimicrobial prophylaxis. The risks and benefits of continuing antimicrobial prophylaxis after the conclusion of the operative procedure, including dosing and duration, need to be further evaluated.

Additional clarification is needed regarding targeted antimicrobial concentrations and intraoperative monitoring of antimicrobial serum and tissue concentrations to optimize efficacy.

The role of topical administration of antimicrobial agents as a substitute for or an adjunct to i.v. antimicrobial prophylaxis needs to be further evaluated.

Additional data are needed to guide the selection of antimicrobial agents for prophylaxis, particularly combination regimens, for patients with allergies to b-lactam antimicrobials.

Data are also needed to devise strategies to optimize antimicrobial prophylaxis in patients and facilities with a high risk or high prevalence of resistant organisms implicated in SSIs (e.g., MRSA).

Optimal strategies for screening for S. aureus and decolonization for certain procedures need to be identified. Finally, outcomes studies are needed to assess the impact of using quality measures and pay-for-performance incentives designed to reduce surgical morbidity and mortality.

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