Antimicrobial Use in Surgical Prophylaxis

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Objectives

• Identify surgical situations requiring prophylaxis
• Identify likely pathogens for each surgical situation
• Be able to choose appropriate antibiotics, dosing, timing, and duration for each surgery

A big problem!

• Surgical site infections (SSIs) are common
• 2-5% clean extra-abdominal and up to 20% intra-abdominal operation patients will develop SSI
• CDC estimates 500,000 SSIs occur annually in U.S.
• Considerable health care costs

Patients with SSIs are....

• 60% more likely to spend time in an ICU
• Five times more likely to be readmitted to the hospital
• Have twice the mortality of non-SSI patients

Prophylaxis vs. Treatment

• Surgery is done under controlled conditions
• Perforation or damage to area is absent
• There are no breaks in technique or major spillage
• Ex. Controlled operations of intra and extra abdominal areas

• Perforation or gross damage to site is present
• Tissue being operated on is actively infected (puss, positive cultures)
• Major spillage of GI contents
• Ex. Infected abscess, ruptured appendix

Problem pathogens extra-abdominal

• Often the result of skin contaminants
• S. aureus, S. epidermidis, Strep species
• MRSA and MRSE may complicate issue
Problem Pathogens
intra-abdominal

- A big party with a lot of guests
- Problematic when the bowel is perforated
- *E. coli*, *Klebsiella*, *Enterococci*, *Bacteroides fragilis*, other anaerobes
- Resistance in *Enterococcus* on the rise

Antimicrobial prophylaxis for surgery: An advisory statement from the National Surgical Infection Prevention Project

- 3 Performance Measures for National Surveillance and Quality Control
  - Proportion of patients who/whose:
    - Have parenteral antimicrobial prophylaxis initiated within 1 hour before the incision
    - Are given a prophylactic antimicrobial agent that is consistent with current published guidelines
    - Prophylactic antimicrobial is discontinued within 24 hours of the end of surgery

Surgical Care Improvement Project

- Specifics
  - Developed collaboratively by over 30 organizations
  - National goal: reduce preventable surgical morbidity and mortality
  - Program includes 3 SIP antibiotic goals
  - Additional anti-infection measures
    - Glucose control
    - Proper hair removal
    - Maintenance of normothermia
  - Measures are monitored by JCAHO
  - Failure in reporting is penalized

Antimicrobial Prophylaxis for Surgery: An Advisory Statement for the National Surgical Infection Prevention Project
Bratzler, DW et al CID 38:1706-1715, 2004

- General Recommendations
  - Timing of the first dose
  - Duration of antimicrobial prophylaxis
  - Screening for Beta-lactam allergy
  - Antimicrobial Choice
  - Additional Agents
  - Antimicrobial Dosing
  - Nonantimicrobial methods

Risk factors for SSI

- Age
- Underlying disease
- Prolonged operation time
- Suture in bowel
- Use of plates and screws
- Immunosuppression
- ICU stay
- others
### Antibiotics for prophylaxis

- Spectrum should cover expected problem organisms
- Should be inexpensive and easy to use
- Available in IV formulation
- Minimal side effects
- Easy to redose if necessary

### Beta Lactam allergy

- Evidence suggests that true incidence of beta lactam allergy is lower than reported
- Discern between true allergy (hives, anaphylaxis) and not (stomach upset)
- Allergy testing may be useful
- Spares vancomycin

### Cefazolin

- First generation cephalosporin
- Available IV and is inexpensive
- Good coverage of gram positive organisms and some gram negatives
- Won’t cover MRSA
- Renally eliminated

### Cefoxitin, Cefotetan

- Cephalosporins with anaerobic activity
- Also has some coverage for gram + and - organisms
- Inexpensive and available IV
- Cefotetan is now off the market
- Renally eliminated

### Clindamycin

- Good choice for beta lactam allergy
- Strong gram + and anaerobe coverage
- No gram - coverage
- Inexpensive and IV

### Metronidazole

- Strong anaerobe coverage
- Coverage will be insufficient if used alone
- Helpful if additional anaerobic coverage is needed
- Inexpensive and IV
Vancomycin
- Useful in beta lactam allergy and if MRSA is a concern
- Covers only gram + organisms
- Overuse in recent years has been accompanied with rise in resistance
- Available IV and is inexpensive
- Renally eliminated
- Use requires justification

Newer agents
- Carbapenems, linezolid, extended spectrum penicillins
- These agents are generally not used for prophylaxis
- Available IV but considerably more expensive (ex. Linezolid=$80/day)

Timing is Everything
- 1st dose should begin within 60 minutes before incision
  - With fluoroquinolones or vancomycin, infusion should begin 120 minutes before incision to prevent ADR
  - No consensus that infusion must be complete before incision
  - When proximal tourniquet is required, antibiotic administration should be complete prior to inflation

Timing is Everything
- Studies show that giving abx post incision has same infection rate as no abx at all!
- Goal of prophylaxis is to maintain drug levels above MIC for duration of operation (depending on agent used)

Duration
- Majority of evidence demonstrates that antimicrobial prophylaxis after wound closure is unnecessary
  - Studies comparing single vs multiple dose prophylaxis have not shown benefit of additional doses
  - Prophylaxis should end within 24 hours of surgery
    - ASHP recommendation for cardiothoracic surgery up to 72 hours
    - Bratzler et. al suggests discontinuing within 24 hours

Dosing
- Weight should be a consideration
- Rebolusing may be necessary in longer operations
- If operation exceeds two half lives of selected agent, then patient should receive a second dose
Redosing interval

- Cefazolin 2-5h
- Cefoxitin 2-3h
- Cefotetan 3-6h
- Clindamycin 3-6h
- Metronidazole 6-8h
- Vancomycin 6-12h

Choosing the right drug

- Think about the surgical site and the bacteria involved
- Pick a drug that will cover likely organisms
- Dose appropriately

Gynecological and Obstetrical

- Abdominal or vaginal hysterectomy
  - Cefotetan or cefoxitin
  - Ampicillin/sulbactam
  - Metronidazole monotherapy
    • Less effective as a single agent for prophylaxis
  - Beta-lactam allergy
    - Clindamycin plus gentamicin, aztreonam, ciprofloxacin or levofloxacin (750mg)
    - Metronidazole combined with gentamicin, ciprofloxacin or levofloxacin (750 mg)
    - Clindamycin monotherapy

- Cesarean Section
  - Low risk for post operative infection
    • Low benefit but recommended
    • Similar agents to hysterectomy
  - High risk for post operative infection
    • C-section after rupture of membrane and/or onset of labor, emergency operation for which preoperative cleansing may have been inadequate
    • Similar agents to hysterectomy
    • Antimicrobials are not usually administered until after the cord is clamped

Orthopedic

- Total joint (hip and knee) arthroplasty
  - Cefazolin or Cefuroxime
  - Beta-lactam allergy
    • Vancomycin or Clindamycin
  - Antibiotics D/C within 24 hours
    • No evidence that continuing antibiotics until all catheters & drains removed will lower infection rates

Cardiothoracic and Vascular

- CV Surgery
  - Cefazolin or Cefuroxime
  - Beta-lactam allergy
    • Vancomycin or Clindamycin
  - Studies have not shown an advantage in continuing antibiotics until invasive lines & drains removed
    • Recognize potentially devastating consequences of infection
    • Workgroup recommends ≤ 24 hrs of antibiotic
Colorectal Surgery

• Oral bowel preparation
  – Neomycin plus erythromycin or neomycin plus metronidazole
    – Started no more than 18 to 24 hrs before surgery
    – 1 gm 19, 18 and 9 hours before surgery
• Mechanical bowel preparation
  • Cefotetan or Cefoxitin or Cefazolin plus metronidazole for parenteral prophylaxis
  • Ampicillin/sulbactam
  • Penicillin allergy
    – Clindamycin plus gentamicin, aztreonam, or ciprofloxacin or levofloxacin (750mg)
    – Metronidazole plus gentamicin or ciprofloxacin or levofloxacin (750mg)

Resistance

• Overuse of antibiotics has resulted in startling rise in microbial resistance
• Incidence of MRSA in ICU > 50%
• VRE approaching 30% of all isolates
• Rise of extended spectrum and metallo beta lactamases has rendered some gram negatives nearly untreatable

Other therapies

• Wash your hands!
• Maintain aseptic technique
• Aggressive glucose control may decrease risk
• Supplementation oxygen and temperature control may also be useful

Antibiotic impregnated bone cement

• Used in joint arthroplasty
• Study by Fang-Yao, et al found cefuroxime impregnated cement lowered risk of deep infection after primary total knee arthroplasty (p=0.0238)
• Should be used in conjunction with preoperative antibiotics

Role of pharmacist

• Advise surgical team on appropriate drug for operation
• Ensure dose, duration, and rebolusing is correct
• Limit unnecessary antibiotic use to decrease cost, adverse events, and resistance

Conclusion

• SSI is a common and problematic complication of surgical operations
• Choosing the appropriate drug, duration, and timing is important for success
• Consider other therapies to maximize outcomes
References