Antibiotic prophylaxis against postoperative wound infections

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Hospital-acquired infections pose a large health burden. Fortunately, much can be done to improve infection control. The value of antibiotic prophylaxis for certain types of surgery is backed by strong evidence, and clear guidelines for its implementation have been issued by surgical societies.

This article reviews the evidence for antibiotic prophylaxis in surgeries with minimal expected contamination of the wound site; discusses the timing, type, and duration of antibiotic administration; and highlights topics of controversy in preventing and managing perioperative infections. Methods of instituting new standards for a hospital team are also discussed.

SURGICAL SITE INFECTIONS CAN BE REDUCED IN THE OPERATING ROOM

Surgical site infections represented the second largest group of nosocomial infections in the United States from 1990 to 1996, according to the National Nosocomial Infections Surveillance System of the Centers for Disease Control and Prevention (urinary tract infections were the largest group, primarily associated with Foley catheters).[1]

The risk of surgical site infection can be reduced by a number of strategies in the operating room, including:

- Optimizing oxygen tension
- Maintaining normal temperature
- Managing fluids
- Controlling blood glucose (especially important for patients undergoing coronary artery bypass graft surgery)
- Not shaving the operative site (or, if shaving is necessary, timing it as soon as possible before surgical incision).

Another factor that is more difficult to control is surgical technique and experience: complication rates tend to be much higher while a surgical team is learning a new procedure compared with after it becomes routine.

ANTIBIOTIC PROPHYLAXIS

Antibiotic prophylaxis is another important method for reducing the incidence of hospital-acquired infections. Because their use in this setting is preventive, antibiotics should be limited to operations in which minimal microbial contamination of the surgical site is expected (ie, clean or clean-contaminated wound classes).

Evidence for the value of antibiotic prophylaxis against infection in surgery is long-standing. In the 1950s, Miles et al[2] injected bacteria intracutaneously in guinea pigs and varied the timing of administration of a single dose of streptomycin and penicillin. Antibiotic administration was effective for infection prevention only in a 2-hour period around the time of bacterial injection, which they termed the "decisive" period.

Burke[3,4] found that the decisive period applied to prophylactic administration of either penicillin, chloramphenicol, erythromycin, or tetracycline from 1 hour before to 2 hours after infection with staphylococci in an animal model.

Hojer and Wetterfors[5] showed that prophylactic administration of doxycycline reduced septic complications following colectomy, with the biggest impact noted in surgeries in which obvious contamination did not occur.

For which procedures is prophylaxis worthwhile?

Since these early studies, antibiotic prophylaxis has proved beneficial for a variety of procedures—gastrointestinal (including appendicitis), oropharyngeal, vascular (abdominal and leg), open heart, obstetric

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and gynecologic, orthopedic hardware placement, and craniotomy, as well as some clean procedures.

Other operations, including many plastic surgery procedures and other less-invasive clean procedures, do not warrant routine antibiotic prophylaxis because the baseline rate of infections is so low. In such situations, the costs of prophylaxis may not justify the benefits.

Choosing an appropriate antibiotic

Antibiotics should be chosen on the basis of their effectiveness against the pathogens most likely to be encountered rather than against every possible pathogen. Skin florae (eg, *Staphylococcus* organisms) are the usual target, so first-generation cephalosporins are most often chosen. Intravenous administration is most common, although a combination of oral and intravenous administration can also be used.

Specific prophylactic antibiotic regimens are becoming standardized through guidelines published by societies such as the Infectious Diseases Society of America, the American Society of Health System Pharmacists, and the Surgical Infection Society, and are available on their Web sites.

TIMING OF PROPHYLACTIC ANTIBIOTICS

Give first dose before incision

Antibiotics should be administered before an incision is made to ensure that antimicrobial levels in the tissue are adequate and maintained for the duration of the procedure.

Stone et al[6] randomly assigned 400 patients undergoing elective gastric, biliary, or colonic operations to one of four regimens: antibiotics administered either 12 hours preoperatively, just before an operation, after an operation, or not at all. The incidence of wound infections was reduced significantly in patients given antibiotics preoperatively. Patients given antibiotics postoperatively had an almost identical infection rate to those not given antibiotics.

Classen et al[7] retrospectively monitored the timing of antibiotic prophylaxis in nearly 3,000 patients undergoing clean or clean-contaminated procedures. Patients who received prophylaxis in the 2-hour period before surgery had the lowest rate of infection, whereas those given prophylaxis more than 2 hours before surgery had a rate comparable to those who received prophylaxis from 3 to 24 hours postoperatively.

Beta-lactam drugs (eg, cefazolin and cefoxitin) have the advantage of an intravenous route of administration with anesthesia induction, leading to high muscle levels at the time of surgery even if given just minutes before the incision.[8]

Continue no longer than 48 hours postoperatively

The consensus of the National Surgical Infection Prevention Project, representing more than a dozen nursing and surgical societies, is that prophylaxis should not extend beyond 24 hours after wound closure.[9] The American Academy of Orthopaedic Surgeons has also issued such a statement, explicitly stating that evidence does not support continuing prophylactic antibiotics until all drains or catheters are removed.[10] The Society of Thoracic Surgeons recommends no more than 48 hours of antibiotic prophylaxis for cardiac surgery[11] (at The Cleveland Clinic, we use prophylaxis for 24 hours).

Most studies have demonstrated efficacy of postoperative antibiotic prophylaxis for only 12 hours or less: whenever short and long courses are compared, the shorter course has proven equally effective.[12–14] A single dose is as effective as multiple doses,[15] and antimicrobial prophylaxis after wound closure is unnecessary.

Prolonged antibiotic prophylaxis beyond 48 hours is not only ineffective in reducing infections but increases antimicrobial resistance[12] and the risk of colitis due to *Clostridium difficile*.

Full therapeutic dose needed

The full therapeutic dose of antibiotic should always be given. The upper range of the dose should be considered for large patients or those undergoing long operations.

Forse et al[16] found that when morbidly obese patients undergoing gastroplasty were given the standard dose (1 g) of intravenous cefazolin, blood and tissue levels of the drug were lower than those found in patients of normal weight. When they increased the dose to 2 g in morbidly obese patients, the wound infection rate dropped from 16.5% to 5.6%.

Redose for long surgeries

Patients undergoing surgery that extends beyond two half-lives of an antibiotic should be redosed intraoperatively.

Scher[17] randomly assigned more than 800 patients undergoing gastrointestinal surgery to one of three regimens: cefazolin (half-life, 2 hours) 1 g preoperatively, cefazolin 1 g preoperatively and a second dose 3 hours later, and cefotetan (half-life, 3 to 4.6 hours) 1 g preoperatively. Patients who underwent surgeries that lasted longer than 3 hours and were given only one dose of cefazolin had a significantly higher infection rate than patients in the other groups.

Zanetti et al[18] similarly found that intraoperative redosing of cefazolin resulted in a lower risk of surgical site infection following cardiac surgery.

Ohge et al,[19] after examining pancreatic tissue con-

centrations of cefazolin at various times in patients undergoing pancreatectomy and determining adequate levels to inhibit bacteria, recommended that a second dose of cefazolin be given 3 hours following initial administration of the drug.

Despite evidence that redosing reduces infection risk, only 12.2% of patients in the National Surgical Infection Prevention Project who underwent surgery for longer than 4 hours received an additional antibiotic dose during the procedure.[9]

VANCOMYCIN IN CARDIAC SURGERY

Vancomycin prophylaxis for cardiac surgery is controversial. Critics of using vancomycin cite that it is increasingly associated with resistance by enterococcal and staphylococcal organisms. It has a narrow spectrum of activity, being effective only against gram-positive bacteria, and no good evidence exists that it actually reduces rates of surgical wound infection. It must be infused over 60 minutes, which can add time to procedures. Furthermore, patients often become allergic to vancomycin. Finally, it has a vasodepressor effect, which can pose problems for patients with cardiac disease.

Supporters of its use argue that cephalosporin-resistant pathogens (methicillin-resistant *Staphylococcus aureus* [MRSA] and *Staphylococcus epidermidis*) are also being observed in incision wounds. Kernodle and Kaiser[20] found that vancomycin is superior to cephalosporins in preventing *S aureus* intermuscular infections in guinea pig models.

The Society for Healthcare Epidemiology of America has issued guidelines[21] recommending routine surveillance cultures of patients at high risk for colonization with MRSA, but no current consensus exists on what constitutes unacceptable levels.

Known carriers of MRSA should probably be treated preoperatively with vancomycin for prophylaxis. At this point, there are no guidelines absolutely contraindicating the use of vancomycin, and the decision on its use is left up to hospitals and doctors.

CLOSING THE ADHERENCE GAP

In some states, legislation has been enacted that requires public disclosure of health care-associated infection rates. Although neither advocating nor opposing such laws, the Healthcare Infection Control Practices Advisory Committee[22] recommends that states in which public reporting has been established should select one or more of the following outcomes measures:

- Central line insertion practices
- Surgical antimicrobial prophylaxis
- Influenza vaccination among patients and health care workers
- Central line-associated bloodstream infections
- Surgical site infections following selected operations.

Evidence is sufficient for many issues in antibiotic prophylaxis that the focus should be on adherence to guidelines.

At The Cleveland Clinic, we have achieved more than 92% compliance with administering prophylactic antibiotics within 60 minutes of cardiothoracic surgeries. For noncardiac procedures, however, the compliance rate was less than 50% over the time studied (January through September 2004).

To implement change, objectives need to be clearly stated and backed by a strong team of stakeholders that includes surgeons. Standards need to be set, and a process established to measure the intervention, provide feedback, and make corrections.

A number of health care organizations are finding the Six Sigma methodology for customer-oriented quality improvement helpful when applied to preventing surgical site infections. By identifying and analyzing all of the component steps of prophylactic antibiotic administration, and then monitoring them for improvement, the Six Sigma approach aims to reduce variation and focus on critical elements to achieve sustainable improvement.

The advent of electronic medical records also offers the opportunity to better measure interventions through the establishment of real-time databases in operating rooms, to allow more extensive and timely accessing and recording of data.

SUMMARY

Prophylactic antibiotics should be given as close to the time of incision as possible to ensure that tissue antimicrobial levels are adequate and maintained for the duration of the procedure. The choice of antibiotic should be based on the organisms most likely to be encountered—usually staphylococcal skin florae. The choice of vancomycin over a cephalosporin may be justified in patients who are known carriers of MRSA. A full therapeutic dose of antibiotic should be used for prophylaxis. Morbidly obese patients should be given twice the standard dose. Redosing during an operation is recommended if the duration of the procedure exceeds two half-lives of the antibiotic administered. Prophylactic antibiotics should not continue to be administered more than 48 hours postoperatively.

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