Timing of prophylactic antibiotics in TJA

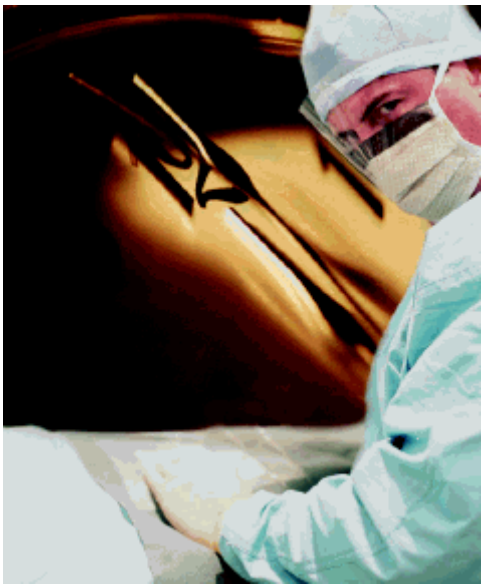
Recommendations exist, but questions persist

By Terry A. Clyburn, MD

The literature on the timing of a preoperative dose of prophylactic antibiotics is clear and supported by excellent laboratory and clinical studies. The classic 1961 article by Burke, using an animal model, revealed what he termed the "effective period"—a period of about two hours prior to the creation of the wound in which the antibiotic could be administered and still be effective. When the antibiotic was administered outside that window or after the wound became contaminated, it was not effective.

Burke stated "failure to administer the first dose of antimicrobial prophylaxis within the two-hour window of time before incision is associated with a two- to six-fold increase in rates of surgical site infection."[1] Several other authors have concluded that to prevent infection, there must be bactericidal levels in the tissue at the time of surgery.[2,3] Many other studies support antibiotic administration as the single greatest factor in lowering the infection rate in total hip arthroplasty.[4-6]

Despite this body of evidence, questions persist about the appropriate timing of prophylactic antibiotics. There has been some concern that dosing immediately before surgery may not result in adequate bactericidal levels during surgery. Both the National Surgical Infection Prevention Project (SIPP) and the AAOS recommend that antibiotic prophylaxis be initiated one hour prior to incision to maximize the effective period. If vancomycin is used, the dose should be administered two hours prior to incision to accommodate the extended infusion time.



One study reported bone and serum concentrations of five cephalosporins, administered over a five-minute period in the operating room (OR) immediately prior to total hip and total knee procedures, and continued for 48 hours. Researchers noted a trend between the serum concentration and the bone concentration. Antibiotics with greater concentration in bone also had higher serum levels and longer half lives (cefazolin and ceforamide).[7] Another study examined the concentration of cephalothin and cefamandole in serum, bone, synovial fluid and wound drainage in 29 total knee replacements and 28 total hip replacements. The antibiotics

were administered with the induction of anesthesia, and high concentrations of antibiotics were found in all samples. The authors concluded: “Because antibiotics penetrate bone rapidly, it is unnecessary to start antibiotics prior to the time of surgery.”[8]

Tourniquets

It may be theorized that inflating the tourniquet minutes after administering the antibiotic would result in a lower dose of antibiotic in the knee area.[9] However; the preponderance of evidence indicates that the bone concentrations of cephalosporin administered in the OR are well above the minimum inhibitory concentration (MIC) for the targeted organisms.

Schurman specifically studied the effect of the tourniquet,[8] finding that concentrations of the same antibiotic at the hip and knee were not significantly different even though a tourniquet was used for the knee replacement procedures. In another analysis of bone concentrations of cephalosporins administered immediately preoperatively, results revealed the bone concentration of cefazolin, which has a half-life of 42 minutes, to be 60 times the MIC for penicillin-resistant *Staphylococcus aureus*.[10]

Yet another study found that the bone concentration of antibiotic was highest 60 minutes after antibiotic administration, and therefore recommended administration of the initial dose in the “anteroom” prior to surgery.[3]

On-call to OR

Another popular option is to order that antibiotics be administered when the patient is “on-call” to the OR, but this practice has been shown to be unreliable. Many factors contribute to the variability of this option, including system problems at hospitals.

Despite the proven need to start antibiotics preoperatively, two studies done in the 1980s show poor compliance.[11,12] One study found that antibiotics were given immediately prior to surgery (within four hours) in only 49 percent of cases and were given more than four hours prior in 10 percent of cases. Furthermore, only 59 percent of 29 total joint cases received antibiotics before surgery.[12] Results of a 1989 study examining priorities in surgical antibiotic prophylaxis led the authors to conclude “…on call dosing is no longer acceptable because it may result in premature administration of the antibiotic regiment and insufficient tissue concentrations of drug during the decisive interval.”[13]

It appears that the preoperative dose may be effective if given within the two-hour “effective period” prior to initiation of the surgical incision. However, it has been found that serum, tissue and bone concentrations of antibiotics are adequate and that clinical infection rates are excellent if the antibiotic is initiated in the OR.

There is also no untoward effect of raising the tourniquet shortly after such dosing. These facts, coupled with the problems that exist with control of dosing when antibiotic administration is ordered “on-call” to the OR, suggest that dosing in the OR of cephalosporins under the guidance of the anesthesiologist and the surgeon is preferred.

Vancomycin and resistant organisms

As concern over methicillin-resistant organisms increases, surgeons are using prophylactic vancomycin.[14,15] Vancomycin is normally infused over a period of at least 30 minutes to prevent the development of “red man syndrome.”[16] I have pretreated patients with H1 and H2 histamine receptor blockers so as to allow more rapid infusion.

Vancomycin should be infused prior to incision and prior to tourniquet inflation. As Laura J.

Prokuski, MD, said in her article on selection of prophylactic agent (*Bulletin*, June 2005), the decision to use vancomycin must be carefully considered and based on an institutional evaluation of the risk of surgical infection with methicillin-resistant *S. aureus* or *S. epidermidis*. If this decision is made, the vancomycin must be ordered in time to be administered over a 30-to-60-minute period, prior to surgery. This requires compliance throughout the preoperative system in the hospital or surgical center.

The AAOS Advisory Statement on "Recommendations for the Use of Intravenous Antibiotic Prophylaxis in Primary Total Joint Arthroplasty" provides additional information on the appropriate selection, timing and duration of prophylactic agents for total joint arthroplasty. It is available on the AAOS Web site.

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