

The Judicious Use of Antibiotics in Large Laboratory Animals

INTRODUCTION

The increasing incidence of antibiotic resistant bacteria has caused major revisions in the way antimicrobials are used in both human and veterinary medicine. Because the emergence of resistance has important clinical implications and resistance patterns are directly affected by antibiotic exposure, the rational use of antimicrobials in laboratory animals is critical.

Given that the field of medicine is constantly evolving as new information is published, periodic review, updating and revision of antimicrobial guidelines are to be expected. The guidelines may not be appropriate for all clinical situations. Veterinarians must exercise professional judgment and consider individual circumstances and available resources when determining the appropriateness of prophylactic antibiotics and the best selection when indicated.

IMPORTANCE OF ASEPSIS IN SURGERY

When considering the use of antimicrobials for prophylaxis, the risks contributing to the development of post-operative infections must be considered. **Antimicrobial use is not a substitute for proper aseptic technique, and all recovery surgery must be performed aseptically.** The surgeon's experience and the length of the procedure have a strong impact on wound infection rates.

GOALS OF SURGICAL PROPHYLAXIS

Prophylaxis refers to the prevention of an infection through the preemptive use of antibiotics. Ideally, an anti-infective drug for surgical prophylaxis should achieve the following goals:

1. Prevent post-operative infection of the surgical site, morbidity and mortality
2. Reduce the duration and intensity of post-operative care required
3. Produce no adverse effects

To achieve these goals, an antimicrobial drug should be:

1. Active against the pathogens most likely to contaminate the wound
2. Given in an appropriate dosage and at a time that ensure adequate concentrations at the incision site during the period of potential contamination
3. Safe
4. Administered for the shortest effective period to minimize adverse effects and development of resistance

Typically, prophylactic antimicrobials are not indicated for clean surgical procedures when aseptic technique is properly followed. Prophylactic antimicrobials for procedures involving prosthetic placement is justified because of the potential for severe complications. Timing of antibiotic administration and rational selection of appropriate antibiotics must be considered. Effective antimicrobial use is based on two criteria: (1) which microorganisms are most likely to cause wound infections and (2) which antibiotics are most likely to be effective

against potential offending microorganisms. Coagulase-positive *Staphylococcus* species and *Escherichia coli* are the preponderant aerobic bacteria isolated from veterinary surgical patients.

PROPHYLAXIS IN VETERINARY PATIENTS

At present, cefazolin, a first generation cephalosporin, at 22mg/kg IV is the antibiotic of choice for prophylaxis in veterinary orthopedic surgery. Antibiotics should be administered at the time of anesthetic induction, repeated every 2 hours, and discontinued at the completion of surgery (Johnson 2007).

Surgical microbial prophylaxis in animals is largely based on human studies due to the lack of controlled clinical trials in veterinary patients. The optimal duration of antimicrobial prophylaxis in veterinary medicine is unknown. However, the vast majority of published evidence in human medicine demonstrates that antimicrobial prophylaxis after wound closure is unnecessary (Giguere 2006). Prolonged use of prophylactic antimicrobial agents is associated with the emergence of resistant bacteria and is more likely to result in adverse effects.

PROPHYLAXIS IN HUMAN PATIENTS

The use of prophylactic antibiotics in human neurosurgery remains controversial (AHSP 1999, Cacciola 2001, Jones 2005, Savitz 2002). However, meta-analysis of randomized studies have demonstrated the efficacy of prophylactic antibiotics in patients experiencing craniotomies (Barker 1994). Importantly, clean surgical procedures carry a risk of less than 5% for post-operative wound infections. In humans, *S. epidermidis* and *S. aureus* are the predominant isolates from post-surgical infections (AHSP 1999), similar to that found in veterinary patients. According to the American Society of Health-System Pharmacists, cefazolin continues to be the drug of choice for antimicrobial prophylaxis in humans due to the low overall frequency of cefazolin failure as a result of resistance including for elective craniotomies and orthopedic surgeries with implantation of internal devices (AHSP 1999).

Current recommendations in neurosurgery include the prophylactic use of antibiotics for up to 24 hours (Iacob 2010). The antibiotic selected should have a narrow spectrum of activity based on microbes likely to infect the surgical site and the prophylactic use of broad spectrum antibiotics for long durations is to be avoided (Iacob 2010). Cefazolin is commonly used in human craniotomies (Klekner 2003) and shown to be efficacious when repeated at 2-4 hour intervals during surgery. Because of the preponderance of Gram positive pathogens, cefazolin has been used perioperatively to prevent infection and has been efficacious when administered as a single dose prior to surgery (Dempsey 1988). Cefazolin remains above the MIC for most bacteria in the serum for approximately 6 hours and in wound excretion for 12 hours following the last dose (Klekner 2003).

For patients in which MRSA is a significant concern, human neurosurgeons choose cefuroxime (a cephalosporin similar to cefazolin) combined with gentamicin (Hammond 2002) at induction. In this report, only one MRSA infection was prevented per 421 patients treated compared with cefuroxime alone with an assumed 15% prevalence of MRSA. Single dose administration an antibiotic (usually a cephalosporin) with cleansing of the surgical site with

rifamycin or a similar drug also has demonstrated efficacy in preventing post-operative infections in clean neurosurgery (Cacciola 2001).

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