Veterinary Practices of Infectious Disease Treatment and Control: Non-Food Animals

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Controlling bacterial infections is perhaps the most common drug therapy administered to non-food animals in veterinary medicine. Without appropriate antibacterial drugs to control and treat infections, it would be practically impossible to practice rational health care to these animals. Veterinarians rely on effective, inexpensive, and convenient antibacterial drugs to treat primary infections or to augment other treatment modalities. The control of bacterial infections in the non-food animals is in the public interest because most of these patients are companion animals. It would be inhumane, and unhygienic to allow these infections to go untreated.

INFECTIONS TREATED

The most common species treated by veterinarians in a small animal practice are dogs and cats. However, rodents, exotic birds, and reptiles and other exotic animals also are frequently presented to some veterinary practices. The most common infections treated in pets are skin infections, urinary tract infections, wound infections, and respiratory tract infections. In horses, the most common infections treated are wound and respiratory infections, and occasionally enteric diseases. The other important use of antibacterial drugs in these non-food animals is for prophylaxis to prevent infections when animals are undergoing treatment or surgery for another condition.

Bacteria Encountered

In small animals, infections are caused by a wide variety of bacterial pathogens. Among the most common are infections caused by Staphylococcus intermedius, and Escherichia coli. Other bacteria that are less frequent, but also important are Pasteurella multocida, Klebsiella, Pseudomonas aeruginosa, Enterobacter, enterococci (Enterococcus spp.), and beta-hemolytic streptococci. In horses, infections are most frequently caused by streptococci, Staphylococcus aureus, and E. coli. Pseudomonas aeruginosa and Klebsiella also cause infections in horses.

RESISTANCE PROBLEMS

Bacterial drug-resistance presents a significant problem to veterinarians, but the incidence of resistance has not reached the crisis that has been publicized in human medicine[1]. The most common bacteria to develop serious resistance in the non-food animals are E. coli, Pseudomonas aeruginosa, and enterococci. Resistance also develops among other bacteria of the Enterobacteriaceae.

There is an impression that drug-resistant bacterial infections have become more common in the last ten years. Increased reliance on antibiotics may have contributed to the current incidence of resistance, but there is a lack of documentation to determine the role of antibiotic use on development of resistance in this group of animals. Some of the drug-resistant bacteria cause nosocomial infections in veterinary hospitals, but ordinarily, the nature of veterinary practice minimizes the opportunity for serious spread of nosocomial infections.

Many veterinarians believe that the apparent increase in infections caused by resistant bacteria is attributed an increase in veterinary skill and technology that allows us to treat more severe, debilitating diseases in recent years. For example, in small animal practice, it is more common for veterinarians to manage patients with severe illness, organ failure, and cancer than it was ten years ago. Geriatric animals are more likely to be treated by veterinarians because there are new developments in anti-inflammatory drugs, nutrition, and cancer treatment that may prolong an animal's life. Therefore the incidence of resistance may be a reflection of a change in the patient population in the last ten years.

It is also possible that greater use of antibiotics in all areas of medicine has contributed to a larger pool of drug-resistant bacteria. Too much availability of antibiotic drugs without prescription is a continuing problem in veterinary medicine. For example, through various outlets to which pet owners or horse owners have access, many once-valuable antibiotics can be easily obtained.

Control of Resistant Infections

In veterinary hospitals, spread of resistant infections is controlled by isolating patients, and keeping the in-hospital stay as short as possible. In the Veterinary Teaching Hospital at North Carolina State University there is an Infectious Disease Control Committee that monitors the incidence and spread of resistant infections in the hospital. By isolating animals with resistant infections, and adhering to strict decontamination procedures for the animal's cage or stall, spread of resistant infections has been controlled.

TRANSFER OF RESISTANCE FROM ANIMALS TO PEOPLE

It has been suggested that the family pet may be a potential source of resistant bacteria or resistant plasmids for people. In one survey [2], enteric bacteria from dogs that had not been treated with antibiotics were shown to have a high frequency of drug resistant plasmids. In another study, 80% of the Salmonella isolates from random-source cats were shown to have plasmids coding for antibiotic drug resistance [3]. It seems, therefore, that there is ample opportunity for drug resistant plasmids to contaminate people. Despite these findings, there is no published evidence that people that own pets have higher numbers of drug-resistant bacteria, or that treatment of bacterial infections in these people are more refractory to treatment than the general population. There is no evidence that antibiotic use, or emergence of drug-resistant bacteria in non-food animals, has caused a public health risk.

Staphylococcal Infections in Animals

Because staphylococcal infections in animals are common, their potential to become resistant and contribute to staphylococcal infections in people has received special attention. Infections in people are caused by Staphylococcus aureus, but almost all staphylococcal infections in small animals are caused by Staphylococcus intermedius. This bacteria is a common cause of wound and skin infections in dogs, for which treatment has usually included a cephalosporin, potentiated amoxicillin (amoxicillin + clavulanate), or a fluoroquinolone, among other drugs. Methicillin-resistant S. aureus (MRSA) are important nosocomial pathogens in human hospitals and resistance to fluoroquinolones developed rapidly among S. aureus after the introduction of these drugs to human medicine [1]. There has been a fear that S. intermedius may acquire resistance from human S. aureus, or that resistance generated in the treatment of canine skin infections could pass to human staphylococci and jeopardize human therapy [4].

Staphylococcal resistance due to beta-lactamase synthesis has increased [4], and beta-lactamase sensitive drugs are no longer considered effective for treating staphylococcal infections in animals. However, methicillin resistance among canine staphylococci is extremely rare and resistance to other drugs has not increased. Lloyd and colleagues [4] demonstrated that despite widespread use of potentiated amoxicillin, cephalosporins, oxacillin, and fluoroquinolones to treat staphylococcal infections in dogs, there was no increase in the resistance to these drugs from 1980 to 1996.

People are exposed to Staphylococcus from small animals (S. intermedius) because of their obvious close relationship in most households. Humans are obviously exposed, because sera from a human blood bank possessed antibodies to S. intermedius [5]. But, this bacteria is not pathogenic to people and transfer of plasmids from S. intermedius of animals to S. aureus of people has not been demonstrated. Plasmids coding for methicillin resistance can be transferred from human Staphylococcus aureus to animal S. intermedius [6], but this is not a common mode for S. intermedius to acquire resistance.

ANTIBACTERIAL DRUGS ADMINISTERED

The most common antibacterial drugs administered for routine infections by veterinarians include the penicillins, cephalosporins, fluoroquinolones, trimethoprim-sulfonamides, and tetracyclines. Drugs also administered occasionally for specific infections include metronidazole or clindamycin for anaerobic infections, erythromycin or azithromycin for gram-positive or intracellular infections, and the aminoglycosides for infections caused by gram-negative infections.

Use of Human Label Drugs

In veterinary medicine human-labeled drugs, are used widely. Their use is primarily to provide drugs for specific infections for which there are not equivalent veterinary products, or to provide dose forms of a drug that are not available. The use of human drugs is allowed under the provisions of the 1994 Animal Medicinal Drug Use Clarification Act (AMDUCA). The reason that veterinarians choose to administer a human generic version of a drug is often a practical one. For example to treat a large dog, a course of therapy with a human generic formulation of a drug may be more convenient because of larger tablet sizes compared a veterinary version of an equivalent drug, and less expensive. Some drugs are administered because there is no equivalent veterinary drug that meets the same criteria for spectrum of action, and/or pharmacokinetic profile. Examples include metronidazole, doxycycline, cefazolin, and azithromycin.

The use of drugs that are ordinarily reserved for resistant infections in small animals include several human drugs, such as the second-and third-generation cephalosporins (for example, cefotaxime, and cefixime), the carbapenem imipenem-cilastatin, and the glycopeptide vancomycin [7]. In the Veterinary Teaching Hospital at North Carolina State University, we rely on these drugs only when resistance has been documented to other available drugs. We restrict the in-house use of injectable third-generation cephalosporins, carbapenems, and vancomycin, to decrease the opportunity for inducing resistance.

Use of Fluoroquinolones

Much of the discussion at this symposium has focused on fluoroquinolones. Recently, enrofloxacin surpassed other drugs as the most commonly prescribed veterinary drug for small animal patients. Two new fluoroquinolones, orbifloxacin and difloxacin were introduced to veterinary medicine within the past year.

Fluoroquinolones are prescribed most often for infections in dogs and cats. They are also commonly prescribed to treat infections in exotic, zoo, and aquatic animals. In these animals they are popular because of they can be conveniently administered and their spectrum of activity includes the gram-negative bacteria that cause serious infections. Fluoroquinolones have been administered to horses, but the use is limited because of the expense, and because administration to young horses may cause joint injury.

There is no data published on the incidence of resistance to fluoroquinolones in small animals that has been induced since their introduction. However, there is an impression among veterinarians that resistance among Pseudomonas aeruginosa, Escherichia coli, Klebsiella, and Enterobacter may occur in a patient with chronic administration. In one paper, Pseudomonas aeruginosa resistance to fluoroquinolones was reported to be 10% [8]. (Note: Treatment of infections caused by Pseudomonas aeruginosa is not included in product labeling for any of the veterinary fluoroquinolones.) It has not been shown that fluoroquinolone resistance is transferred among small animals, or that resistance is transferred to people as a result of fluoroquinolone administration.

To reduce the incidence of resistance to fluoroquinolone in non-food animals, adequate doses should be administered. Higher doses, to maximize the peak concentration:MIC ratio are suggested to be necessary to reduce resistance [9]. High doses of the fluoroquinolones may be necessary in veterinary patients to treat infections that have unusually high MIC [10, 11]. The new initiative that allows for more flexible dosing of fluoroquinolones is welcome [12]. Veterinarians now have dosing guidelines that can be used to administer higher doses to treat infections that have a propensity to develop resistance.

CONCLUSION

Drug-resistant bacteria are primarily a problem documented in individual animals, and spread of resistance among animals in a veterinary hospital, or to people has not been well-documented, except for spread of nosocomial infections in some veterinary teaching hospitals [13]. Although drug-resistant bacteria have emerged and can become a therapeutic challenge in non-food animal patients, the judicious use of currently-available drugs has allowed veterinarians to treat these infections effectively. The most important challenges facing veterinarians that treat infections in non-food animals is to have the availability of safe and effective drugs in formulations that can be conveniently administered to their patients.

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