

Topics in Drug Therapy

Issues regarding the use of vancomycin in companion animals

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The emergence and dissemination of multidrug-resistant bacterial pathogens is an increasing problem in veterinary medicine. Although the origin and means of dissemination have not been fully identified, infections caused by organisms such as MRSA are being reported more frequently.^{1,2} This phenomenon is of concern for a variety of reasons, including the effects on animal morbidity and mortality rates and the potential for zoonotic transmission. Additionally, as the incidence of multidrug-resistant bacterial infections increases, there may be increased pressure to use newer antimicrobials and those used primarily in human medicine. One such antimicrobial, of which use is commonplace in human medicine but currently rare in veterinary medicine, is vancomycin.

Case Reports

In any field of human or veterinary medicine, administration of drugs with which clinicians have little experience is associated with a potential for inappropriate use. On 2 recent occasions, this has been highlighted to the author regarding the use of vancomycin for MRSA infections in dogs; the 2 cases involved consultations about dogs that were receiving vancomycin orally for treatment of severe soft tissue infections caused by MRSA. Both dogs had wound infections of the distal portion of a limb. Following lack of response to empirical treatment with β -lactam antimicrobials and on the basis of results of routine bacterial culture and susceptibility testing, MRSA infection was diagnosed in both dogs. For both animals, administration of vancomycin was subsequently chosen over other treatment options because of the desire to use an orally administered antimicrobial and because microbial susceptibility to vancomycin was reported by the diagnostic laboratory at which culture and susceptibility testing was performed. Unfortunately, in either case, the veterinarian did not appear to practice any degree of due diligence regarding use of a drug of which he or she had no prior experience. This is clear because vancomycin is not absorbed after oral administration in humans³ and there is no evidence suggesting that this is different in companion animals. Accordingly, in the author's opinion, the 2 dogs were treated with an expensive nontherapeutic regimen (costs totaling > US \$1,000 to 2,000) that, at best, only resulted in unnecessary financial burden on the own-

ABBREVIATIONS

MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
VRE	Vancomycin-resistant enterococci

er and, at worst, contributed to morbidity or death of these dogs. Furthermore, the potential for emergence of vancomycin resistance both in the targeted pathogen and, perhaps more importantly, in the commensal microflora was considerable. In hindsight, the legal and ethical implications of inappropriate use of antimicrobials, particularly drugs such as vancomycin, should be clear and of concern for practicing veterinarians.

Vancomycin

Vancomycin is a glycopeptide antimicrobial. It is bactericidal with a spectrum that includes activity against most gram-positive aerobes and anaerobes but with little effect against gram-negative bacteria. In human medicine, this antimicrobial is administered parenterally for the treatment of many multidrug-resistant, gram-positive pathogens (eg, MRSA). It is also often used for treatment or prophylaxis in patients that are allergic to penicillins and cephalosporins. Vancomycin is poorly absorbed after oral administration,³ and this route of administration is only useful against enteric organisms such as *Clostridium difficile*. For parenteral administration, it must be administered IV in dilute form via slow infusion.

No formulation of vancomycin is approved for use in any veterinary species, and there is currently little objective information regarding the use of vancomycin in veterinary medicine. There are a few case reports or case series in which the use of vancomycin in animals (other than humans) has been described,^{4,5} yet there is limited guidance available to veterinarians faced with the option of administration of this drug. Furthermore, reports^{4,5} of the use of vancomycin in animals do not necessarily indicate that its administration was prudent or effective; in 1 report,⁵ clinical response was apparent but elimination of the causative bacterium was not achieved with vancomycin administration in a cat. To the author's knowledge, there is no information regarding how often vancomycin is used in veterinary medicine; however, anecdotal information suggests that the drug is being used for the treatment of various conditions, including parenteral administration for MRSA infections and oral administration for *C difficile* infections in both small animals and horses.

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Vancomycin-Resistant Organisms

The main concerns regarding vancomycin resistance involve VRE. Despite introduction of vancomycin in the late 1950s, it was not until the 1990s that VRE became a major problem.⁶ This was perhaps a result of widespread use of vancomycin in humans that began in the 1980s and 1990s for treatment of *C difficile* and MRSA infections. From 1989 to 1993, there was a 23-fold increase in the incidence of VRE infection in humans in the United States.⁷

Vancomycin-resistant enterococci appear to be an emerging concern in veterinary medicine, both in veterinary clinics and in the general animal population. Although presently uncommon, there are increasing numbers of reports⁸⁻¹² of VRE infection or colonization in dogs, cats, horses, pigs, and poultry. The origin of VRE in animals is unclear but likely involved both de novo development of vancomycin resistance in enterococci of animal origin and transmission of VRE from colonized or infected humans to their animal contacts. The latter is of concern because there is evidence that the epidemiology of VRE infection in humans is changing, with increasing numbers of reports of VRE in people in the general population.¹³ As has been apparent with findings regarding MRSA, it is likely that increased presence of VRE in humans in communities will result in increased exposure of animals (particularly pets) to those organisms. Although it has not been objectively evaluated, it is logical to assume that treatment of animals with vancomycin could encourage both emergence and dissemination of VRE, particularly in an environment of increased VRE exposure. The higher apparent prevalence of VRE in animals in Europe has been ascribed to the use of avoparcin, another glycopeptide, in food animals^{10,14}; this further suggests that the use of glycopeptides in animals may be associated with VRE dissemination. Like other enterococci, VRE can be part of animals' normal commensal intestinal microflora. Therefore, it is possible for the VRE burden to increase in an individual animal or a population in the absence of clinical signs. Colonized animals could potentially transmit VRE, resulting in further colonization or the development of opportunistic infections in susceptible hosts, whether human or veterinary species.

Protocols for Restriction of Vancomycin Use

In some respects, focusing on the rare use of drugs such as vancomycin in animals may appear strange considering its widespread use in humans. The overall risk of emergence of vancomycin-resistant organisms with subsequent animal or public health problems is likely low; however, any additional pressure toward dissemination of important pathogens such as VRE is unwanted. Furthermore, perceived misuse of vancomycin could result in increased pressure to restrict extralabel use of antimicrobials in veterinary medicine.

Concerns regarding antimicrobial use and antimicrobial resistance in veterinary medicine have prompted various groups to develop prudent use guidelines.^{15,16} Such guidelines have typically been rather general and have not addressed specific issues such as the use of

vancomycin or similar antimicrobials in animals. A consensus statement issued by the American College of Veterinary Internal Medicine raised issues regarding voluntary restriction of antimicrobial use in veterinary medicine.¹⁷ Although this did not call for a formal ban on administration of drugs such as vancomycin, it recommended that veterinarians assign drugs into different use categories (ie, primary, secondary, or tertiary use). Drugs that are critically important in human medicine and used against multidrug-resistant pathogens would be restricted to the tertiary use category; those drugs would only be administered when there were no potentially effective primary or secondary drug options. Additionally, the consensus statement recommends that veterinarians consider whether administration of certain antimicrobials that are of such importance in human medicine should be voluntarily prohibited in other animals.

Because of concerns about the use of vancomycin, some veterinary hospitals are implementing formal or informal mechanisms to control or regulate its use. For example, a restriction-of-use protocol for vancomycin has been implemented at the Ontario Veterinary College. For a vancomycin prescription to be filled at that institution, the criteria that must be met are as follows: results of bacterial culture must indicate the infective organism, there must be no other treatment options based on the organism's antimicrobial susceptibility and patient factors, the organism must be susceptible to vancomycin in vitro, the infection must not be treatable by use of local antimicrobial or antiseptic agents alone, the infection must be life-threatening, there must be a reasonable chance for survival of the animal following treatment, and approval for use must be obtained from designated individuals within the institution who have expertise in infectious diseases and infection control. Both cases described in this report would not have met these criteria because of the availability of other antimicrobial treatment options. Moreover, a requirement to consult with specialists and pharmacy oversight would have prevented inappropriate oral administration of vancomycin in those dogs. Since the restriction-of-use protocol for vancomycin was introduced at the Ontario Veterinary College in 2001, vancomycin has only been used once; in that instance, the treatment was administered to a dog with multidrug-resistant enterococcal peritonitis. In several other situations at that institution, vancomycin use has been discussed with infection control personnel; however, a better treatment option was identified. In addition to directly reducing the frequency of vancomycin prescription, a policy such as this can be useful by increasing general awareness of the concepts of prudent use of antimicrobials among veterinarians and clinic staff. Beyond restriction policies, it is appropriate for veterinarians to determine whether they consider administration of vancomycin judicious in any case.

Overview

Because of increasing concerns about the use of antimicrobials in veterinary medicine and the ongoing emergence of multidrug-resistant bacteria, veterinarians need to take a proactive approach to prudent anti-

microbial use in general and to prudent use of specific antimicrobials such as vancomycin. Veterinarians and veterinary practices should consider the implications of the administration of drugs such as vancomycin, ideally in advance of a situation in which use of those drugs might be indicated. Development of written protocols regarding antimicrobial use can be a useful tool for improving patient care; furthering education of veterinary staff; increasing communication among veterinarians, pharmacists, and infection control personnel; and facilitating prudent antimicrobial use overall.

If veterinarians decide to use drugs such as vancomycin, it is imperative that they take the time to adequately understand the properties of the drug. Veterinary-specific information can sometimes be obtained from peer-reviewed sources or recent antimicrobial treatment texts.¹⁸ General information can be obtained from various sources such as the US Pharmacopeia Antimicrobial Monographs.¹⁹ If useful information (eg, dosing recommendations and safety issues) is not available for the intended animal species, then it is important for veterinarians to reassess whether use of the drug is appropriate.

Undoubtedly, challenges involving the selection and use of antimicrobials will continue to increase as infections with multidrug-resistant organisms become more common. An understandable desire to deliver what is perceived to be optimal veterinary patient care may drive the use of drugs that are critically important in human medicine. Paradoxically, if that type of use increases, so may the pressure to restrict veterinarians' access to antimicrobials. A proactive approach should be taken by veterinarians to ensure that all antimicrobials are administered with the principles of prudent use in mind. It is beyond the scope of this report to determine whether vancomycin should be used in animals at all; however, the author recommends that each veterinary facility should develop a policy regarding the use of vancomycin that will, if not prohibit its use, at least restrict it to situations in which its administration is absolutely necessary.

Veterinarians should remain aware of their responsibilities when administering any drug in an extralabel manner. It is the onus of the prescribing veterinarian to be aware of safety and efficacy issues regarding drugs they use in their patients. Proper use of antimicrobials such as vancomycin is of importance for patient care, public health, and protection of the relatively broad rights of veterinarians to prescribe antimicrobials. Failure to do so could result in patient morbidity and death, increased risks of zoonotic disease transmission, and compromising restrictions on extralabel drug use in veterinary medicine.

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