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The Challenge of Methicillin Resistant Bacteria - Therapy and Prevention Strategies

Professor David Lloyd
Department of Veterinary Clinical Sciences, Royal Veterinary College, Hawkshead Campus, North Mymms, UK.

Introduction

Methicillin-resistant bacteria are difficult to treat successfully because they are commonly resistant to many antimicrobial agents. Indeed, there may be no registered veterinary drugs that are effective. Thus early identification, prompt and effective treatment, and prevention of transfer to associated people and animals are essential. This presentation follows on from the previous lecture on infection and diagnosis and will focus on the treatment and prevention of infections by methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant Staphylococcus pseudintermedius (MRSP), and on hygiene measures designed to reduce to a minimum transfer and infection to associated veterinary staff, owners and animals.

Clinical Infection in Dogs and Cats

MRSA infections in dogs and cats have tended to be associated with wounds, postoperative infection, particularly where implants are involved, and skin including the ear. Such infections generally follow a course which is typical of methicillin-sensitive S. aureus (MSSA) although complications related to treatment failure and antimicrobial resistance are more common. Nevertheless, there is some evidence from a retrospective study that MRSA may more commonly be associated with deep infections when compared with MSSA. MRSP infections are clinically similar to those caused by meticillin-sensitive S. pseudintermedius and S. aureus. Staphylococcal infections, particularly of the skin, are generally secondary to other underlying diseases and thus a critical component of the successful treatment of these diseases is the diagnosis and resolution of the underlying problems.

Risk factors for MRSA infection of pets appear to mirror those for human hospital-associated MRSA infections (HA-MRSA) which include carriage of MRSA, contact with carriers, hospital admission and invasive procedures. In dogs and cats a UK case control study showed that contact with human MRSA carriers was the most important factor, then repeated antimicrobial therapy, surgery and duration of hospitalisation. The importance of contact with human carriers focuses attention on human carriage and there is now ample evidence that veterinary staff have higher carriage rates, with or without known contact with MRSA cases. Carriage rates of up to 27% have been demonstrated in referral hospital staff and a recent study has reported 9% carriage amongst UK first opinion veterinary staff. Contamination of veterinary premises is also likely to be important. A very recent report from the United States showed that MRSA was present in 16% of small animal hospital environmental sites sampled during a period where no MRSA outbreaks were present in the hospital.

In dogs, S. pseudintermedius is part of the resident flora of the nares, oropharynx, and anal ring. From these resident sites, it can be spread to the skin, to sites of infection, to other dogs in the household, and to in-contact humans. However, if the mucosal population is eliminated with topical antibiotics, the cutaneous population drops markedly emphasising the importance of mucosal colonisation. There is now evidence of transfer of MRSP from pets to in-contact humans and dogs, and into their environments both in clinics and in homes. Although carriage by humans seems to be a transient phenomenon there is potential for rare infections with MRSP to develop, with resultant therapeutic difficulties. In addition, canine-derived MRSP must be considered as a potential source for SCCmec transfer and possibly other mobile determinants of antimicrobial resistance to susceptible staphylococci on human skin and mucosae. Transfer to the environment and persistence of MRSP can occur at a high frequency; van Duijkeren et al’ found that 70% of households with dogs having current or recent MRSP infection were positive for MRSP.
Because MRSP is adapted to living in dogs, it is more likely to persist when acquired even when clinical infection has resolved, and can then be promoted when antimicrobial therapy is given and eliminates competitors. For this reason it presents a higher risk to veterinary practice than MRSA which tends to be lost when animals are maintained in clean environments.9

Dealing with MRSA and MRSP in Small Animal Practice

These observations focus attention on the importance of both personal and environmental hygiene, the need for responsible antimicrobial usage, and the adoption of practice protocols which will minimise transfer and selection of methicillin-resistant staphylococci. These measures require a change of approach in many veterinary clinics and hospitals. However, an increasing amount of information and guidelines for the management and prevention of such infections is becoming available on the internet and can greatly facilitate this process.

Essential actions in the clinic are similar for both these organisms and include 1) early recognition of the problem, 2) selection of appropriate treatment protocols, 3) adoption of stringent hygiene protocols to avoid transfer to other animals, staff and environments used, and 4) information and advice to the owner, including warnings of zoonotic risks, especially to individuals with compromised immunity.

Early recognition requires use of culture and sensitivity tests and these should be carried out routinely where cases of MRSP are being seen quite often or where MRSP (or MRSA) infected cases are in contact. Particular care is necessary when an animal under treatment with systemic antimicrobials is in contact with an MRSP case. In such cases repeated testing may be required.

Effective systemic treatment in cases with meticillin resistant staphyloccocal infection may be very difficult and selection of drugs will depend on sensitivity testing and may require the use of agents that are not registered for dogs. Fortunately, the commonest MRSA clones affecting dogs and cats tend to be susceptible to potentiated sulphonamides and tetracyclines. (Loeffler et al RVC outbreak) these drugs can be used at registered dose rates and are effective provided that underlying diseases can be controlled. Methicillin-resistant strains of \textit{Staphylococcus schleiferi} are generally less resistant1 than the MRSA clones and thus registered veterinary systemic antimicrobials are usually available for their treatment also. Unfortunately, the dominant European clone of MRSP is susceptible only to amikacin, fusidic acid, rifampicin, vancomycin, teicoplanin and linezolid,10,11 none of which is licensed for systemic use in pets. All of these drugs are classified in the 2009 World Health Organisation (WHO) Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) as critically or highly important and thus they should not be used in animals.

However topical therapy can be successful in superficial pyoderma associated with MRSP;12 topical antimicrobial creams and gels containing fusidic acid (or mupirocin although this should be avoided if possible because of its importance in human medicine) used 3 times daily, and shampoos containing agents such as chlorhexidine and benzoyl peroxide used every 2 to 3 days may be effective. Again, it is essential to deal with underlying causes and possible sources of reinfection otherwise recurrent infection is likely.

Guidelines for Infection Control and Prudent Antimicrobial Use

There is now an impetus to define measures to control infections and use antimicrobials in animals in responsible ways so as to reduce levels of resistance. Guidelines are being created at different levels of complexity varying from general concepts to specific recommendations for individual disease conditions and specific organisms. The Federation of European Companion Animal Veterinary Associations (FECAVA) has established a Working Group on Hygiene and the Use of Antimicrobials in Veterinary Practice to bring together and co-ordinate recommendations within small animal practice in Europe13. This group has produced a poster, “FECAVA Guidelines for Hygiene and Infection Control in Veterinary Practice”, which outlines under 8 headings the essential approaches. This is available on the Internet (http://www.fecava.org/files/952.pdf) and translated versions are already available from FECAVA member societies in several different languages.

In the UK, both the British Veterinary Association and the British Small Animal Veterinary Association have published recommendations on prudent use of antimicrobials.14,15 The BVA has produced a downloadable poster suitable for display which lists an 8 point plan providing actions and advice...
suitable for veterinary practice. The key points are a) development of protocols which ensure that antimicrobials are used only when necessary, b) selection of appropriate antimicrobials following sensitivity tests if possible, and compliance with correct dosage and administration, c) limitation of prophylactic and perioperative use, and d) maintenance of records of treatment outcomes so that therapeutic regimens can be evaluated and modified if necessary. Selection of appropriate drugs and their correct use is, of course, of vital importance. When treatment must be instituted rapidly or there is a high level of confidence that the causative organism and its sensitivity can be predicted, appropriate "first line" drugs can be selected. Otherwise, sensitivity tests should be carried out and "second line" drugs may be required. An important component of this process is client education conveying the dual message that both avoidance of non-essential antimicrobial administration and full compliance with dosage regimens of prescribed courses of antimicrobial drugs reduce the risk of increasing bacterial resistance. To this list must be added the need for rigorous hygiene so that as resistant organisms are encountered, in infected animals or in healthy carriers, transmission to other patients or humans is prevented.

References


