Outpacing the resistance tsunami: Antimicrobial stewardship in equine medicine

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Antimicrobial resistance is not on most equine practitioner's radar but AMR is emerging as an important issue in equine medicine. We are moving from the antimicrobial era through the antimicrobial resistance era into the era of antimicrobial stewardship. This shifting paradigm in our relationship with antibiotics is part of the global responsibility that all users have to preserve for the long term the rather small range of antimicrobial drugs available to treat bacterial infections.

Antimicrobial stewardship refers to an approach that promotes, improves, monitors and evaluates judicious antimicrobial use (AMU) to preserve the future effectiveness of antimicrobials and to promote and protect human and animal health. It is a term that is preferred to the previously used terms judicious or prudent use, since it includes the idea of not using antimicrobials. The general mindset of **good stewardship practice (GSP)** is a **"5R" approach**: Responsibility, Reduction, Refinement, Replacement, and Review. A **5R stewardship approach is an active, dynamic, process of continuous improvement** in AMU, a pragmatic ethic with many steps of different sizes. All veterinary users of antimicrobials are now inevitably forming part of the global "One Health" strategy to address AMR. This strategy, as endorsed in the 2017 pan-Canadian Framework for Action for Tackling Antimicrobial Resistance and Antimicrobial Use, includes surveillance, infection prevention and control, stewardship, and innovation.

Antimicrobial stewardship (AMS) is a rapidly evolving field, with greatest activity and leadership in large tertiary care human hospitals where AMR problems are most visible. Nevertheless, there is increasing focus in both human and veterinary medicine on primary care physicians and veterinarians, since they are the major users of antimicrobials. In Canada, the move to veterinary prescription only for antimicrobials in food animals is a major shift in responsibility for stewardship and GSP. It seems likely that, within a short time, provincial veterinary regulations will require all practices to develop AMS policies and that regulators will monitor and evaluate AMU by veterinarians against agreed benchmarks.

A practical approach to antimicrobial stewardship in equine medicine

The concept of AMS is of a dynamic process of continuous improvement in how we use antimicrobials and of reduction in their use to where the benefits are clear and substantial. Figure 1 is an illustration of some of the different elements of GSP. The different elements will be discussed.



Figure 1: An approach to antimicrobial stewardship for equine practitioners

Practice guidelines: The British Equine Veterinary Association (BEVA) has developed an award-winning approach to AMS, Protect ME, and is the best veterinary stewardship approach currently available: <u>www.beva.org.uk/protectme</u>. Two-thirds of British equine practices have adopted the ProtectME approach. The brilliance of the approach is that it requires practices to think through their AMS approaches and to engage the entire veterinary team; it's adopt an approach rather than adopt a defined practice. Protect ME offers a comprehensive approach for a practice to develop its AMS policies and practices: the acronym stands for **P**ractice policy; **R**educe prophylaxis; **O**ther options; Types of drug and bacteria; **E**mploy narrow spectrum; **C**ulture and sensitivity; Treat effectively; **M**onitor use, compliance and resistance; **E**ducate. For example, under Practice policy it recommends making a list of first-line drugs, with dosages; under monitoring, it suggests assigning functions of resistance reporters, resistance monitors and resistance leaders to engage the whole veterinary team, and provides templates or wall charts where resistance data can be entered. BEVA offers an Equine Antibiotic Resistance Champion plaque for the clinic if you meet certain criteria.

Infection control: The emergence and spread of methicillin-resistant *Staphylococcus aureus* (MRSA), particularly clonal type CMRSA 5, in horses represents a serious example of an AMR problem that is encountered both in equine hospitals and in the community. Infections include soft tissue infection, incision infections, bone and joint infections, as well as disseminated infections. Other clonal types, notably the livestock-associated strain ST398, may also become problematic. MRSA are resistant to all beta-lactam antibiotics. Nasal colonization is common in horses and infection with these strains is common in equine personnel, including veterinarians. In one study, there was a strong correlation between high nasal colonization of equine veterinarians and lack of handwashing. Good infection control is fundamental in reducing the spread of infections, including of resistant bacteria.

Clinical microbiology : Greater use of clinical microbiology data to guide selection of antimicrobials is an obvious approach to GSP, but is currently hampered by delays in obtaining data and cost. There is considerable effort being made to speed the process, particularly through rapid DNA-based approaches. Protect ME recommends such testing before the use of Category 1 antimicrobials, those of critical importance in human medicine (fluoroquinolones, third-generation cephalosporins).

Resistance and use surveillance: On-going monitoring of resistance and use is an important part of the "continuous improvement" mindset of GSP. One equine specific example is of the emergence of macrolide resistance in the foal pneumonia pathogen, *Rhodococcus equi*. On some farms resistance in isolates is as high as 40%, seriously impairing the ability to treat infection. A unique type of macrolide resistance gene, *erm*₄₆, has been spreading in *R. equi* and in soil non-pathogenic rhodococcal species on horse breeding farms around the world. It has been the practice on many farms to use ultrasound to detect incipient lung abscesses, and then to treat foals with azithromycin. Recently it has become clear that many foals will develop small lung abscesses but will recover spontaneously, without treatment, even if abscesses are as large as 10 cm. This is an outstanding example where not treating unnecessarily, despite the temptation, will prevent the development of resistance and preserve antimicrobials. We still need to find out how to know which foals will go on to developing clinical disease, which is part of the conundrum of *R. equi* infection.

Pharmacokinetics and pharmacodynamics: Knowing the difference between concentration-(aminoglycosides, fluoroquinolone) and time-dependent antimicrobial drugs is an important pharmacokinetic consideration both in optimal dosing and in the prevention of the emergence of resistance. One survey found that inappropriate dosing generally was common in equine medicine.

Regulations: Regulations should be followed. They are particularly important in relation to human health considerations. Protect ME suggests that use of vancomycin and carbapenems should be avoided in horses.

Education: Staff and owner education posters and related materials are available on the Protect ME website.

Summary

Many aspects of antimicrobial stewardship, including regulatory monitoring, evaluation and certification are in their infancy. Equine practitioners will however be expected to hold to a high standard of AMS, as part of the broad changes around how we use antimicrobial drugs so as to preserve them for the foreseeable future.

References

BEVA offers free access to papers on resistance in equine medicine:

https://www.beva.org.uk/Home/News-Archive/entryid/755/free-antimicrobial-research-collectionpublished-online-for-equine-vets