Survey of marbofloxacin susceptibility of bacteria isolated from cattle with respiratory disease and mastitis in Europe

S. Kroemer, D. Galland, V. Guérin-Faublée, H. Giboin, F. Woehrlé-Fontaine

Context
The primary aim of antibiotic treatments is to eliminate pathogenic bacteria from infected individuals, but it is also important from the perspective of both veterinary and human health that such treatments minimise the risk of antibiotic resistance emerging among pathogenic or commensal bacteria. This is particularly true for the veterinary use of critically important antibiotics such as fluoroquinolones.

Injectable fluoroquinolones have two major indications for use in adult cattle: bovine respiratory disease (BRD) and acute mastitis caused by *Escherichia coli*. For cattle practitioners, systematic susceptibility testing of the bacterial agents involved in these diseases is not always achievable. Therefore, knowledge of the distribution of susceptibility among pathogenic bacteria, and changes in susceptibility over time, is an important tool to help judicious use of antibiotics.

This paper describes a survey of the susceptibility to the fluoroquinolone antibiotic marbofloxacin of bacterial isolates from cases of BRD and mastitis in cattle in Europe between 2002 and 2008.

Main conclusion
The susceptibility to marbofloxacin of pathogenic bacteria involved in BRD and mastitis appeared to be stable over the seven years of this survey and was similar to previously published results. Moreover, the susceptibility of these pathogens remains very high.

Approach
A monitoring programme has been conducted in Europe since 1994 to survey the marbofloxacin susceptibility of bacterial pathogens isolated from cattle. This programme, involving a network of veterinary surgeons and microbiology laboratories, has enabled the susceptibility of 3851 bacterial strains isolated from bovine mastitis and BRD cases before any antibiotic treatment, between 2002 and 2008, to be established. Marbofloxacin minimum inhibitory concentration (MIC) values were determined by a standardised microdilution method, following Clinical and Laboratory Standards Institute guidelines.

Results
Among the respiratory pathogens, *Pasturella multocida* (751 strains) and *Mannheimia haemolytica* isolates (514 strains) were highly susceptible to marbofloxacin (MIC ≤0.03 µg/ml for 77.39 per cent of the strains) and only 1.75 per cent of *M haemolytica* strains were resistant (MIC ≥4 µg/ml). *Histophilus somni* isolates (73 strains) were highly susceptible to marbofloxacin (MIC 0.005 to 0.06 µg/ml). For *Mycoplasma bovis* (171 strains), MIC ranged from 0.5 to 4 µg/ml.

Among mastitis pathogens, the majority of *E coli* isolates (95.5 per cent of 617 strains) were highly susceptible to marbofloxacin. *Staphylococcus aureus* (568 strains) and coagulase-negative *staphylococci* (250 strains) isolates showed homogenous populations with MIC centred on 0.25 µg/ml. *Streptococcus uberis* (660 strains) and *Streptococcus dysgalactiae* (217 strains) were moderately susceptible, with MIC centred on 1 µg/ml.

Interpretation
There was no significant change in the resistance to marbofloxacin of bacterial pathogens involved in BRD or mastitis from 2002 to 2008, with year on year or compared with the previous period of the survey (1994 to 2001). *H somni* remained the most susceptible respiratory pathogen, with very low MIC values, whereas *M haemolytica* continued to be the least susceptible of the bovine respiratory Pasteurellaceae, as has been commonly described. The susceptibility to marbofloxacin of *M bovis* resulted in a single population of isolates centred on a MIC value of 1 µg/ml, which had not changed since the beginning of the survey. *P multocida* and *M haemolytica* strains were distributed into a susceptible wild-type population and two subpopulations; the first subpopulation corresponded to bacteria with reduced susceptibility resulting from a single genetic mutation, whereas the second population corresponded to bacteria with a high level of resistance, implying multiple chromosomal mutations, as has been previously described for resistance to fluoroquinolones. These resistant subpopulations tended to decrease in prevalence from 2006 to 2008.

Isolates of *E coli* from cases of mastitis showed a similar distribution, with a predominant highly susceptible wild-type population. In other studies, subpopulations of *E coli* with reduced susceptibility or resistance to marbofloxacin were commonly observed among isolates of digestive origin and seemed to emerge sporadically in mastitis cases. However, in the present study the number of these resistant strains among isolates from mastitis did not increase significantly between 2002 and 2008, or during the period from 1994 to 2001. Within the scope of this epidemiological survey, *Staphylococcus* and *Streptococcus* strains were simultaneously monitored, in order to have a complete overview of the major mastitis pathogens: they presented with reduced susceptibility levels, characteristic of these bacterial species, without evolution over the years.

As for all fluoroquinolone antibiotics, the use of marbofloxacin is restricted to the treatment of individual cases and should be reserved for the treatment of clinical conditions that have responded poorly, or are expected to respond poorly, to other antimicrobials. It is also recommended to base the use of marbofloxacin on antimicrobial susceptibility testing. The results presented here should help to guide decision making by veterinary surgeons.

Significance of findings
This comprehensive epidemiological survey provides a complete description of marbofloxacin susceptibility patterns in key pathogens involved in BRD and mastitis. At a time when the use of critically important antibiotics in veterinary practice is regularly challenged, this study provides clear data on changes in the fluoroquinolone susceptibility of pathogenic bacteria isolated from adult cattle.
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Veterinary Record 2012 170: 53 originally published online November 24, 2011
doi: 10.1136/vr.100246

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