
C. R. Müntener¹, K. Mühlemann², V. Perreten³

¹ Institute of Veterinary Pharmacology and Toxicology, University of Zurich, ² Institute for Infectious Diseases, Medical Faculty, University of Bern, ³ Institute of Veterinary Bacteriology, University of Bern

We would like to comment on the publication by Decristophoris et al. in Schweiz. Arch. Tierheilk. 2011, 153: 405–409 about the treatment of a dog infected with methicillin-resistant *Staphylococcus pseudintermedius* (MRSP). The authors rightly describe the treatment of MRSP as being critical because of its resistance to all beta-lactams and, often, other classes of antibiotics. The antibiogram presented in the publication convincingly demonstrates this fact, the bacterium involved presenting resistances to 9 different classes of antibiotics. However, we strongly disagree with the use of rifampicin as monotherapy to treat an infection caused by MRSP, even if it seems to have been successful in the case presented.

Rifampicin is an antibiotic primarily used against mycobacteria but also effective against some Gram-positive bacteria, especially staphylococci or some selected Gram-negative bacteria like *Brucella* sp. (McEvoy, 2011). Its primary mode of action is the suppression of the initiation of chain formation for RNA synthesis through inhibition of the DNA dependent RNA polymerase. The specific binding site of the antibiotic is the beta subunit of the enzyme. Rifampicin is bacteriostatic to bactericidal, depending on the concentration achieved at the site of infection (McEvoy, 2011). Resistance to rifampicin can be achieved by diverse mechanisms but mutation is one of the most frequent. In most cases, single mutations of the *rpoB* gene encoding the beta-subunit of the polymerase affect the highly conserved rifampicin-binding site (Tupin et al., 2010). In staphylococci, resistance to rifampicin has been described both in human and veterinary medicine (Aubry-Damon et al., 1998; Kadlec et al., 2011). In *S. aureus* isolates, the in vitro mutation rate under rifampicin selection was determined at $10^{-7}$ to $10^{-4}$ and it was shown that resistance does not arise by sequential independent events, but rather in a single-step fashion (Aubry-Damon et al., 1998). A similar rate of $4.74 \times 10^{-7}$ was shown in another study without a statistically significant difference between methicillin-susceptible and methicillin-resistant strains (Schmitz et al., 2000). On the human medicine side, a systematic review on rifampicin use for the eradication of *S. aureus* showed that 17% of patients harbored *S. aureus* strains which developed a resistance to rifampicin after treatment with different regimens containing this antibiotic (Falagas et al., 2007).

On the veterinary medicine side, a recent publication described rifampicin-resistance in canine MRSP isolates (Kadlec et al., 2011). The study investigated consecutive isolates from 9 different dogs at 5 Dutch animal hospitals prior to and after therapy with rifampicin. Twenty-one isolates were multidrug-resistant and exhibited at least one mutation in the *rpoB* gene. The data specifically showed that rifampicin resistance was emerging rapidly under therapy. For this reason, and even if successful treatment of canine pyoderma by rifampicin monotherapy has already been described in another publication (Şenürük et al., 2005), this antibiotic should never be used alone.

Current recommendations for use of rifampicin in human medicine emphasize that rifampicin might be useful for the treatment of serious infections associated with biofilm (e.g. prosthesis infection) caused by methicillin-resistant staphylococci but should always be used in combination with another anti-infective agent (McEvoy, 2011). The risks of using rifampicin alone should also be considered in relation to recent studies from Japan linking its use to the development of intermediary resistance to both vancomycin and daptomycin in methicillin-resistant *S. aureus* (MRSA). Both antibiotics are currently used as drugs of last resort for the treatment of infections caused by multidrug-resistant Gram-positive bacteria in human medicine (Cui et al., 2010; Watanabe et al., 2011). We therefore entirely support the conclusion of Kadlec and co-workers (2011) who recommended not to use rifampicin monotherapy for the treatment of infections.
caused by MRSP. As even combinations may not prevent the development of resistances (Aubry-Damon et al., 1998), the sensibility against rifampicin should also be determined during therapy if possible. For these reasons, empirical therapy of such infectious diseases is not recommended. S. pseudintermedius has a zoonotic potential and severe infections caused by MRSP in humans have been reported in the USA and Switzerland (Kempker et al., 2009; Stegmann et al. 2010). It is therefore in the interest of public health to avoid rapid selection of antibiotic resistance in bacteria from animals and keep antibiotics of major importance for the treatment of life-threatening diseases in humans only.

References


Corresponding author

Vincent Perreten, Prof. Dr.
Institute of Veterinary Bacteriology
University of Bern
Länggassstr. 122
CH-3012 Bern
Tel.: +41 (0)31 631 24 30
Fax: +41 (0)31 631 26 34
vincent.perreten@vetsuisse.unibe.ch

Received: 10 December 2011
Accepted: 14 December 2011