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Infections Caused by Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant *Staphylococcus aureus* (VRSA) in Domestic Animals

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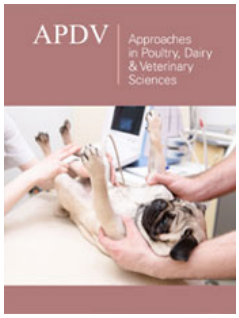

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Abstract

Bacteria of the genus *Staphylococcus* are considered common etiological agents of infectious processes. *Staphylococcus aureus* is one of the major pathogens that cause human and animal infections due to its high prevalence in hospital and community infections since it belongs to the normal microbiota of the skin and nasal fossae of humans and healthy animals. In addition, the incidence of multidrug-resistant strains (MDR) of the S aureus species are related to high morbimortality rates in domestic animals worldwide. The identification of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Staphylococcus aureus* (VRSA) in domestic animals is relevant not only from the epidemiological point of view, but also to enables the development of strategies to control and prevent infections caused by these microorganisms in veterinary practice, in order to reduce their effects on human public health. In this context, the present study aimed to elucidate the link between MDR strains of *S aureus* and infections in domestic animals.

Keywords: Bacterial infections; Resistance; *Staphylococcus aureus*; MRSA; VRSA; Domestic animals

Introduction

Bacterial infectious diseases are among the leading causes of morbimortality of domestic and wild animals, besides food contaminants [1,2]. Among the main microorganisms that cause infections in mammals, the *Staphylococcus aureus* stands out as the most important pathogen in animals and humans. This microorganism is associated with superficial and deep infections of the skin and soft tissues, causing toxin-mediated diseases such as staphylococcal scalded-skin syndrome, toxic shock syndrome and abscess-forming bacteremia, as well as serious infections such as osteomyelitis, pneumonia, meningitis, arthritis, endocarditis, septicemia and infectious mastitis [3,4].

Recent studies have shown a worrying prevalence of infections caused by strains of *S aureus* with resistance to numerous classes of antimicrobials in animals. Bacterial resistance is an inevitable consequence of natural selection, but some factors may accelerate its occurrence, including inadequate use of antimicrobial agents in human and animal health [5-7]. Considering the existence of microorganisms that have mechanisms of self-protection to certain classes of antimicrobials, it is known that besides mutations in the DNA of bacteria, the origin of acquired resistance of microorganisms that cause infection comes from the transfer of resistance genes [8,9]. Over the decades, bacteria that have clinical and veterinary importance have become resistant to one or even to several classes of antimicrobials. These resistant microorganisms were called multidrug resistant (MDR) [5,9,10].

Interaction between animals and humans, especially domestic animals, increases the possibility of contamination of these animals by pathogenic microorganisms. The environment

shared by both can be a way of contact with the pathogens. In Brazil, about 40% to 60% of *S aureus* isolated from clinical samples from animals are methicillin-resistant *Staphylococcus aureus* (MRSA). In the last decades there has been a significant increase in the presence of MRSA in domestic animals that have a significant ability to transfer resistance factors to human strains. The presence of multidrug-resistant *Staphylococcus aureus* in animals are a public health concern, especially due to the ability to cause infectious processes of difficult treatment [11,12]. Therefore, it is important to understand the association between dissemination and contamination of resistant antimicrobials between humans and animals, with the aim to control the dissemination of zoonoses [13-16].

Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant *Staphylococcus aureus* (VRSA)

Some bacterial species have resistance profiles widely distributed throughout the world, such as MRSA [3,17]. The presence of strains of resistant staphylococci was observed shortly after the use of penicillin G in medical practice in 1941. In the 1950s, about 80% of *S aureus* isolates collected from human and animal infections were resistant to penicillin G, due to the production of inactivating penicillinase enzymes. Currently strains of staphylococci isolated from community-based infections are resistant to drugs such as ampicillin, amoxicillin, benzylpenicillin, and carbenicillin. In order to combat staphylococci, we used methicillin, oxacillin, its derivatives and the first and second generation cephalosporins [3]. With the emergence of MRSA strains, glycopeptide antimicrobials, such as vancomycin, were widely used as a therapeutic option in infections caused by MRSA. However, in 1996, *S aureus* strains with intermediate resistance to vancomycin (VISA) were identified and subsequently the emergence of strains of *S aureus* resistant to vancomycin (VRSA). Some authors claim that resistance to vancomycin is related to the thickening capacity of the cell wall of these microorganisms, preventing the passage of the drug [18-20]. The mechanism of resistance to glycopeptides is not well defined, however, many authors support the hypothesis that it is through the acquisition of mobile genetic elements (transposons) of vancomycin-resistant *Enterococcus* that cause changes in the metabolism and cell wall of *Staphylococcus*, precluding the drug to enter the microorganism [20,21].

Antibiotic resistance associated with the biofilm formation capacity of these microorganisms contributes to the success of *S aureus* as a pathogen in animals and humans. Biofilms can be defined as structures formed by microbial cell aggregates that present a high degree of communication and coordination, enwrap in an exopolysaccharide matrix, responsible for the protection of the microorganism cells of the host immune response and the activity of antimicrobial compounds. These resistance factors do not act independently of each other and the phenotype of biofilm production expressed by clinical isolates of *S aureus* is influenced by the acquisition of resistance genes [3,22,23].

Infections Caused by MRSA and VRSA in Domestic Animals

Studies indicate that the first isolates of MRSA in animals are related to the association of the prevalence of *S aureus* as pathogen of infectious mastitis in cattle and horses, with the use of beta-lactams by intramammary route in the treatment of these infections. The MRSA profile has already been identified in several species, such as cats, dogs, horses, goats, pigs and chickens. Moreover, outbreaks of MRSA infections in these animals have been reported [24]. Dougka et al. [25] analyzed 53 strains of *S aureus* isolated from dogs and cats of a veterinary clinic in Greece and identified the presence of the MRSA profile in 16 of these isolates.

Studies investigating the dynamics of colonization by resistant strains of *S aureus* in domestic animals evidenced a transitory colonization of these microorganisms among these animals. In addition, they showed a high clonal relationship between isolates in domestic and human animals from the same region [16,25,26]. Grinberg et al. [16] identified a high clonal association between 15 MRSA strains from animals and colonization isolates from humans that had contact with these animals through pulsed field electrophoresis (PFGE). Animal and human isolates were classified as the EMRSA-15 subtype. Zhang et al. [26] described a high clonality relationship between 21 clinical isolates of MRSA from dogs and cats and 1 colonization isolate from the nasal region of a veterinarian in China. Furthermore, 4 of the 22 isolates analyzed showed resistance to gentamicin and tetracycline. The study evaluated the presence of the *mecA* gene through the Polymerase Chain Reaction method (conventional PCR) and identified the presence of this gene in all 22 isolates.

The presence of the VRSA resistance profile has been described so far only in cattle, goats and pigs [27,28]. Bhattacharyya et al. [28] reported the first case of vancomycin resistance in bovine and caprine animals after investigation of the VRSA profile in 352 milk samples obtained from cattle (269) and goats (63) with clinical and subclinical infectious mastitis. Among the isolates analyzed, 2 showed resistance to vancomycin by broth microdilution, with minimum inhibitory concentration (MIC) values of 16μg/ml and 32μg/ml and 5 isolates presented the VISA profile, with values of MIC of 8μg/ml. None of these VRSA/VISA isolates presented the *vanA* and *vanB* genes and all 7 isolates showed resistance to oxacillin and cefoxtin, besides the presence of the *mecA* gene.

Conclusion

The zoonotic potential and the creation of animal reservoirs for the reinfection of humans by MRSA and VRSA strains are evident and have become worrying. Thus, studies describing the risk factors associated with the transmission of resistant strains of *S aureus* among domestic animals have become increasingly recognized as necessary. Infections caused by MRSA and VRSA are emerging and challenging due to the potential to evolve into severe cases and death. Hence, the identification of MRSA and VRSA in domestic animals is relevant not only from the epidemiological point of

view, but also because it enables the development of strategies to control and prevent infections caused by these microorganisms in veterinary practice, in order to reduce their effects on public health.

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Conflict of Interest

None declared.

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