Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Food of Animal Origin: A New Challenge in Food Safety?

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Abstract

**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) causes a wide range of infections, sometimes fatal, and represents a major problem in both human and veterinary medicine. The global spread of intensive farming and the high and indiscriminate use of antimicrobials has favoured the selection and circulation of MRSA in livestock and, consequently, in food of animal origin. The presence of MRSA is well documented in foodstuff, such as, beef, pork, poultry and rabbit meat as well as fish, raw milk and table eggs. The strains mostly isolated from food are animal associated, i.e. CC398; however, human strains have also been isolated from foodstuff. Some of these MRSA strains are capable of synthesizing staphylococcal enterotoxins.

**Objective of the Study:** In this review, the origin and the significance of MRSA in food of animal origin are discussed from a food safety point of view.

**Keywords:** MRSA; Antimicrobial-Resistance; Food Safety

Introduction

Antimicrobial resistance (AMR) in bacteria is a great challenge for the XXI century [1]. The WHO stated that “the post-antibiotic era, in which common infections and minor injuries can kill, far from being an apocalyptic fantasy, is instead a very real possibility for the 21st Century” [2]. Antimicrobial pressure in a bacterial population promotes the selection, survival and spread of resistant bacteria. In fact, AMR occurs due to a mutation in the bacterial genome which enables the microorganism to survive in the presence of antimicrobial molecules, thus rendering them ineffective; it could also arise due to the acquisition of an antimicrobial-resistance pattern through DNA fragments from other microorganisms via conjugation, transformation or transduction.

The emergence of intensive farming, where a lot of animals are confined in restricted spaces, has led to increased stress levels in these animals forced to live in conditions which are far from ideal. This condition facilitates the transmission of microbial pathogens between animals, leading to the arise of infectious diseases with a significant economic loss for farmers. To curb this problem, the extended use of antimicrobials for prophylaxis and metaphylaxis (other than for therapeutic purposes), largely used in the intensive farming, should be significantly reduced. In addition, in many countries the use of antimicrobials as growth promoters is still permitted [3]. In fact, every year 131.109 tons (73%) of all antimicrobials sold worldwide are used in animals [4]. Under this extraordinary selective pressure, some
populations of pathogenic or harmless bacteria have emerged and reached human beings and are having several effects on them: first of all, infections which are difficult to treat and are sometimes fatal [5]. The secondary side effect of AMR is that farmed animals represent a great reservoir of antimicrobial resistant genes which may increase the chance of other bacteria acquiring them by gene exchange with the animal microbiota or through the environment. Therefore, the presence of AMR bacteria in livestock, food-producing animals and food derived thereof represents an important source of AMR bacteria for humans [6]; in fact, consumers might acquire infections caused by these microorganisms, via handling or consuming contaminated foods [7]. In this framework, among others, an important theme is debated by food-safety experts: the role of methicillin-resistant Staphylococcus aureus (MRSA) as a foodborne pathogen.

Molecular epidemiology of MRSA

MRSA is a well-known human and animal pathogen which can cause severe infections [8] so much so that the WHO has included it on the list of antibiotic-resistant "high priority pathogens" [9]. Methicillin resistance is due to the synthesis of the penicillin binding protein 2a (PBP2a), a protein encoded by the mecA gene, with a low affinity for methicillin and oxacillin and practically for all the β-lactams antibiotics [10,11]. The epidemiology of MRSA can be divided into three major phases: during the ‘80s, MRSA infections were mostly considered a nosocomial problem affecting hospitalized patients presenting several risk factors such as catheterization and prolonged hospitalization [12]. The main clonal complexes (CCs) isolated from these patients were CC5, CC8, CC22, CC30 and CC45 [13]; these multidrug-resistant strains were called Hospital-Acquired (HA)-MRSA [14]. Subsequently, in the late ‘90s, a spread of MRSA infections in the community was observed (Community-Acquired (CA)-MRSA); the people affected were non-hospitalized patients living in a community, such as prisoners, military personnel or athletes (sharing the same space), with unknown risk factors [15,16]. The main strains involved belonged to the Sequence Type (ST) 1, 8 and 80; although these strains were not multi-drug resistant, they were more virulent due to the synthesis of the Panton-Valentine leukocidin (PVL) [17]. Finally, in the early 2000s, a high prevalence of MRSA was observed in Dutch pig breeders, in which it was 760 times higher than in the rest of the population. Further investigations showed that pigs were highly colonized by MRSA and that the isolates mainly belonged to the CC398; these strains were called Livestock-Associated (LA)-MRSA [18].

Characteristics and epidemiology of LA-MRSA

The overuse of antibiotics in pig farming has contributed to the selection and emergence of LA-MRSA. The origin of LA-MRSA CC398 is in question. It is likely that a human methicillin susceptible S. aureus (MSSA) strain ST398 has acquired the mecA gene from other staphylococci, probably coagulase negative staphylococci (CNS), and has adapted to pigs by losing human-specific immunomodulators (bacteriophage ϕSa3) and pvl genes [19].

CC398 was also isolated in other animals, including cattle, poultry, rabbits, horses and dogs, as well as humans, worldwide [20]. These strains showed the presence of SCC-mec type IV or V and the possible presence of genes coding for Staphylococcal enterotoxin(s) [21].

LA-MRSA strains harboring SCC-mec types IV and V are resistant to several classes of antibiotics, because of the selective pressure linked to the large use of antimicrobials in animal farming. However; although LA-MRSA CC398 can cause human and animal infections, it shows low virulence for humans because they have not the ability to synthesize the PVL. In fact, despite the high exposition level in countries with high pig density, few human infections caused by LA-MRSA are reported [22].

On the other hand, the substantial spread of LA-CC398 in farmed animals might represent a risk for humans, in whom it could reacquire the virulence genes that would enable the inter-human spread of MRSA infections [23].

Recently, a LA-MRSA CC9/CC398 spa type t899 has been described; this represents a unique genotype with a CC398 chromosomal back bone and a smaller CC9 region, which contains the staphylococcal protein A [19]. This genotype has been isolated from colonized or infected poultry and humans, which means that a subpopulation of CC9/CC398 carrying the ϕSa3 phage has adapted to humans and poultry [24]. This raises the possibility that ϕSa3-positive CC9/CC398 isolates more than the ϕSa3-negative ones might be disseminated, via the foodborne route and via human-to-human transmission.

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MRSA in food of animal origin and its significance for food safety

Many authors have reported the presence of MRSA in food of animal origin worldwide: it has been found with different prevalence in meats such as pork (0.004 - 50%), poultry (0.7 - 43.8%), beef (1 - 15.2%), lamb (6.2%) and wild boar (25%), as well as in raw milk (1.7 - 17.6%), table eggs (11%) and fish (13.5%) [8,25-34]. On the other hand, it is important to stress that human MRSA strains, too, have been isolated from food, because of contamination during food handling [35]; in fact, depending on the epidemiology of the geographical area considered, about 0.7 - 1.5% of human beings are colonized by MRSA [36-38]. Therefore, nowadays, it is well known that there exists an interchange between human and animals' MRSA clones [39] but it is still unclear whether there is a foodborne risk linked to food contaminated by MRSA. However, in 1994 the 1st foodborne outbreak at the University Hospital Rotterdam, where 5 out of 27 patients died, occurred; the outbreak was caused by a human strain isolated from a worker who contaminated the food during meal preparation [40]. Also, in 2001 there was the 1st food poisoning outbreak caused by a staphylococcal enterotoxin C (SEC) producing MRSA isolated from roasted pork contaminated by food handlers [41].

Conclusion

The spread of MRSA in the food chain represents a risk for consumers who might be colonized or acquire infections by handling and/or consuming contaminated foods [7]. In particular, CC398 S. aureus strains have been found in pork, chicken products, and raw turkey meat. It may be transmitted to humans from meat products by handling contaminated foods or by the cross contamination of household surfaces due to poor kitchen hygiene [42]. The therapeutic options for treating the infections caused by MRSA could be dramatically reduced because this organism is frequently multi-drug resistant. Moreover, MRSA should also be considered to be a new professional bio-hazard in the production chain of food of animal origin; thus, slaughterhouse workers, veterinarians and transport workers are at greater risk of colonization by LA-MRSA [43-46]. Several actions should be taken to reduce the public health impact of MRSA along the food chain; for example, it would be useful to implement the good hygienic practices (GHP) in farms and in food production plants as well as in domestic kitchens using appropriate training programs for breeders, food business operators and consumers. Health authorities should introduce continuous surveillance of the proper use of antimicrobials in food-producing animals and the adoption of GHP by food producers along the meat and milk production chain. Finally, to better assess the significance of MRSA as a foodborne pathogen and the related public health risks, it would be useful to investigate: i) the MRSA prevalence in less investigated food-producing species, such as buffaloes and camels, which produce a large amount of milk worldwide; ii) the ability of MRSA to survive in the human stomach and intestine; iii) the ability of MRSA to survive and multiply in food of animal origin, especially in ready-to-eat foods, such as cheeses and fermented meats.

Bibliography


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