MDR BACTERIA: A REVIEW OF IMMENSE RELEVANCE IN VETERINARY MICROBIOLOGY

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ABSTRACT

Large amounts of antibiotics used in animal therapy, as well as for farm animals and even for fish in aquaculture, resulted in the selection of pathogenic bacteria resistant to multiple drugs. Multidrug resistance in bacteria may be generated by one of two mechanisms. First, these bacteria may accumulate multiple genes, each coding for resistance to a single drug, within a single cell. This accumulation occurs typically on resistance (R) plasmids. Second, multidrug resistance may also occur by the increased expression of genes that code for multidrug efflux pumps, extruding a wide range of drugs. This review discusses on the various aspects of multidrug resistance in pathogenic bacteria as applicable to veterinary microbiology and therapeutics.

Keywords: Bacteria, Multidrug resistance, Veterinary microbiology

Number of References : 22

INTRODUCTION

Multiple drug resistance (MDR), multi-drug resistances or multi resistance is a condition which enables bacteria, viruses, fungi or parasites in resisting distinct antimicrobials, like antibiotics, antifungal drugs, antiviral medications, antiparasitic drugs and wide variety of chemicals [1] having structure and function which are employed for the eradication of various organisms. Microorganisms exhibit variable degrees of MDR. Nowadays, the terms extensively-drug resistant (XDR) and pandrug-resistant (PDR) have been introduced. Vancomycin-Resistant Enterococci (VRE), Methicillin resistant *Staphylococcus aureus* (MRSA) [2], Extended-spectrum β-lactamase (ESBLs) producing Gram negative bacteria , *Klebsiella pneumoniae* carbapenemase (KPC) producing Gram-negatives , Multi drug -Resistant gram negative rods such as *Enterobacter species*, *E.coli*, *Klebsiella pneumonia* , *Acinetobacter baumannii*, *Pseudomonas aeruginosa* are the most commonly available multi-drug-resistant organisms (MDROs) or bacteria *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumonia* , *Acineto bacter baumanii* , *Pseudomonas aeruginosa* and Entero bacter species comprise the group of gram positive and gram negative bacteria of particular importance which have been dubbed as the ESKAPE group [3].Multi-drug-resistant tuberculosis is also of prime importance of discussion in this field. Mastitis is a multi-etio pathogenic condition of mammary gland affecting dairy cows and remains the most economically important disease of dairy industries around the world. It is characterized by physical, chemical and microbiological changes in the milk and pathological changes in the glandular

tissues of the udder.The indiscriminate uses of antibiotics and irrational treatment of bovine mastitis with different antibiotics have invited serious complication like multiple drug resistance. Till date different types of antibiotics have been tried against the pathogens in bovine mastitis with or without identification and drug sensitivity testing. Methicillin-resistant *Staphylococcus aureus* (MRSA) is infrequently reported in bovine mastitis. Due to the indiscriminate use of antibiotics without proper identification of the causative pathogen and drug sensitivity testing in mastitis cases, the emergence of multidrug resistant pathogens has accelerated [4]. After the very first report of involvement of MRSA in mastitis by Devriese *et al.*[5], MRSA has been described in mastitis very occasionally [2, 6 - 8]. For treatment of mastitis, methicillin resistance, which is caused by the expression of the *mecA* gene, is of particular interest. Indeed, this mechanism confers resistance to almost all types of β-lactam antibiotics active against *S. aureus*, and these antibiotics are still frequently used in mastitis treatment [9]. MRSA is an important pathogen in human medicine, but can also colonize and cause infections in a variety of animal species also [10].The most extensive antimicrobial resistance studies involving mastitis isolates have investigated *Staphylococcus aureus* .Methicillin-resistant *Staphylococcus aureus* (MRSA) is reported in bovine mastitis cases. Methicillin resistant *Staphylococcus aureus*

have zoonotic importance. Detection of the *mec*A gene by polymerase chain reaction (PCR) is the gold standard for identifying methicillin-resistant *Staphylococcus aureus* (MRSA) [11].*Mechanism involved in the resistance of bacteria to antibiotics*

Various microorganisms by the mechanism of spontaneous mutation or by DNA transfer have survived for thousands of years by their ability to adapt to antimicrobial agents. By this property these bacteria oppose the action of certain antibiotics, rendering the antibiotics ineffective [12].

The several mechanisms as used by the bacteria in attaining multi-drug resistance are not related to the glycoprotein cell wall, efflux mechanisms to remove antibiotics [13], increased mutation rate as a stress response,enzymatic deactivation of antibiotics, Decreased cell wall permeability to antibiotics and altered target sites of antibiotic,

Staphylococci[14], enterococci, gonococ ci, streptococci [15], salmonella, as well as numerous other Gram negative bacteria and *Mycobacterium tuberculosis* show multi-drug resistance. Antibiotic resistant bacteria are able to pass on the resistance genes and so generations of antibiotics resistant bacteria and produce transfer copies of DNA that code for a mechanism of resistance to other bacteria even distantly related to them [16]. This process is called horizontal gene transfer.

Resistance to Antiviral therapeutics

Influenza virus has become increasingly MDR; first to amantadenes, then to neuraminidase inhibitors such as oseltamivir, (2008-2009: 98.5% of Influenza A tested resistant), also more commonly in immunoincompetent people. HIV is the prime example of MDR against antivirals, as it mutates rapidly under monotherapy. Cytomegalovirus can become resistant to ganciclovir and foscarnet under treatment, especially in immunosuppressed patients. Herpes simplex virus, mostly in the form of cross-resistance to famciclo vir and valacyclo vir in immune suppressed patients rarely becomes resistant to acyclovir preparations.

Resistance to Antifungal drugs

When prolonged/ long term treatment of fungal infections in performed with azole preparations, requiring treatment with a different drug class, Yeasts such as *Candida species* can become resistant. *Scedosporiumprolificans* infections are resistant to multiple antifungal agents and prove to be uniformly fatal [17].

Anthelmintic resistance

Many parasitic helminthes of veterinary importance have genetic features that favor development of anthelmintic resistance, this becoming a major worldwide constrain in livestock production. The development of anthelmintic resistance poses a large threat to future production and welfare of grazing animals. Development of variable degrees of resistance among different species of gastrointestinal nematodes has been reported for all the major groups of anthelmintic drugs. It has been observed that frequent usage of the same group of anthelmintic; use of anthelmintics in sub-optimal doses, prophylactic mass treatment of domestic animals and frequent and continuous use of a single

drug have contributed to the widespread development of anthelmintic resistance in helminthes. The degree and extent of this problem especially with respect to multidrug resistance in nematode populations is likely to increase. Maintaining parasites in refugia and not exposed to anthelmintics, seems to be a key point in controlling and delaying the development of resistance, because the susceptible genes are preserved [18, 19]. The prime example for MDR against antiparasitic drugs is malaria. *Toxoplasmagondii* can also become resistant to artemisinin, as well as atovaquone and sulfadiazine, but is not usually MDR [8]. Antihelminthic resistance is mainly reported in the veterinary literature in connection to the practice of livestock drenching [20]. In 2012, artemisinin-resistant *Plasmodium falciparum* emerged in western Cambodia and western Thailand. *Plasmodium vivax* hasbecome chloroquine and sulfadoxine-pyrimethamine resistant a few decades ago [21].

CONCLUSION

To limit the development of antimicrobial resistance, it has been suggested to use the appropriate antimicrobial for an infection, to identify the causative organism(s), selection of an antimicrobial targeting the specific organism, to complete the optimum duration of antimicrobial treatment and using the correct dose for eradication, as sub-therapeutic dosing is associated with resistance, as demonstrated in food animals [22].

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