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A Review on How Animals Contribute as a Factor to Antibiotic Resistance

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Abstract

The development and spread of antibiotic resistance have become a major cause of concern. Over a past few decades, no major new types of antibiotics have been produced and almost all known antibiotics are losing their activity against pathogenic organisms. Overuse and misuse of antimicrobials in animals and humans is contributing to the rising threat of antibiotic resistance as some types of infections in humans have already developed resistance to most of the antibiotics available for treatment. The surge in the growth of multi drug resistant bacteria in animals and animal products holds as a consequence to the inappropriate use of antimicrobials. The food chain is an important contributor to the development and dissemination of antibiotic resistant pathogens. The resistance is transmitted to humans directly by contact or indirectly posing risk to human health.

Keywords: Antibiotic Resistance; Food supply Chain; Transmission; Global interest

List of abbreviations: AR: Antibiotic Resistance; MRSA: Methicillin Resistant Staphylococcus Aureus; WHO: World Health Organisation

Introduction

Antibiotics are medicines that inhibit or kill the growth of bacteria which contribute to prevent infections and save lives. Antibiotic resistance (AR) occurs when the bacteria develop some changes that mitigates the effectiveness of drugs or chemicals designed to cure or prevent infections and inherit the ability to survive and grow. The rapid surge in the development of AR is the main cause of concern as it specifies the ability of an organism to resist the killing effects of an antibiotic to which it was normally susceptible and now is has become an issue of global interest. Key contributors responsible for AR include: (1) Inadequate or improper diagnosis (2) Poor quality control of available antibiotics (3) clinical misuse (4) Ease of availability [1]. In recent years, enough evidence highlighting a link between excessive use of antimicrobial agents and antimicrobial resistance from animals as a contributing factor to overall burden of AR has emerged. The main reasons for the use of antibiotics in food producing animals include prevention of infections, promotion of growth and improvement of production of farm animals. The mechanism of action of antibiotic resistance is varied and each one is further explained. The more an antibiotic is used, the more likely are resistant populations to develop among bacteria of an increasing number of animals [2]. The indiscriminate use of antimicrobials would lead to treatment failures and could also act as a source of gene pool for transmission to humans. The relationship of drug-resistant bacteria in people to antibiotic use in food animals continues to be debated [3].

Discussion

Mechanism of Antimicrobial Resistance

Antibiotic use has always been related to growth of resistance. Indeed, whenever an antibiotic is consumed, it eliminates susceptible bacterial cells, leaving or selecting those unusual strains that proceed grow in its presence through Darwinian selection process. Those resistant variants then increase and become the predominant bacterial populations, and transmit their resistance genes to offspring (Apata, 2009; Holmes *et al.*, 2016) [4]. The bacteria pass along the mutated genes by either reproduction or by releasing DNA upon death which is then picked up by other bacteria surrounding it. For example, strands of staphylococcus aureus are developed into methicillin resistant staphylococcus aureus (MRSA) which is resistant B-lactam antibiotic. The centres for Disease Control and Prevention conservatively estimates that at least 23,000 people die annually in the USA as a result of an infection with an antibiotic-resistant organism [5].

The major mechanism of action of antimicrobial resistance include: [5]

1) Decreased uptake- Decreased entry of the drug into the bacterial cell wall. Bacteria have developed mechanisms to stop the antibiotic from reaching its intracellular or periplasmic target by decreasing the uptake of the antimicrobial molecule. The prime example of the efficiency of this natural barrier is the fact that vancomycin, a lipopeptide antibiotic, is not active against gram-negative organisms due to lack of penetration through the outer membrane.

2) Target Modification- Alteration or interference with the antimicrobials target molecule. One of the foremost successful bacterial strategies to deal with the presence of antibiotics is to supply enzymes that deactivate the drug by adding specific chemical moieties to the compound or they eradicate the molecule itself, thus making the antibiotic unable to interact with its target.

3) Antibiotic inactivation- The main mechanism of B-lactam resistance relies on the destruction of compounds by the action of B-lactamases. These enzymes destroy the amide bond of the B-lactam ring, making the antimicrobial ineffective.

4) Increased influx- Increased export of the drug from the bacterial cell. The production of complex bacterial machineries capable to extrude a toxic compound out of the cell also can end in antimicrobial resistance. This mechanism of resistance affects a wide range of antimicrobial classes including protein synthesis inhibitors, fluoroquinolones, B-lactamases, carbapenems and polymyxins.

Presence of Resistant bacteria in Animals

The main reasons for the use of antibiotics in food animals include prevention of infections, treatment of infections, promotion of growth and improvement in production in farm animals. Resistant bacteria are developed in humans in the course of use of antibiotics in order to treat infections. Evidence which identified prevalence surveys reporting antibiotic resistance rates in animals for common indictor pathogens: Escherichia coli, Campylobacter, nontyphoidal Salmonella and Staphylococcus aureus. The highest resistance rates were observed with the foremost commonly used classes of antimicrobials in animal production: Tetracyclines, Sulphonamides and Penicillin [6]. A prospective in vivo study in 1975 was performed to evaluate the effect of introducing low-dose-in-feed oxytetracycline on intestinal flora of chickens. The results showed not only colonisation of the chickens with tetracycline-resistant and other drug-resistant Escherichia coli strains but also acquisition of resistance in E. coli in the intestinal flora of the farm family [3]. The new WHO recommendations aim to help preserve the effectiveness of antibiotics that are important for human medicine by reducing their unnecessary use in animals. In some countries, approximately, 80% of total consumption of antibiotics is within the animal sector, largely for growth promotion in healthy animals [6]. Poultry is one of the most widespread food industries worldwide. Chicken is the most ordinarily farmed species with over 90 billion plenty of chicken meat produced annually. A large diversity of antimicrobials is used to raise poultry in most countries which are also considered to be essential in human medicine. The indiscriminate use of such essential antimicrobials in animal production is likely to accelerate the development of resistant bacteria [6]. A study to detect the presence of MRSA in broilers and the surrounding air in Germany reported the prevalence of MRSA in air as high as 77% in broilers. This pattern of resistance was also reported in India with 1.6% of staphylococcal isolates containing MEC-A resistant gene [6]. Meat products antibiotic-resistant salmonella, Campylobacter, E-coli and multidrug resistant staphylococcus have been detected in may different types of retail meat and poultry products, as well as in farm animals and the farm environment. Nearly half (48.4%) of Salmonella isolated from chicken breasts were resistant to three or more classes of antibiotics and more than 30% were resistant to five or more classes of antimicrobials [6].

The emergence of AR along the food supply chain is thus a serious global public health issue, with several studies having reported food animals being colonised and contaminated by antibiotic resistant strains such as methicillin-resistant staphylococcus aureus (MRSA), antibiotic resistant campylobacter. For example, Alexander *et al.* showed that drug-resistant Escherichia coli was present on beef carcasses after evisceration and after 24h within the chiller and in beef stored for 1 to eight days. Others isolated ciprofloxacin-resistant Campylobacter spp. from 10% to 14% of consumer chicken products. MRSA has been reported to be present in 12% of beef, veal, lamb, mutton, pork, turkey and other samples purchased in the consumer market in the Netherlands as well as cattle dairy products in Italy. Likewise, extensive antibiotic resistance has been reported for bacteria including human pathogens from farmed fish and market shrimp [7].

Transmission in Humans

Evidence that antibiotic use in food animals may result in antibiotic-resistant infections in humans has existed for several decades. Associations between antibiotic use in food animals and the prevalence of antibiotic-resistant bacteria isolated from those animals have been detected in observational studies as well as randomized trials [7]. Antibiotic resistant bacteria of animal origin have been observed in environment surrounding livestock farming practices, on meat products available for purchase in retail food stores and as the cause of clinical infections and subclinical colonisation in humans. It is estimated that the volumes of antimicrobials used in food animals exceeds the use in the human worldwide and nearly all the classes of antimicrobials that are used for humans are also being used in food animals including the newest classes of drugs such as third and fourth generation cephalosporins, fluoroquinolones, and streptogramins (Aerestrup *et al.*, 2008) [7] .

Transmission of resistance from animals to humans can take place through a variety of routes, where food-bourne route is probably the most important (enteric bacterial pathogens such as salmonella, campylobacter occur through this route) whereas the other resistant pathogens through direct contact between animals and humans maybe a major route of transmission [8].

The emergence of AR in the food chain is considered as a cross-sectoral problem as AR and AR genes can easily spread at each stage of food- production chain and cause infections in humans. As disease-causing bacteria are often transferred from food producing animals to humans, the food supply chain is taken into consideration as a route of transmission for the resistant bacteria or the resistant genes. Antibiotic resistant genes from foodborne bacteria were transferred in the laboratory to human resident and pathogenic bacteria by gene transfer (HGT) mechanisms, leading to acquired resistance in recipient strains [9]. A number of antimicrobial-resistant pathogens have emerged in the food production chain: extended beta-lactamase producing Salmonella and Escherichia coli, transmissible quinolone resistance in Salmonella and E. coli and animal associated methicillin-resistant Staphylococcus aureus (MRSA), which can transmit to and cause infections in humans. These emergences can all be associated with the use of antimicrobial agents in food animals and they have led to renewed attention to the use of certain types of antimicrobials in food animals that are considered critically important for human health (Aerestrup *et al.*,2008; Xia *et al.*,2010) [9].

In addition, human population maybe directly exposed to antibiotic resistant bacteria via contact or consumption of contaminated food products. Recently, numerous reports have been described the presence of large quantities of antibiotic resistant bacteria in various food products (ready to eat meat, cooked meat, bulk milk) and various animal sources such as cattle, poultry, swine, goat and sheep) [10].

It is generally accepted that adequate cooking destroys bacteria in food. Although, in a research conducted, it was assumed that as with salmonellae, inadequate cooking cross contamination occurs with other bacteria as well as resistant strains [10]. Salmonella species are widespread in nature and frequently cause food poisoning in humans. Epidemiological studies show that foods of animal origin are often involved. Salmonellosis in humans involving antibiotic-resistant strains of bovine origin has occurred (Anderson 1968, Threlfall *et al.* 1978) [16]. Furthermore, there is a little doubt that resistance can be transferred through plasmids from certain resistant microorganisms to others that were originally sensitive. These in turn have been shown to be transmissible to other animals and in isolated cases, to humans (Levy *et al.*1976 a, b; Hirsh 1977). This resistance transfer or "infectious drug resistance" has led on the part of some individuals to fear the resistant strains could be transferred to other animals and humans thereby creating a reservoir of pathogens, which when involved in clinical infections, would be unresponsive to antibiotic treatment. Some of the antibiotic resistance genes identified in food bacteria have also been identified in humans, providing indirect evidence for transfer by food handling or consumption. In 2001, Sorensen *et al.* confirmed the risk of consuming meat products colonized with resistant bacteria, showing the resistant Enterococcus faecium of animal origin ingested via chicken or pork lasted in human stool for up to 14 days after ingestion. Donabedian *et al.* found overlap within the pulsed-field gel electrophoresis (PFGE) patterns of gentamicin-resistant isolates from humans and pork meat additionally as in those of isolates from humans and grocery chicken. They identified that when a gene conferring antibiotic resistance was present in food animals, the same gene was present in retail food products from the same species [11].

Conclusion

Antibiotic resistance to bacteria is rising dangerously to high levels which makes it difficult to treat common infections. The prevalence of multi-drug resistant bacteria has been identified in poultry products, cattle, dairy products and various other animal sources. The transmit of these antibiotic resistant bacteria to humans via different routes pose a risk to both handlers, consumers and a threat to global and public health. Preventive measures need to be adapted to lower the impact and limit the spread of resistance worldwide.

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