Manipal Journal of Pharmaceutical Sciences

Volume 7 | Issue 1 Article 9

3-1-2021

How do the animals contribute as a factor to Antibiotic Resistance? – A Review

Gore S
Clinical Pharmacy, Bharati Vidyapeeth University, Pune,

Review Article

How do the animals contribute as a factor to Antibiotic Resistance? – A Review

Sania Gore

Email: saniagore44@gmail.com

Abstract

Antibiotic resistance is emerging as a serious concern over the past few decades. There has not been any significant production of new types of antibiotics in recent times and the existing ones are turning out to be non-effective against pathogens. The reason behind the increase in antibiotic resistance is due to the large scale and improper use of antimicrobial agents in animals and humans. Most of the pathogens causing infections in humans are now resistant to the recommended antibiotics which are prescribed for treatment. The surge in the growth of multidrug-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 rise and spread of antibiotic resistant pathogens. The resistance is transmitted to humans directly by contact or indirectly, posing risk to human health.

Key words: Antibiotic resistance, food supply chain, transmission, global interest

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 increase in AR is the primary cause of concern, as it specifies an organism's ability to withstand the killing effects of an antibiotic that it was usually susceptible to and has now become a global problem. Key contributors responsible for AR include (1) Inadequate or improper diagnosis; (2) Inferior quality control of antibiotics; (3) Misuse in the clinical use of the antibiotics; (4) The fact that they are easily available.1 It has now been well established that the primary factor for AR is a connection between overuse of antibiotics and resistance against the same coming from animals. Antibiotics are being overused in food-producing/farm animals to prevent infections, promote growth and improve their production. The mechanism of action of antibiotic resistance is varied and each of those is further explained. It is expected that with excessive use of an antibiotic, more resistant populations will appear among bacteria in a larger number of animals.2 The indiscriminate use of antimicrobials would lead to treatment failures and could also serve as a gene pool for human transmission. The correlation between drug-resistant bacteria in humans and the use of antimicrobials in food animals remains a controversial topic.[3]

Sania Gore

Clinical Pharmacy, Bharati Vidyapeeth University, Pune, Maharashtra State, India

Date of Submission: 14-Aug-2020, Date of Revision: 25-Feb-2021, Date of Acceptance: 03-Mar-2021

Mechanism of antimicrobial resistance

The use of antibiotics has always been related to the development of antimicrobial resistance. On the use of an antibiotic, susceptible microbes are killed and others are selectively left behind which are able to grow when the antibiotic is present. This brings into play the Darwinian selection process, whereby the selected resistant strains comprise the predominant population and move on to transmit their resistant genes down the generation.[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,

How to cite this article: Gore S. How do the animals contribute as a factor to Antibiotic Resistance? – A Review. *MJPS* 2021; 7(1): 101-104.

strands of staphylococcus aureus are developed into methicillin resistant staphylococcus aureus (MRSA), which is a resistant B-lactam antibiotic. An estimate given by the Centre for Disease Control and Prevention shows that a minimum of 23,000 annual deaths in the USA is due to an infection caused by an antibiotic-resistant organism.[5]

The major mechanism of action of antimicrobial resistance include: [6]

1) Decreased uptake - Bacterial mechanisms to decrease the entry of the drug into the bacterial cell wall and prevent it from reaching its intracellular target. A chief example is vancomycin, which is inactive against gram-negative bacteria because it is not able to penetrate through the outer membrane.

2) Target Modification - Alteration or interference with the antibiotic molecule. One of the foremost bacterial strategies to deal with antibiotics is to deactivate the drug enzymatically, either by adding some chemical group to the antibiotic molecule or by eradicating the molecule.

3) Antibiotic inactivation - An example of this is the B-lactam resistance, which is the inactivation of antibiotics by the action of enzymes called B-lactamases, which cleave the amide bond in the B-lactam ring, thus making it ineffective.

4) Increased efflux - Increased export of the drug from the bacterial cell by complex bacterial machineries. This mechanism of resistance has been observed in a variety of antimicrobial classes including B-lactamases, protein synthesis inhibitors, carbapenems, fluoroquinolones and polymyxins.

Presence of resistant bacteria in animals

Resistant bacteria are developed in humans in the course of the use of antibiotics in order to treat infections. There have been surveys that have reported that antibiotic resistance exists in animals for common pathogens such as Campylobacter, Escherichia coli, Staphylococcus aureus and nontyphoidal Salmonella. The maximum resistance rates occurred against antimicrobials, which are extensively used in animal production: Tetracyclines, Penicillin and Sulphonamides.[7] In 1975, a prospective in vivo study was carried out to understand if the introduction of "low-dose-in-feed" oxytetracycline has any effect on the intestinal flora of chickens. It was found out that Escherichia coli strains which were tetracycline and other drug-resistant have colonised the chickens together with resistant E. coli in the intestinal flora of the farm family.8 WHO recommends to help to maintain the efficacy of antibiotics needed for human medicine by reducing their excessive use in animals. In some countries, about 80% of antibiotics are used in the animal sector, mainly for promoting their growth.[9] Poultry, being a widespread food industry worldwide, produces over 90 billion chicken meat annually. In most countries, a wide variety of antimicrobials are used to raise poultry, which is also regarded as important in human medicine. Such is the rate of overuse that it forms the reason for the development of resistant bacteria.[10] A study carried out in Germany has reported that the air surrounding broilers constitute about 77% MRSA. A similar trend was also reported in India where the MEC-A resistant gene was present in almost 1.6% of staphylococcal isolates.[11] Meat products containing antibiotic-resistant Salmonella, Campylobacter, E. coli and multi-drug resistant Staphylococcus have been detected in many different types of retail meat and poultry products, and also 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.[12]

Therefore, the rise of AR along the food supply chain is a global and critical public health concern, with several findings stating that antibiotic-resistant strains, for example, "methicillin-resistant Staphylococcus aureus" (MRSA), antibiotic-resistant Campylobacter are colonizing in food animals. Alexander et al. showed that beef carcasses after evisceration or beef after 24 hours chilling or 1-8 days storage contained drug-resistant Escherichia coli. In separate studies, 10-14% of consumer chicken products have been contaminated with ciprofloxacin-resistant Campylobacter spp. Reports on 12% of meat samples (lamb, beef, mutton, veal, turkey, pork and others) from the Netherlands have shown colonisation of MRSA. Similarly, cattle dairy products in Italy, farmed fish and market shrimp have also shown contamination and colonization of antibiotic-resistant bacteria including human pathogens.[13]

Transmission in humans

The fact that antibiotic-resistant infections in humans is a consequence of the use of antibiotics in animals used as food is well proven. Observational studies and randomized trials have shown that there exists a correlation between antibiotic use in food animals and the prevalence of antibiotic-resistant bacteria isolated from those animals.[14] The environment around livestock and meat products contain antibiotic-resistant bacteria and of animal origin and is the cause of clinical infections and subclinical colonisation in humans. The quantity of antimicrobials used in animals for food purpose is estimated to surpass human use worldwide, and almost all classes of antimicrobials used for human use are often used in animals, as well as drugs of new generations such as cephalosporins, fluoroquinolones and streptogramins of the third and fourth generations.[15]

The food borne route is the most significant of the various routes through which transmission of resistance from animals to humans can take place. Enteric bacterial pathogens such as Salmonella and Campylobacter are transmitted through this route, whereas another major route through which resistant pathogens may be transmitted is direct contact between animals and humans.[16]

AR is thought to be a "cross-sectoral problem" as AR and these genes can spread easily at each point of the food production process to cause infections in humans. The food supply chain is taken into consideration as a major route of transmission for the resistant bacteria or genes as they are transferred from food animals to humans often. Antibiotic-resistant genes from foodborne bacteria have been transferred in the laboratory via gene transfer mechanisms (HGT) to human resident and pathogenic bacteria, leading to acquired resistance in recipient strains.[17] "Transmissible quinolone resistance" and "extended beta-lactamase" producing Salmonella and Escherichia coli and animal associated MRSA have risen in the food production chain, which can infect humans. Antimicrobial agents in animals used as food can all be related to these outbreaks and contributed to consideration of use of some forms of antimicrobials that are regarded as relevant for human health.[18]

In addition, direct exposure to AR organisms can occur via contact or ingestion of food which are contaminated. The existence of excessive amounts of antibiotic-resistant bacteria in a number of food products (bulk milk, cooked meat and ready to eat meat) and products of animal origins such as beef, sheep, goat, poultry and swine has been identified in numerous reports recently.[19]

The fact that proper cooking destroys bacteria in food is well accepted. However, research has shown that with improper cooking, cross-contamination occurs with other bacteria as well as resistant strains.[20] 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.[21] Furthermore, there is a little doubt in the transfer of resistance from resistant microorganisms to sensitive ones through plasmids. In turn, these have been transmitted to other animals and humans too in isolated cases This resistance transfer or "infectious drug resistance" has been the cause of concern as it could create a reservoir of pathogens, which when involved in clinical infections, would not show response to antibiotic treatment. Few genes found in bacteria present in eatables for antibiotic resistance are also present in humans, establishing an indirect proof of transmission by food handling or intake. Sorensen and group in 2001 showed that resistant Enterococcus faecium was present in human stool up to 14 days after consumption of contaminated meat, thus proving that it is a risk to consume food colonized with resistant bacteria. Donabedian et al. studied gentamicin-resistant isolates from humans, pork meat and grocery chicken and found similarity in the pattern of pulsed-field gel electrophoresis (PFGE). They identified that when an antibiotic resistance gene occurs in animals used as food, the same gene existed in those retail food merchandise.[22]

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 transmission of these antibiotic-resistant bacteria to humans via different routes continue to act as a risk factor for handlers and consumers as well as a health hazard globally. Preventive measures need to be adapted to lower the impact and limit the spread of resistance worldwide.

References

1. Chokshi A, Sifri Z, Cennimo D, Horng H. Global Contributors to Antibiotic Resistance [published correction appears in J Glob Infect Dis. 2019 Jul-Sep;11(3):131]. J Glob Infect Dis. 2019;11(1):36-42.
2. Phillips, I. Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data. Journal of Antimicrobial Chemotherapy. 2003;53(1):28–52.
3. Marshall, B. M., & Levy, S. B. (2011). Food Animals and Antimicrobials: Impacts on Human Health. Clinical Microbiology Reviews.2011;24(4):718–733.
4. Founou LL, Founou RC, Essack SY. Antibiotic Resistance in the Food Chain: A Developing Country-Perspective. Front Microbiol. 2016; 7:1881.
5. Munita JM, Arias CA. Mechanisms of Antibiotic Resistance. Microbiol Spectr. 2016;4(2):10.1128/microbiolspec.VMBF-0016-2015.
6. Munita JM, Arias CA. Mechanisms of Antibiotic Resistance. Microbiol Spectr. 2016;4(2): 10.1128/microbiolspec.VMBF-0016-2015.
7. Van Boeckel TP, Pires J, Silvester R, et al. Global trends in antimicrobial resistance in animals in low- and middle-income countries. Science. 2019;365(6459): eaaw1944.
8. Marshall, B. M., & Levy, S. B. (2011). Food Animals and Antimicrobials: Impacts on Human Health. Clinical Microbiology Reviews 2011:24(4):718–733.
9. Christian lindmeier, C.L. Stop using antibiotics in healthy animals to prevent the spread of antibiotic resistance. [Online]. Available from: https://www.who.int/news-room/detail/07-11-2017-stop-using-antibiotics-in-healthy-animals-to-prevent-the-spread-of-antibiotic-resistance [Accessed 7 July 2020].
10. Agyare, C., Etsiapa Boamah, V., Ngofi Zumbi, C., & Boateng Osei, F. Antibiotic Use in Poultry Production and Its Effects on Bacterial Resistance. Antimicrobial Resistance - A Global Threat. 2019.
11. Agyare, C., Etsiapa Boamah, V., Ngofi Zumbi, C., & Boateng Osei, F. (2019). Antibiotic Use in Poultry Production and Its Effects on Bacterial Resistance. Antimicrobial Resistance - A Global Threat.
12. H Wang, JC Mcentire, L Zhang, X Li & M Doyle. The transfer of antibiotic resistance from food to humans: facts, implications and future directions. [Online], 2012, 31 (1), 249-260 Available from: https://pdfs.semanticscholar.org/cf91/29eb968ac86a10a57fb21b7528def76d42db.pdf [Accessed 7 July 2020].
13. Marshall, B. M., & Levy, S. B. (2011). Food Animals and Antimicrobials: Impacts on Human Health. Clinical Microbiology Reviews, 24(4):718–733.
14. Landers TF, Cohen B, Wittum TE, Larson EL. A review of antibiotic use in food animals: perspective, policy, and potential. Public Health Rep. 2012;127(1):4-22.
15. Wegener HC. Antibiotic Resistance—Linking Human And Animal Health. In: Institute of Medicine (US). Improving Food Safety Through a One Health Approach: Workshop Summary. Washington (DC): National Academies Press (US); 2012. A15. Available from: https://www.ncbi.nlm.nih.gov/books/NBK114485/
16. Wegener HC. Antibiotic Resistance—Linking Human And Animal Health. In: Institute of Medicine (US). Improving Food Safety Through a One Health Approach: Workshop Summary. Washington (DC): National Academies Press (US); 2012. A15. Available from: https://www.ncbi.nlm.nih.gov/books/NBK114485/
17. H Wang, JC Mcentire, L Zhang, X Li & M Doyle. The transfer of antibiotic resistance

Gore S: How do the animals contribute as a factor to Antibiotic Resistance? – A Review

from food to humans: facts, implications and future directions. [Online], 2012, 31 (1), 249-260 Available from: https://pdfs.semanticscholar.org/cf91/29eb968ac86a10a57fb21b7528def76d42db.pdf [Accessed 7 July 2020].

18. Wegener HC. Antibiotic Resistance—Linking Human And Animal Health. In: Institute of Medicine (US). Improving Food Safety Through a One Health Approach: Workshop Summary. Washington (DC): National Academies Press (US); 2012. A15. Available from: https://www.ncbi.nlm.nih.gov/books/NBK114485/
19. Founou LL, Founou RC, Essack SY. Antibiotic Resistance in the Food Chain: A Developing Country-Perspective. Front Microbiol. 2016; 7:1881.
20. Phillips, I. (2003). Does the use of antibiotics in food animals pose a risk to human health? A critical review of published data. Journal of Antimicrobial Chemotherapy, 53(1):28–52.
21. Founou LL, Founou RC, Essack SY. Antibiotic Resistance in the Food Chain: A Developing Country-Perspective. Front Microbiol. 2016; 7:1881.
22. Marshall, B. M., & Levy, S. B. Food Animals and Antimicrobials: Impacts on Human Health. Clinical Microbiology Reviews 2011; 24(4):718–733.