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"Antimicrobial Drug-Resistance of Zoonotic Foodborne Pathogens and Consequences on Public Health"

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Mini Review

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Abstract

The emergence of antimicrobial drug-resistant bacteria and their dissemination in the community represents a real challenge to Public Health, both today and for the years ahead. Antimicrobial resistant zoonotic foodborne pathogens are a particular problem and there are worldwide numerous instances of severe foodborne illnesses caused by such bacteria. Some of these bacteria show increased virulence and therefore morbidity and mortality. In the majority of such infections the incriminated foods are of animal origin. Application of improved hygiene standards along the food production chain, "from farm to fork", is of paramount importance to control the dissemination of all zoonotic foodborne pathogens, and thus the drug resistant ones. The establishment of thresholds in foods of certain foodborne pathogens to selected antimicrobials may also be a useful tool in combating antimicrobial resistance dissemination.

Introduction

The contribution of antimicrobials to the achievements of human and veterinary medicine and surgery is widely accepted. Antimicrobials have also had a significant contribution in increasing life expectancy, by reducing the effects of bacterial infections. Unfortunately, from the early beginnings of the discovery of antimicrobials the risk of developing resistant strains from their overuse and misuse was recognized. Many pathogens have already become resistant to multiple classes of antibiotics and infections from resistant bacteria have become common and represent a serious global problem to public health. The reduced effectiveness of antimicrobials undermines the ability to manage and control bacterial infections, particularly those secondary infectious complications, common in vulnerable patients undergoing chemotherapy for cancer, dialysis for renal failure, organ transplantation and other surgeries [1].

A direct relationship between antimicrobial consumption and the emergence and dissemination of resistant bacterial strains has been demonstrated in numerous epidemiological studies [2]. In bacteria, genes conferring antimicrobial resistance can be inherited from close relatives or can be acquired by mutation, or horizontal transfer, from non-relatives on mobile genetic elements, such as plasmids. An example is the recently reported emergence of colistin resistant *E. coli* in animals and humans due to the horizontal transfer of the *mcr-1* gene by plasmid-mediated polymyxin resistance [3]. Furthermore, antimicrobials can eliminate drug-sensitive competitors favoring undisturbed resistant bacteria reproduction as a result of natural selection [4].

In the food industry antimicrobials have been essential to ensure the good health and welfare of livestock, especially in intensive farming, but the overuse, misuse and the use of low doses of antimicrobial drugs as growth promoters have contributed to the emergence of resistant bacteria. These resistant bacteria can be transferred to the human population through food, the environment (i.e., water, manure, sludge-fertilized soil and air), or by direct human-to-animal contact [5]. Food contamination with these pathogens can occur at any of the multiple steps along the complex food production chain, including production, processing, distribution and preparation. Over all these observations demonstrate that antimicrobial resistance is of importance to both medical and veterinary science and emphasize the need for coordinated actions.

Foodborne Pathogens and Diseases

Foodborne diseases are considered a major source of morbidity and mortality especially in susceptible population groups, such as infants, the elderly and immunocompromised persons [6]. The World Health Organization estimates that 1.5 billion cases, and more than three million deaths, occur in children every year due to food and water contamination [7]. According to the Centers for Disease Control and Prevention [8], from the 31 known foodborne pathogens, eight account for the vast majority of illnesses and among these are non typhoidal *Salmonella*, *Campylobacter* spp., *Clostridium* spp., *Staphylococcus aureus, Listeria monocytogenes* and Enteropathogenic *Escherichia coli.* In the European Union a total of 5,251 foodborne outbreaks were reported between May 2013 and May 2014 [9]. These outbreaks involved 45,665 human cases, 6,438 hospitalizations and 27 deaths. The most common bacterial causative agents were *Salmonella* (1,048 outbreaks) and *Campylobacter* (444 outbreaks). However, these estimates are generally considered conservative, and it is recognized that the global burden of foodborne diseases is significant.

Antimicrobial Resistance in Food Pathogens

The majority of foodborne infections are mild and usually self limiting, but treatment with antibiotics and other antimicrobial drugs can be lifesaving in invasive and complicated cases. Outbreaks caused by drug-resistant bacteria are no longer emerging problem, but rather an established one. Antimicrobial resistance can make these drugs ineffective for treatment of these infections and thus potentially represents a serious threat to public health.

Antimicrobial resistant *Salmonella* (such as *Salmonella* Typhimurium DT 04) causing foodborne human disease are well documented and are clearly a foodborne threat (www.who.int/foodsafety/publications/micro/en/report). Typically the implicated foods are of animal origin but it is now accepted that fresh produce can be the source. Human infections with fluoroquinolone-resistant *Campylobacter* species have become increasingly common [10]. Overall 20-30% of campylobacteriosis cases are associated with the handling and consumption of poultry meat by case control studies while 50-80% are attributed to the poultry reservoir as a whole by molecular epidemiology. Fluoroquinolones are often used for the treatment of bacterial infections in poultry. Antimicrobial resistant *Salmonella* and *Campylobacter* cause an estimated 410,000 infections in the US alone each year [11]. *Shigella* spp. resistant to ciprofloxacin has been incriminated for foodborne outbreaks in Brazil [12]. A multi-state cluster of infections of *Shigella sonnei,* resistant to ciprofloxacin, has recently been reported in the US [13]. Ciprofloxacin is the recommended antimicrobial medication to treat shigellosis in adults. Methicillin-resistant *S. aureus* (MRSA) strains have been isolated from foods incriminated in staphylococcal food poisoning (SFP) [14,15].

Unfortunately information on outbreaks of foodborne illness due to antimicrobial-resistant bacteria is limited because, in many countries, isolated bacteria are not routinely tested for antimicrobial resistance and, even if tests are performed, results are often not required to be reported to health authorities.

The vast majority of antimicrobial–resistant foodborne outbreaks are caused by consumption of contaminated foods of animal origin or multi-ingredient foods. There is convincing evidence that antimicrobial use in food producing animals is the major contributing factor to the emergence of many antimicrobial–resistant zoonotic foodborne bacteria and that foods contaminated with such bacteria serve as vehicles for human infection [11].

For years there has been accumulating evidence about the public health impact of antimicrobial resistance in foodborne bacteria such as *Salmonella* and *Campylobacter* [16,11]. This impact relates to the reduction in effectiveness of the antimicrobials at early empirical treatment, as well as restriction of treatment choice, even after confirmation of microbiological diagnosis.

Antimicrobial resistance may also be related to increased virulence. Several epidemiological studies have shown the correlation of increased morbidity and mortality in resistant foodborne pathogens [16]. Moreover, after the consumption of contaminated food, resistant foodborne bacteria may asymptomatically colonize the intestine tract. Then, if for some reason antimicrobial therapy is performed during this colonization, severe clinical disease may subsequently develop.

The establishment of thresholds of selected foodborne bacteria resistant to certain antimicrobials on foods is one option under consideration to control the dissemination of antimicrobial resistance. In general, the prudent use of antimicrobials in veterinary medicine, especially in livestock, the exclusion of antimicrobial drugs as growth promoters, the improvement of hygiene at all stages of food production chain, based on the principle "from farm to fork", and the reduction of the microbial pathogen load in foodstuffs of animal origin, will all contribute to the control and prevention of foodborne antimicrobial resistant bacteria.

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