



Antibiotics Resistance among Major Foodborne Bacterial Pathogens (Review Article)

Author

Dr. Adnan Bashir Bhatti, M.D.

Department Of Medicine, Capital Development Authority (CDA) Hospital, Islamabad, Pakistan

Email: dr.adnanbashir@gmail.com

Abstract

Bacteria-mediated food poisoning is a major contributing factor for the increase in a total number of hospital visits, stays, and emergency room (ER) visits among otherwise healthy people. In most cases, bacterial food poisoning is self-limiting in healthy adults; however, the condition often requires medical interventions in children and immunocompromised patients. Salmonella, Escherichia coli, Staphylococcus aureus, Campylobacter, Vibrio, Listeria monocytogenes and Shigella are the major bacterial pathogens that are responsible for food poisoning. One of the major challenges faced by physicians with food poisoning cases is the emergence of antibiotic resistance which renders antibiotic treatment ineffective. The following review addresses these issues with a brief overview of each pathogen, the major reasons for the emergence of antibiotic resistance, and suggestions on how we can prevent the incidence of antibiotic resistance.

Introduction

Discovery of antibiotics by Alexander Fleming marked a new era in the history of modern medicine ^[1]. Many lives have been saved with this “wonder drug” but lately the glory of antibiotics is diminishing with the worldwide incidence of antibiotic resistance among bacterial pathogens ^[2]. This is especially true and worrisome in the case of bacterial pathogens that cause food poisoning.

Naturally susceptible bacteria acquire resistance by a variety of ways which can be summarized into two subtypes ^[3].

Changes in genetic makeup leading to increased production of antibiotic-degrading enzymes, formation of efflux pumps on the bacterial surface which actively pump out antibiotics, changes on bacterial membrane surfaces such that it prevent

antibiotics from entering bacterial cells and molecular alterations in bacterial organelles upon which antibiotics act ^[4].

Transfer of genetic materials from resistant bacteria to non-resistant bacteria (horizontal gene transfer). The newly acquired genetic material helps bacteria produce enzymes which deactivate antibiotics. For example, plasmid-mediated beta-lactamases, production of substitute enzyme for enzymes that are targeted by antibiotics ^[4].

According to WHO, about 600 million people equating to an approximate of 1 in 10 people in the world contracts food poisoning and almost 420,000 lives are lost per year. Food contamination can happen due to a variety of reasons including pathogenic bacteria, viruses, protozoan parasites and toxic chemicals ^[5]. Among them, bacterial pathogens are of special

importance largely owing to the rapid spread of multi-drug resistance. The most common bacterial pathogens responsible for food poisoning include *Salmonella*, *Escherichia coli*, *Staphylococcus aureus*, *Campylobacter*, *Vibrio*, *Listeria monocytogenes* and *Shigella*.

Salmonella

Salmonella is a Gram-negative bacterial pathogen that is accountable for infecting millions of people worldwide in the form of food poisoning [6]. As of 2010, an approximate of 93.8 million people are reported to be infected and the mortality rate is about 155,000 deaths per year [7].

Signs and symptoms

Salmonellosis or enteritis results in the development of abdominal cramps, diarrhea, and fever with 12 to 72 hours post-infection [8].

Source of infection

The major source of infection is contaminated water and food of animal origin [9].

Pathogenic *Salmonella* species:

Salmonella Choleraesuis, *S. Enteritidis*, and *S. Typhimurium* are the major serovars of *Salmonella* genus that is responsible for salmonellosis [10].

Course of infection and drug of choice

The infection is often reported to be uncomplicated and patients have a spontaneous recovery without any treatment within in 3 to 7 days. However, the infection can prove to be fatal for those with a weak immunity (children, elderly and immunocompromised patients) [11-12]. Antibiotics like trimethoprim/sulfamethoxazole, ceftriaxone, cefotaxime, or fluoroquinolones are used for treating adults. Ampicillin and amoxicillin are the major drug of choice for treating patients who are at risk of complications [13].

Antibiotic resistance in *Salmonella*

The global scale increase in the incidence of antibiotic resistance among *Salmonella* strains often hinders successful management of salmonellosis. Results from a various study conducted across the globe have suggested an

observable hike in the incidence of antibiotic resistance from about 20%–30% in the 1990s to as high as 70% in some places within a decade [14]. In 1999, a multi-drug resistant form of *S. Typhimurium* (phage type 104 (DT104)), was isolated. It was found out to be resistant towards 5 different types of antibiotics, namely ampicillin, chloramphenicol, streptomycin, sulfonamide, and tetracycline [15]. Soon incidence of resistance to antibiotics like nalidixic acid and fluoroquinolones were reported [16].

Escherichia coli

Escherichia coli (*E.coli*) is gram-negative commensal (beneficial) bacteria found in the intestine for humans and other warm-blooded animals. The subgroup of *E.coli* known as diarrheagenic *E. coli* is the causative organism responsible for food poisoning.

Signs and Symptoms

The major symptoms observed in the case of *E.coli* infection is diarrhea. The infection is more prevalent among patients of pediatric age group [17].

Source of infection

The major source of infection includes contaminated food and water [18].

Pathogenic *E. coli* species

The six pathotypes of *E.Coli* are Shiga-toxin-producing *E. coli* (STEC), Enterotoxigenic *E. coli* (ETEC), Enteropathogenic *E. coli* (EPEC), Enteroaggregative *E. coli* (EAEC), Enteroinvasive *E. coli* (EIEC), and Diffusely adherent *E. coli* (DAEC) [19].

Course of infection and drug of choice

Like salmonellosis, infection is self-limiting and diarrhea-induced dehydration is usually managed by oral rehydration therapy. However, in the case of infections which are chronic or relapsing, antibiotics are used to curb the infection. Amoxicillin, ampicillin, cephalothin, cotrimoxazole, streptomycin, sulfonamide, and tetracyclines are the common antibiotics used for treating such cases [20].

Antibiotic resistance in *E.Coli*

Increase in incidence of antibiotic resistant has been reported among all the groups of diarrheagenic *E. coli* from developed as well as developing countries^[19]. Resistance to ampicillin, cephalothin, co-trimoxazole, streptomycin, sulfonamide, or tetracycline streptomycin, trimethoprim, ciprofloxacin, azithromycin, and ceftriaxone have been reported from different parts of the world^[20-25].

Staphylococcus aureus

Staphylococcus aureus (*S. aureus*) is a gram-positive bacterial pathogen which is seen as a persistent commensal on the skin and mucous membrane of 20 to 30% of humans and in about 60% of humans, they are reported to have a sporadic colonization^[26]. It is one among the most common cause of food poisoning and is therefore given high priority in public health programs across the globe^[27].

Signs and Symptoms

Symptoms develop rapidly after consumption of contaminated food, often within a short span of 2 to 8 hours. The major symptoms include nausea, vomiting, painful abdominal cramps and in some cases diarrhea^[28-30].

Source of infection

The pathogen is spread through contaminated food containing toxins produced by *S.aureus*^[31]. The risk of infection is particularly high with consuming contaminated processed meat and dairy product which are stored at higher temperatures^[32]. Food handlers who are carriers of *S. aureus* are attributed to be the major source of contamination of food^[26].

Course of infection and drug of choice

The infected patients usually have a spontaneous recovery within the end of the second day of infection. Severe cases are often reported in infants, elderly or immunocompromised patients where hospitalization and oral or intravenous rehydration is required^[30]. In the case of enteritis and colitis caused by *S. aureus* antibiotics like methicillin and vancomycin is used^[33].

Antibiotic resistance in *S.aureus*

Even though antibiotics are not recommended for treating uncomplicated *S.aureus* induced by food poisoning, several studies have reported the isolation of drug methicillin-resistant *S. aureus* (MRSA) from the various food sources and infected patients. The first report on a community-acquired outbreak of MRSA-induced food poisoning came out in 2002 from the United States^[34]. This was followed by many more reports of MRSA-induced food poisoning in the succeeding years^[35].

Campylobacter jejuni

Campylobacter is a gram-negative food pathogen which is often associated with raw or undercooked meat particularly poultry^[36].

Source of infection

Campylobacter harboring flocks are the major reservoir for the pathogen. Most of the birds are infected and subsequently, upon slaughter their carcasses are often contaminated with *Campylobacter*^[37].

Signs and Symptoms

The major symptoms of infection include diarrhea, cramping, abdominal pain and fever within 2 to 5 days post-infection^[38].

Course of infection and drug of choice

The infection is usually self-limiting in adults and therefore requires only oral rehydration to replenish the fluid lost by diarrhea. However, among young children, elderly and immunocompromised individuals antibiotic treatment is required. Erythromycin, azithromycin, ciprofloxacin, and levofloxacin are the commonly used antibiotics to treat *Campylobacter*-induced food poisoning^[39-41].

Antibiotic resistance in *Campylobacter*

There are a sizable number of studies reporting the isolation of drug-resistant *Campylobacter* from infected patients and food sources^[42-43]. A study from Poland reported the isolation of antibiotic-resistant *campylobacter* from clinical isolates that were resistant towards erythromycin, ciprofloxacin, and tetracycline^[44]. Similarly, a

group of researchers reported the isolation of tetracycline resistant *campylobacter* from clinical isolates of patients residing in Canada^[45].

Vibrio

Vibrio is a gram-negative bacterial pathogen which is often associated with seafood. *Vibrio*-related food poisoning is commonly reported from countries across the world that have long coastline^[46].

Pathogenic *Vibrio* species

The most common species involved in food poisoning include *V. parahaemolyticus* and *V. cholerae*^[47].

Signs and Symptoms

Consumption of the food contaminated with *V. parahaemolyticus* results in acute gastroenteritis with manifestations ranging from stomach pain, nausea, vomiting and fever within a day after consumption.

Course of infection and drug of choice

The infection usually follows a natural course of recovery without any medical interventions except in cases of severely immunocompromised individuals. Tetracycline or ciprofloxacin are the major drug used in such cases^[48]. *V. cholerae* infection results in severe diarrhea and is responsible for an approximate of 100,000 deaths annually. The symptoms usually present itself anywhere between a few hours to 5 days and in severe cases that are left untreated may lead to death within hours of infection. The death of patients can be prevented with rehydrating the person with water and electrolytes either orally or intravenously^[48]. Antibiotics used for treating cholera include doxycycline (adults) and azithromycin (children and pregnant women)^[49].

Antibiotics resistance in *Vibrio*

The incidence of multi-drug resistance is also common among *Vibrio* with latest reports indicative of resistance towards ampicillin, tetracycline, and amikacin. In the *V. parahaemolyticus*^[50], and *V. cholerae* sulphamethoxazole/trimethoprim, erythromycin, and streptomycin are found out to be resistant^[51].

Listeria monocytogenes

Listeria monocytogenes is a gram-positive food pathogen that can infect people through contaminated meat, poultry, and seafood. The infection leads to high mortality among pregnant women, fetuses and immunocompromised patients^[52].

Signs and Symptoms

The major symptoms of *Listeria* infection among this group include abortion, neonatal death, septicemia, and meningitis^[52].

Drug of choice

Upon development of symptoms in the high-risk group, ampicillin/amoxicillin and gentamicin is generally used to manage and stabilize the patient^[53], and in the case of patients with a history of beta-lactam allergy, trimethoprim is used^[54].

Antibiotic resistance in *Listeria*

Several studies among *Listeria* isolated from clinical strains reveal the incidence of antibiotic resistance among this group. Some of the reports on incidence of drug-resistant *Listeria* include isolation of fluoroquinolone-resistant bacteria from human cases of listeriosis in France^[55], isolation of chloramphenicol, erythromycin, streptomycin, and tetracycline resistant *Listeria* from clinical isolates^[56], and a report on high prevalence of clindamycin-resistant *Listeria* from clinical isolates from cancer patients^[57].

Shigella

Shigella is a gram-negative bacterial pathogen causing bacillary dysentery. An approximate of 500,000 cases of diarrhea in the United States is a result of ingestion of food contaminated with *Shigella*^[58].

Pathogenic *Shigella* species:

Shigella sonnei, *Shigella flexneri*, *S. boydii*, and *Shigella dysenteriae* are the three major *Shigella* species that are responsible for bacillary dysentery^[59].

Signs and Symptoms

All the classic symptoms of food poisoning are observed in the case of *Shigella* infection, the most common being dysentery and tenesmus (a

painful sensation to pass stools even when bowels are empty).

Course of infection and drug of choice

The infection usually resolves within a few days of infection and therefore does not require any treatment except for rehydration. In the case of high-risk group (children, gay men, and HIV patients) antibiotic treatment is necessary ^[60-62]. Owing to the high incidence of antibiotic resistance among *Shigella* antibiotics are selected only after conducting an antibiotic sensitivity assay.

Antibiotic resistance in *Shigella*

The condition of drug resistance is so severe in the case of *Shigella*, that CDC declared it as an urgent threat in the United States ^[62]. Several reports are available in literature indicative of alarming emergence of antibiotic resistance ^[63-65].

Factors contributing to emergence of antibiotic resistance

The single most important factor contributing towards a higher incidence of multi-drug resistance is the indiscriminate use of antibiotics ^[66]. This scenario can be observed not only in the health care sector ^[67], but also in livestock rearing and management sector ^[68].

The Darwinian principle of survival of the fittest is applicable to bacterial pathogens as well and when exposed to suboptimal quantities of antibiotics, pathogens that are resistant towards the particular antibiotic becomes the dominant group and multiply rapidly and spread ^[69].

Indiscriminate use of antibiotics by physicians and lack of health literacy by patients are the major issues faced in health care sector. It's indeed an alarming fact that a sizable proportion of physician prescribes antibiotics that are not necessary ^[70]. As explained in this review, in the majority of cases, the infection resolves itself without any medical interventions. Antibiotics are necessary only in case of high-risk cases. Similarly, it is also important to take the antibiotic medicine precisely as per the instructions even after complete recovery. Patients tend to

discontinue the antibiotic course once their symptoms are resolved and this usually leads to a relapse of infection which is no more treatable with the antibiotic that they have taken. Another serious issue is the easy availability of antibiotics as over the counter medicine. Patients take medications as per the instructions of untrained pharma shopkeepers and this practice often lead to unnecessary antibiotic therapy which in turn leads to the development of antibiotic resistance ^[70].

The second contributing factor is the incorporation of antibiotics in feed for farm bred animals as growth promoters and for disease treatment and prevention. Constant exposure to antibiotics automatically put selective pressure on bacterial communities and those who gain resistance, survive and become the dominant species. These pathogens in due course of time may reach the humans and result in infections which are no more treatable with antibiotics ^[71].

Conclusion

Antibiotics can be considered as a “double-edged sword” which when used wisely can be the single most proven and effective weapon to combat bacterial infections; on the other hand, unwise use of antibiotics can lead to the future that is similar to the pre-antibiotic era where people die due to trivial bacterial infections. The proactive measure should be coordinated in the global scale to curb the emergence of multi-drug resistances. Physicians should be thoroughly educated about the after effects of the unnecessary use of antibiotics, proper counseling should also be provided to patients under antibiotic treatment, emphasizing the importance of completing the antibiotic course even after the complete recovery and antibiotics should strictly be made accessible only as prescription medication. In addition to that, federal laws should be implemented to prevent the use of antibiotics as growth promoters in the feed of farm bred animals.

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