Original Articles

USE OF ANTIBIOTICS IN THE POULTRY INDUSTRY IN SAUDI ARABIA: IMPLICATIONS FOR PUBLIC HEALTH

Zaki H. Al-Mustafa, PhD; Mastour S. Al-Ghamdi, PhD

Background: The use of antimicrobial agents in food-producing animals has become an important public health issue due to the spread of microbial resistance. This study was aimed at identifying the antimicrobial agents available for poultry use and highlighting their possible impact on public health.
Materials and Methods: Twenty-three randomly selected poultry farms and all veterinary pharmacies in the Eastern Province of Saudi Arabia were surveyed for the antibiotics used or dispensed. Further, a comprehensive literature survey was performed.
Results: Twenty-nine antimicrobial agents were identified as being available for poultry use, of which 22 (75.9%) were important for the treatment of human infections. Enrofloxacin, oxytetracycline, ampicillin, neomycin, sulphamethoxazole, colistin, doxycycline and erythromycin were the most frequently used drugs. Food-borne hypersensitivity reactions and the emergence of microbial resistance, as well as cross-resistance to the various groups of antibiotics in animals and its transfer to human pathogens, are well documented.
Conclusion: The misuse of antibiotics in the local poultry industry poses a serious health risk to the public and may complicate the treatment of human infections. The veterinary use of antimicrobial agents, especially those with dual animal and human applications, should therefore be restricted. The establishment of a government department concerned with food and drug safety is also highly recommended.
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Key Words: Antibiotics, bacterial resistance, poultry, public health.

The use of antimicrobial agents in food-producing animals has recently become a very important public health issue. These agents are being increasingly used for the prevention and therapy of infectious disease in farm animals raised under intensive husbandry methods of production.[1] In addition, they are routinely added at subtherapeutic levels to animal feed for their growth-promoting properties.[2] These practices, however, carry many negative effects, including the stimulation of microbial resistance to antibiotics, with the possible transfer of resistant pathogens from animals to humans.[3,4] Furthermore, the presence of drug residues in animal products may pose a potential health risk to the public.[5]

In previous studies,[6,7] lack of adherence by the local poultry producers to international guidelines for the use of antimicrobial agents recommended by organizations such as the World Health Organization (WHO), Food and Agriculture Organization (FAO), Veterinary Medicines Directorate (VMD) of the European Union, as well as Food and Drug Administration (FDA) of the US was observed. This study was, therefore, aimed at surveying the antimicrobial agents available for poultry use in the Eastern Province of Saudi Arabia, and highlighting their possible impact on public health.

From the Department of Pharmacology, College of Medicine, King Faisal University, Dammam, Saudi Arabia.
Address reprint requests and correspondence to Dr. Al-Mustafa: Department of Pharmacology, College of Medicine, King Faisal University, P.O. Box 2114, Dammam 31451, Saudi Arabia.
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Materials and Methods

A survey of 23 randomly selected poultry farms in the Eastern Province of Saudi Arabia (16 in Al-Ahsa and 7 in Dammam) and all veterinary pharmacies in the area (9 in Al-Ahsa and 7 in Dammam) was conducted. Information about the antimicrobial drugs used in each farm was gathered from farm supervisors using a detailed questionnaire. In addition, veterinary pharmacists were asked to list the most commonly dispensed antimicrobial agents from their pharmacies in descending order of preference. Also, online searches for reports of food allergy due to antibiotic residues, as well as food-transmitted pathogenic organisms and their resistance to antimicrobial agents, were conducted.

Results

Twenty-nine antimicrobial agents were found to be available for poultry use in the Eastern Province of Saudi Arabia (Table 1). Only seven agents (24.1%) (enrofloxacin, tylosin, kitassamycin, spiramycin, flumequin, furaltadone and furazolidone) were of specific use as veterinary drugs, while the remaining 22 agents (75.9%) were also used for the treatment of human infections (Table 1). Some agents were also available in combined preparations. They included lincomycin and spectinomycin (Lincospectin), oxytetracycline and neomycin (Neooxyne, Neoterramycin), trimethoprim and sulphamethoxazole (Septrin), trimethoprim and colistin (TSC), penicillin and streptomycin (Penstrept). Most of the drugs were available in powder form to be dissolved in drinking water. In addition, injection and solution forms were also available (Table 1).

Enrofloxacin was found to be the most frequently used drug in Al-Ahsa, followed by oxytetracycline, ampicillin, neomycin, sulphamethoxazole and colistin. In Dammam, however, colistin was the most frequently used drug, followed by enrofloxacin, erythromycin and doxycycline (Table 2).

Enrofloxacin and oxytetracycline were the most commonly dispensed drugs in both Al-Ahsa and Dammam regions, as indicated by veterinary pharmacists (Table 2).

TABLE 1. *Antimicrobial agents available for poultry use in the Eastern Province of Saudi Arabia.*

Drug	Dosage form		
	Powder	Injection	Solution
Amoxicillin	+	+	–
Ampicillin	+	+	–
Chlortetracycline	+	+	–
Ciprofloxacin	+	+	+
Colistin†	+	+	–
Doxycycline	+	+	–
Enrofloxacin*	+	+	–
Erythromycin	+	–	–
Flumequin*	+	+	+
Furaltadone*	+	–	–
Furazolidone*	+	–	–
Gentamicin	+	+	–
Kanamicin	–	+	–
Kitassamycin*	+	–	–
Lincomycin‡	+	+	–
Nalidixic acid	+	+	–
Neomycin++	+	+	–
Norfloxacin	+	+	+
Oxacillin	+	–	–
Oxytetracycline++	+	+	+
Pefloxacin	+	+	–
Penicillin#	+	+	–
Spectinomycin‡	+	+	–
Spiramycin*	+	+	–
Streptomycin#	+	+	+
Sulfamethoxazole	+	+	+
Tetracycline	+	+	+
Trimethoprim†**	+	+	+
Tylosin*	+	+	+

*Animal use only; + =available; – =not available; **trimethoprim: available in combination with colistin in powder form; ++oxytetracycline: available in combination with neomycin in powder form; ‡lincomycin available in combination with spectinomycin in powder form; †trimethoprim: available in combination with colistin in powder form; #penicillin: available in combination with streptomycin in injection form.

Discussion

Animal exposure to antimicrobial agents may stimulate the emergence of microbial resistance, which might possibly be transferred to human pathogens.[4] In addition, animals might act as a possible source of resistant pathogenic organisms that contaminate humans.[8,9] Furthermore, human exposure to animal products containing significant levels of antibiotic residues may provoke immunological responses in susceptible individuals and cause disorders of intestinal flora.[10]

In the present study, the 29 antimicrobial agents available for poultry were mostly employed for prophylactic or nutritional purposes rather than therapy of infectious disease. Twenty-two (75.9%) of the available antimicrobial agents were noted to be of dual use for both animals and humans, with many being highly important in the treatment of human infections (Table 1).

The fluoroquinolones are relatively new, highly effective therapeutic agents in humans. However, there has been increasing concern over their use in food animals because of the steady rise in microbial resistance observed in both animal and human isolates.[7,10] In this study, enrofloxacin was found to be the most commonly used agent in both studied areas despite the fact that this drug is not recommended for use as a growth promoter or as a prophylactic, since it may cause joint lesions in growing animals.[11] Although enrofloxacin is approved only for veterinary use, its main metabolite, ciprofloxacin, is an important drug for the treatment of human infections. Exposure to one quinolone may stimulate the emergence of cross-resistance to other quinolones, or even to the structurally unrelated aminoglycosides.[10,12]

Tetracyclines, especially oxytetracycline and doxycycline, were found to be among the most commonly used antimicrobials. They are extensively used in poultry feed for growth promotion[2] and for controlling serious *Mycoplasma gallisepticum* infections.[13] Concomitant use of more than one tetracycline drug was previously found to be common practice in poultry farms in both investigated regions.[6] This practice is not only clinically unjustifiable, as these drugs share the same mechanism of action and cover the same microbial spectrum, but may also contribute significantly to the development of resistance to the drugs.

TABLE 2. *The most commonly used and dispensed antimicrobial agents in Al-Ahsa and Dammam regions according to farm supervisors and veterinary pharmacists, respectively. Drugs are listed in descending order of preference.*

Poultry farms supervisors' response		Veterinary pharmacists' response	
Al-Ahsa (n=16)	Dammam (n=7)	Al-Ahsa (n=9)	Dammam (n=7)
Enrofloxacin	Colistin	Enrofloxacin	Enrofloxacin
Oxytetracycline	Enrofloxacin	Oxytetracycline	Oxytetracycline
Ampicillin	Erythromycin	Spectinomycin	Colistin
Neomycin	Doxycycline	Lincomycin	Doxycycline
Spectinomycin	Furazolidone	Neomycin	Neomycin
Sulfamethoxazole	Neomycin	Eryhtromycin	Sulfamethoxazole
Colistin	Lincomycin	Tylosin	Trimethoprim
Amoxicillin	Gentamicin	Ciprofloxacin	Amoxicillin
Doxycycline	Oxytetracycline	Colistin	Furaltadone
Trimethoprim	Norfloxacin	Sulfamethoxazole	Gentamicin
Gentamicin	Spectinomycin	Trimethoprim	Spectinomycin
Norfloxacin	Flumequin	Amoxicillin	Lincomycin
Lincomycin	Furaltadone	Furaltadone	–
Erythromycin	Trimethoprim	–	–
Furaltadone	Amoxicillin	–	–
Furazolidone	Tetracycline	–	–
Tylosin	Sulfamethoxazole	–	–
Spiramycin	Ampicillin	–	–
Penicillin	Penicillin	–	–
–	Kitassamycin	–	–
–	Spiramycin	–	–
–	Tylosin	–	–

Spectinomycin is structurally related to aminoglycosides and used by veterinarians as a broad-spectrum antibiotic against gram-negative bacteria.[11] Both spectinomycin and tetracyclines are widely used in the local poultry industry despite the fact that they are mutually antagonistic, especially when used concurrently.[11] Although spectinomycin has limited applications in humans, veterinary use of the drug was found to be associated with cross-resistance to other antimicrobial agents.[14]

Lincomycin is a lincosamide antibiotic used in poultry for therapy of penicillin G-resistant organisms and anaerobic infections, or for growth promotion.[2] Although this drug is not commonly used in humans, its derivative, clindamycin, is widely employed in the treatment of *Bacteroides fragilis* infections. Resistance to clindamycin, however, has been increasing steadily in recent times.[15]

The macrolide antibiotics, erythromycin and spiramycin, were also widely utilized in both regions as broadspectrum prophylactic and therapeutic antibiotics (Table 2). However, a considerable rise in resistance to macrolides among susceptible organisms such as *Streptococcus pneumoniae*, coupled with cross-resistance to other antibiotics, including clindamycin and tetracycline, has recently been noted.[16]

At least four aminoglycoside drugs were marketed for poultry use in the two investigated regions, with neomycin apparently being the most commonly dispensed drug (Tables 1 and 2). It is used as a growth promoter or prophylactic of enterobacteriaceal infections, as it has poor absorption from the gastrointestinal tract. Aminoglycosides are especially important for the treatment of infections involving gram-negative organisms. In recent years, the incidence of aminoglycoside resistance and cross-resistance has seriously increased.[17] Moreover, aminoglycoside residues in food may also provoke hypersensitivity reactions in susceptible humans.[18]

Colistin (polymyxin E) was among the most commonly used antimicrobial agent in the investigated farms. It may be used to promote growth or to prevent infections caused by gram-negative bacteria, including salmonella.[19] It is an old drug with limited applications in humans because of its potential toxicity. However, there is now renewed interest in the drug, especially as many other agents become redundant due to rising resistance. Colistin is currently recommended for serious nosocomial infections caused by multidrug-resistant gram-negative bacteria, especially *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.[20] However, a tendency for the development of mutual co-resistance to gentamicin and colistin in *E. coli* and *Pseudomonas* strains has been observed.[21]

Penicillin was not as commonly used as enrofloxacin or tetracycline in the two investigated regions. Although penicillin is approved in the US as a feed additive for prophylaxis or growth promotion,[2] its continuous use has been shown to stimulate the emergence of resistant *E. coli* strains in chicks.[22] Moreover, hypersensitivity to penicillin is considered the most common adverse reaction to food-borne drug residues. Penicillin, even at low residue levels, is capable of inducing allergic reactions in a previously sensitized person.[23]

The nitrofuran drugs, furazolidone and furaltadone, were also utilized in both regions, despite the fact that the use of these agents in food-producing animals had been prohibited in many countries, including Saudi Arabia. Furazolidone has very limited applications in humans and may be used as an adjunct in the treatment of some gastrointestinal infections, including multidrug-resistant typhoid fever.[24] More recently, the drug has effectively been employed in multidrug regimen for the eradication of *Helicobacter pylori*.[25]

It is concluded that there is widespread misuse of antibiotics in the local poultry industry. This poses a serious health risk to the public and may complicate the treatment of human infections by stimulating the emergence of microbial resistance. We therefore recommend that the veterinary use of antimicrobial agents, especially those with dual animal and human applications, be restricted. In addition, regular monitoring of bacterial resistance to antimicrobial drugs in both animals and humans is needed. The information should be made available in a national database in order to help health professionals optimize the use of antimicrobial agents. This would necessitate the establishment of a department concerned with food and drug safety.

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