

Drug residues in broiler chickens fed with antibiotics in ration

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ABSTRACT

Daily oral administration of two dose levels of 1 and 2 mg/kg body mass of ampicillin (groups A1 and A2), 50 and 100 mg/kg body weight of oxytetracycline (groups O1 and O2) and 50 and 100 mg/kg body mass sulphadimidine (groups S1 and S2), in broiler feed resulted in an immediate increase in concentrations of antibiotics in plasma and tissues from day 1 until day 40 of the treatment. At day 40 a range of 0.61 to 1.94, 0.24 to 2.25, 1.30 to 6.70 µg/g or µg/ml of A, O and S, respectively was found in tissues or plasma. Withdrawal of medicated feed resulted in a rapid decline in tissue concentration parallel to that of plasma, and withdrawal times were 5 days for (O) and (S) and 6 days for (A).

Key words: antibiotics, residues, broiler, chicken.

Introduction

Administration of drugs to food-producing animals requires not only consideration of effects on the animal but also the effects on humans who ingest food from these animals. In short, after food-producing animals have been exposed to drugs in order to cure or prevent disease or to promote growth, the effects of the residues of such treatment may have on humans should be known. These residues consist of the parent

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compound or compounds derived from the parent drug (or both) including metabolites, and residues bound to macromolecules (WEBER, 1979). Concern has been expressed about possible harmful effects on humans through the use of drugs, as follows: (1) increased microbial drug resistance, (2) drug residues in food, (3) allergic reactions and sensitisation to antimicrobials, and (4) drug toxicity (BLACK, 1984).

In the Saudi poultry industry, birds are frequently raised in conditions where there is high level of stress and where different types of antibiotics are used. This might result in drug residues in meat of chicken. This study was conducted to investigate residue concentration after feeding different levels of antibiotics to chickens and to determine their withdrawal times under Saudi conditions.

Materials and methods

A description of experimental protocol is presented in Table 1. Five hundred one-day-old broiler chicks (Lohman) were obtained from a local hatchery in Al-Ahsa and moved to the poultry unit of King Faisal University. On arrival to the unit the chicks were divided into a control group comprising 50 chicks and six experimental groups each of 75 chicks. The control group received an antibiotic-free diet, while in the experimental groups ampicillin(A), oxytetracycline (O) and

Table 1. Drugs added to broiler chicks diet during the course of experiment

Group (N)	Name of drug	Manufacturer	Dose per kg body mass
C (50)	control	-	-
A1 (75)	Ampicillin	Beecham, The Netherlands	1 mg
A2 (75)	Ampicillin	Beecham, The Netherlands	2 mg
O1 (75)	Oxytetracycline	Terramycine Poultry Formula, Pfizer, USA Batch No. POC1-51310	50 mg
O2 (75)	Oxytetracycline	Terramycine Poultry Formula, Pfizer, USA Batch No. POC1-51310	100 mg
S1 (75)	Sulphadimidine	Sigma, England	50 mg
S2 (75)	Sulphadimidine	Sigma, England	100 mg

sulphadimidine(S) were added to the diet at different rates as shown in Table 1. All chicks were fed *ad libitum* on the same diet up to 40 days of age. Four birds from each group were slaughtered 1, 2, 3, 4, 5, 10, 20 and 40 days during treatment, and 1, 2, 3, 4, 5 and 6 days after withdrawal of

treatment. Blood from plasma, liver, kidney and breast muscle were collected for estimation of antibiotic residues by microbiological methods previously validated and described (NOUWS et al., 1982, 1985).

Data were expanded as means \pm SD. Analysis of variance was used to test withdrawal time of drugs.

Results

Administration of ampicillin (A), oxytetracycline (O), and sulphadimidine (S), in feed to broiler chicks resulted in an immediate

Table 2. Mean (\pm SD) Ampicillin (A) residues ($\mu\text{g/g}$) in plasma, liver, kidney and breast muscle of chicken given antibiotic in feed at a dose of 1 or 2 mg/kg body mass

Time in days		Group							
		Plasma*		Liver*		Kidney*		Muscle*	
		A1	A2	A1	A2	A1	A2	A1	A2
During treatment	1	0.50 \pm 0.05	0.62 \pm 0.05	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
	2	1.45 \pm 0.25	1.95 \pm 0.30	0.74 \pm 0.08	0.80 \pm 0.08	0.76 \pm 0.07	0.81 \pm 0.08	0.58 \pm 0.06	0.65 \pm 0.07
	3	1.62 \pm 0.20	2.00 \pm 0.35	0.76 \pm 0.08	0.81 \pm 0.07	0.78 \pm 0.07	0.83 \pm 0.08	0.60 \pm 0.07	0.73 \pm 0.07
	4	1.55 \pm 0.20	1.85 \pm 0.31	0.75 \pm 0.08	0.82 \pm 0.08	0.79 \pm 0.08	0.84 \pm 0.08	0.61 \pm 0.06	0.74 \pm 0.08
	5	1.55 \pm 0.20	1.93 \pm 0.31	0.75 \pm 0.08	0.83 \pm 0.08	0.78 \pm 0.08	0.85 \pm 0.08	0.60 \pm 0.07	0.73 \pm 0.07
	10	1.39 \pm 0.23	1.89 \pm 0.29	0.76 \pm 0.08	0.82 \pm 0.08	0.79 \pm 0.07	0.85 \pm 0.08	0.61 \pm 0.06	0.72 \pm 0.07
	20	1.45 \pm 0.24	1.95 \pm 0.28	0.74 \pm 0.08	0.82 \pm 0.07	0.77 \pm 0.07	0.85 \pm 0.08	0.59 \pm 0.06	0.72 \pm 0.07
	40	1.53 \pm 0.22	1.94 \pm 0.27	0.76 \pm 0.08	0.81 \pm 0.08	0.76 \pm 0.07	0.85 \pm 0.08	0.61 \pm 0.07	0.73 \pm 0.07
After withdrawal of treatment	1	0.76 \pm 0.06	0.83 \pm 0.07	0.56 \pm 0.04	0.61 \pm 0.04	0.55 \pm 0.04	0.63 \pm 0.04	0.45 \pm 0.04	0.50 \pm 0.04
	2	0.24 \pm 0.3	0.29 \pm 0.3	0.24 \pm 0.03	0.29 \pm 0.03	0.25 \pm 0.03	0.31 \pm 0.04	0.20 \pm 0.03	0.22 \pm 0.03
	3	0.12 \pm 0.2	0.16 \pm 0.3	0.16 \pm 0.03	0.19 \pm 0.02	0.18 \pm 0.03	0.20 \pm 0.03	0.16 \pm 0.03	0.18 \pm 0.02
	4	<0.05	<0.05	0.07 \pm 0.02	0.08 \pm 0.02	0.10 \pm 0.03	0.20 \pm 0.03	0.10 \pm 0.03	0.12 \pm 0.03
	5			<0.05	<0.05	<0.05	0.09 \pm 0.02	0.07 \pm 0.02	0.09 \pm 0.02
	6						<0.05	<0.05	<0.01

*Values represent average from 4 birds at each sacrifice interval

increase in concentration of antibiotics in plasma from the first day of treatment onwards (Tables 2, 3 and 4) and in liver, kidney and breast muscle from the second day of treatment onwards. Concentration of antibiotics in plasma and tissues was constant and correlated well with the dose level. The highest concentrations of antibiotics were found in plasma, followed by kidney and liver, and the lowest levels in breast muscles. At day 40 of treatment a range of 0.61 to 1.94, 0.24 to 2.25, 1.30 to 6.70 $\mu\text{g/g}$

Table 3. Mean (\pm SD) Oxytetracycline (O) residues ($\mu\text{g/g}$) in plasma, liver, kidney and breast muscle of chicken given antibiotic in feed at a dose of 50 or 100 mg/kg body mass

Time in days		Group							
		Plasma*		Liver*		Kidney*		Muscle*	
		O1	O2	O1	O2	O1	O2	O1	O2
During treatment	1	1.65 \pm 0.15	2.10 \pm 0.05	<0.08	<0.08	<0.08	<0.08	<0.08	<0.08
	2	1.75 \pm 0.15	2.25 \pm 0.15	0.62 \pm 0.07	0.71 \pm 0.07	0.65 \pm 0.07	0.72 \pm 0.07	0.22 \pm 0.06	0.45 \pm 0.07
	3	1.60 \pm 0.20	2.05 \pm 0.15	0.59 \pm 0.06	0.70 \pm 0.07	0.67 \pm 0.07	0.73 \pm 0.07	0.28 \pm 0.07	0.50 \pm 0.07
	4	1.70 \pm 0.10	1.95 \pm 0.10	0.61 \pm 0.06	0.68 \pm 0.07	0.66 \pm 0.07	0.71 \pm 0.08	0.26 \pm 0.05	0.55 \pm 0.07
	5	1.74 \pm 0.10	1.85 \pm 0.15	0.60 \pm 0.07	0.67 \pm 0.07	0.65 \pm 0.07	0.75 \pm 0.07	0.27 \pm 0.05	0.52 \pm 0.06
	10	1.69 \pm 0.15	2.15 \pm 0.10	0.62 \pm 0.07	0.69 \pm 0.07	0.66 \pm 0.07	0.74 \pm 0.07	0.28 \pm 0.05	0.52 \pm 0.06
	20	1.68 \pm 0.15	2.15 \pm 0.10	0.62 \pm 0.07	0.67 \pm 0.07	0.65 \pm 0.07	0.73 \pm 0.07	0.26 \pm 0.05	0.55 \pm 0.06
	40	1.66 \pm 0.15	2.05 \pm 0.15	0.63 \pm 0.07	0.68 \pm 0.07	0.64 \pm 0.07	0.75 \pm 0.07	0.24 \pm 0.05	0.52 \pm 0.06
After with-drawal of treatment	1	0.53 \pm 0.06	0.65 \pm 0.06	0.41 \pm 0.06	0.51 \pm 0.06	0.42 \pm 0.04	0.56 \pm 0.06	0.20 \pm 0.04	0.39 \pm 0.06
	2	0.24 \pm 0.3	0.29 \pm 0.3	0.34 \pm 0.05	0.37 \pm 0.05	0.33 \pm 0.03	0.39 \pm 0.04	0.18 \pm 0.04	0.24 \pm 0.04
	3	<0.08	<0.08	0.12 \pm 0.02	0.14 \pm 0.02	0.11 \pm 0.02	0.15 \pm 0.03	0.12 \pm 0.02	0.18 \pm 0.04
	4			<0.08	<0.08	<0.08	<0.08	0.09 \pm 0.01	0.12 \pm 0.03
	5							<0.08	<0.08

*Values represent average from 4 birds at each sacrifice interval

or $\mu\text{g/ml}$ of A, O and S, respectively was found in tissues or plasma. Concentrations of antibiotics in plasma and tissue of control birds (untreated) were below the detection limit of the assays.

One day after withdrawal of medicated feed the concentrations of antibiotics fell significantly ($P<0.001$) in plasma and tissues. Drug

Table 4. Mean (\pm SD) Sulphadimidine (S) residues ($\mu\text{g/g}$) in plasma, liver, kidney and breast muscle of chicken given antibiotic in feed at a dose of 50 or 100 mg/kg body mass

Time in days		Group							
		Plasma*		Liver*		Kidney*		Muscle*	
		S1	S2	S1	S2	S1	S2	S1	S2
During treatment	1	4.95 \pm 0.45	6.2 \pm 0.50	<0.03	<0.03	<0.03	<0.03	<0.03	<0.03
	2	5.60 \pm 0.45	6.5 \pm 0.50	2.10 \pm 0.15	2.85 \pm 0.20	2.25 \pm 0.25	3.20 \pm 0.20	1.30 \pm 0.08	1.90 \pm 0.08
	3	5.35 \pm 0.40	6.6 \pm 0.50	2.10 \pm 0.15	2.90 \pm 0.20	2.30 \pm 0.25	3.10 \pm 0.25	1.45 \pm 0.08	1.85 \pm 0.10
	4	5.45 \pm 0.40	6.7 \pm 0.45	2.20 \pm 0.15	2.85 \pm 0.02	2.35 \pm 0.20	3.25 \pm 0.25	1.40 \pm 0.08	1.80 \pm 0.10
	5	5.30 \pm 0.40	6.6 \pm 0.50	2.16 \pm 0.20	3.10 \pm 0.25	2.40 \pm 0.20	3.25 \pm 0.25	1.45 \pm 0.08	1.85 \pm 0.10
	10	5.35 \pm 0.40	6.5 \pm 0.50	2.12 \pm 0.20	3.10 \pm 0.20	2.30 \pm 0.20	3.30 \pm 0.25	1.50 \pm 0.08	1.93 \pm 0.09
	20	5.25 \pm	6.6 \pm 0.50	2.15 \pm 0.15	2.95 \pm 0.20	2.35 \pm 0.20	3.25 \pm 0.25	1.35 \pm 0.08	1.95 \pm 0.9
	40	5.20 \pm 0.45	6.7 \pm 0.50	2.13 \pm 0.15	2.90 \pm 0.20	2.30 \pm 0.20	3.20 \pm 0.20	1.55 \pm 0.08	1.83 \pm 0.08
After withdrawal of treatment	1	1.39 \pm 0.08	1.60 \pm 0.08	0.95 \pm 0.07	0.05 \pm 0.01	0.98 \pm 0.07	1.15 \pm 0.01	0.75 \pm 0.07	0.85 \pm 0.07
	2	0.18 \pm 0.06	1.21 \pm 0.6	0.50 \pm 0.06	0.65 \pm 0.05	0.55 \pm 0.06	0.70 \pm 0.07	0.40 \pm 0.05	0.50 \pm 0.05
	3	<0.03	<0.03	0.14 \pm 0.02	0.16 \pm 0.03	0.14 \pm 0.02	0.17 \pm 0.04	0.18 \pm 0.04	0.30 \pm 0.03
	4			<0.03	<0.03	<0.03	<0.03	0.08 \pm 0.01	0.10 \pm 0.01
	5							<0.03	<0.03

*Values represent average from 4 birds at each sacrifice interval

concentrations reached about maximal residue level (MRL) in plasma and tissues as follows: for A in plasma on day 4, liver and kidney on day 5, and muscle on day 6; for O in plasma on day 3, liver and kidney on day 4 and muscle on day 5; for S in plasma on day 3, liver and kidney on day 4, and muscle on day 5.

Discussion

This study shows that antibiotics given in feed to chicken attained a level of more than 1 $\mu\text{g/ml}$ in plasma 24 hours after offering medicated feed; levels in tissues are less than that in plasma and occurred 2-3 days later. It is clear that antibiotics achieved high tissue penetrating ability (BAGGOT, 1977). These results corroborate the results of earlier investigations which show that A, O and S are rapidly absorbed from the gastrointestinal tract of chicken (GOREN et al., 1981; ROUDAUT et al., 1987; RAMADAN et al., 1992). However, factors such as the physicochemical properties of the drug, presence of bivalent ions in the gut and nutritional sources may affect absorption from the digestive tract of chicken (HINZ et al., 1972; GILMAN et al., 1991). Some studies reported lower tissue levels (MEREDITH et al., 1965; BLACK 1977), comparable levels (SWEZEY et al., 1980) or higher levels (PAIGE, 1993) of residues in chicken. These differences may be due to difference in route of drug administration or method of drug detection (HENION, 1988; HORWITZ, 1988). At the dose level used, an MRL of all antibiotics were exceeded from the first or second day until the end of treatment.

Drug withdrawal time is the time required for drug residue to reach a safe concentration for human or animal consumption, defined as MRL (BOOTH, 1982). This parameter is generally based on data derived from healthy animals (TESKE et al., 1972) and established on the basis of drug residue levels in various tissues, e.g. kidney or muscle (MERCER et al., 1977). It is clear from this study that withdrawal times required to reach MRL could be 5 days for oxytetracycline and sulphadimidine and 6 days for ampicillin in chicken.

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SAŽETAK

Tovnim pilićima dnevno je u hrani tijekom 40 dana davan antibiotik ampicilin u količini 1 i 2 mg/kg tjelesna mase (skupine A1 i A2), oksitetraciklin u količini 50 i 100 mg/kg tjelesne mase (skupine O1 i O2), te sulfadimidin također 50 i 100 mg/kg tjelesne mase (skupine S1 i S2). Koncentracija spomenutih antibiotika i sulfadimidina naglo se povećala u plazmi i tkivima pilića već drugi dan nakon davanja, te ostala na povećanoj razini tijekom čitavog razdoblja davanja. Nakon 40. dana davanja, ampicilin je u različitim tkivima ili plazmi dokazan u koncentraciji od 0,61 do 1,94, oksitetraciklin od 0,24 do 2,25 te sulfadimidin od 1,30 do 6,70 g/g ili g/ml. Koncentracija oksitetraciklina i sulfadimidina smanjila se u tkivima i krvi 5., a ampicilina 6. dana nakon prestanka davanja u hrani.

Ključne riječi: antibiotici, rezidue, tovni pilići
