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**EFFECT OF SULFONAMIDE, BAYTRIL AND FLORFENICOL ADMINISTRATION
IN POULTRY WITH COLIBACILLOSIS: A BIOCHEMICAL AND
HEMATOLOGICAL STUDY**

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ABSTRACT

Avian colibacillosis is an infectious disease caused by the bacteria *Escherichia coli* (*E.coli*). It is one of the leading causes of mortality and morbidity associated with economic losses in the industry throughout the world today. Avian colibacillosis can affect all avian species, at all ages and in all types of poultry production (broilers, breeders, layers, turkeys etc.). Economic losses can be due to decreased hatching rates, mortality, lowered production, carcass condemnation at processing and treatment costs. The aim of present study was to compare of biochemical and hematological parameters after administration of sulfonamide, florfenicol and Baytril antibiotics in poultry with colibacillosis. In present study, 6 broiler farms with colibacillosis were selected and drugs were administrated. Sulfonamides were administrated at the dose of 300 cc per 1000 liter drinking water for 4 days and florfenicol was administrated at the dose of 1 L per 1000 liter drinking water for 4 days. Data showed that administration of sulfonamide and florfenicol yield to non-significance decrease in ALP. Also, these drugs decrease blood glucose significantly. As well as, data showed that administration of drugs increase level of uric acid significantly. At the end, total protein and albumin were increased subsequent administration of drugs. Hematological data showed that there is no significant difference among groups in term of eosinophil, hematocrit and hetrophils while lymphocytes and WBS were decreased significantly. As well as, levels of monocytes increased significantly subsequent use of drugs. Data showed that administration of Baytril increased amounts of ALP and Glc and decreased Uric acid but made

no changes on Total protein and albumin values. In hematological assay, there was no different between Baytril and two other antibiotics ($P < 0.05$).

Keywords: Broiler Chickens, Sulfonamides, Florfenicol, Baytril, Colibacillosis, Hematological and Biochemical Parameters

INTRODUCTION

Avian colibacillosis is an infectious disease caused by the bacteria *Escherichia coli* (*E.coli*). It is one of the leading causes of mortality and morbidity associated with economic losses in the industry throughout the world today [1]. Avian colibacillosis can affect all avian species, at all ages and in all types of poultry production (broilers, breeders, layers, turkeys etc.). Economic losses can be due to decreased hatching rates, mortality, lowered production, carcass condemnation at processing and treatment costs.

Although *E.coli* is considered a normal inhabitant of the gut flora, it is capable of acquiring virulence factors to gain the ability of colonizing the internal organs, and producing avian colibacillosis. Virulence factors include the ability to resist phagocytosis (an important immune system mechanism used to remove pathogens and debris), utilization of highly efficient iron acquisition systems, production of colicin toxins, and adherence to respiratory epithelium [2]. Strains capable of this are termed avian pathogenic *E.coli* (APEC).

Multiple serotypes are associated with this disease but most commonly seen are serotypes O1, O2, and O78. The number of published APEC serotypes, however, is increasing. Colibacillosis can cause problems within a flock as either a primary or a secondary pathogen. In birds, contrary to mammals, colibacillosis is usually a localized or systemic disease and not an enteric disease. It commonly causes yolk sac infection, omphalitis, airsacculitis, salpingitis, pericarditis, peritonitis, perihepatitis, arthritis, and septicemia. In broilers, colibacillosis involving the respiratory tract is the most commonly encountered disease at slaughter [1]. It manifests mainly as a respiratory infection with peritonitis and pericarditis. The infection is considered airborne with the air sacs probably being an important port of entry.

In laying hens, *E.coli* infections commonly present as acute or subacute fibrinous salpingitis, oophoritis and peritonitis. These findings are often accompanied by lesions caused by cloacal cannibalism indicating that vent pecking is an

important predisposing factor. Bacterial infections are generally more prevalent in laying hens in litter-based housing systems, including free-range birds, than in caged birds [3].

In young chicks, *E. coli* is a common isolate from birds displaying depression, septicemia, and variable mortality. The navel is often inflamed and swollen and abnormal yolk material with peritonitis may be seen on necropsy. Unabsorbed, infected yolk sacs often result in chicks with reduced weight gain.

Large numbers of *E. coli* are maintained in the poultry house environment through fecal contamination. Initial exposure to pathogenic *E. coli* may occur in the hatchery from infected or contaminated eggs, but systemic infection usually requires predisposing environmental factors or infectious causes. Stress due to other infections, toxins, or nutritional deficiencies compromise the bird's immune system defenses allowing colibacillosis development. Colibacillosis often develops subsequent to infection with other agents such as infectious bursal disease, mycoplasmosis, coccidiosis, Newcastle disease, infectious bronchitis, etc. or secondary to environmental stressors.

Prevention strategies include controlling predisposing infections that suppress the

immune system and improving environmental factors through management of feed, water, temperature, litter, lighting, and ventilation. Optimal brooding conditions are fundamental in reducing the overall impact of colibacillosis. Additionally, birds need to be protected against pathogens that promote infections with APEC. This is possible by using Mycoplasma-free birds, implementing solid control programs for helminthiasis and coccidiosis, and protecting the birds against viral diseases such as IBD by using appropriate vaccinations. Additionally, biosecurity is essential in preventing disease introduction. Suitable housing infrastructure, the correct use of a transition zone (for changing clothes/shoes, and washing hands), and pest control (rodent feces can be source of pathogenic *E. coli*) are all imperative [4]. Careful control of humidity, sanitation, and temperature in the incubator is important for prevention of *E. coli* in young chicks. Only clean eggs without cracks should be set.

The use of antibiotics to treat colibacillosis may be recommended in some cases in accordance with susceptibility testing. Resistance has been a problem with many drugs such as tetracycline, streptomycin, aminoglycosides and sulfa drugs [5]. Resistance to fluoroquinolones was reported within several years of the approval of this

class of drugs for use in poultry. There is concern that genes conferring resistance to extended-spectrum beta-lactams will emerge in avian pathogenic *E. coli* strains and reduce the efficacy of ceftiofur, which is currently used on a limited basis [4].

Baytril is a powerful antibiotic that is effective for a large number of bacterial & mycoplasmal infections, including pasteurellosis, mycoplasmosis, coli-bacillosis, coli-septicaemia and salmonellosis. Baytril is the brand name for Enrofloxacin, which is a powerful bactericidal medicine in the Fluoroquinolone class. CRD is a common problem that has some symptoms that make chickens seem to have a "cold." Birds that get well still become chronic carriers and may have symptoms re-appear during later times of stress. CRD is usually caused by *Mycoplasma Gallisepticum* (MG), *Mycoplasma Synoviae* (MS) and/or Infectious Coryza, though it may be possible for *E. coli*, chronic Infectious Laryngotracheitis (ILT), and other conditions to be involved. Baytril can be very useful in treating many cases of CRD / Air Sacculitis [6].

Sulfonamides are produced by chemical synthesis. They have bacteriostatic activity against a broad spectrum of pathogens. They interfere with RNA and DNA, which are necessary for cell growth and replication.

Sulfonamides, such as trimethoprim, are effective against *Staphylococcus* species, *Streptococcus* species, *Pasteurella*, *Salmonella*, and *E coli* [7, 8].

Florfenicol is a synthetic, fluorinated analogue of chloramphenicol which lacks chloramphenicol's associated human health risk. It has been used in Asia for aquaculture since the 1980's [9]. In early 1996, an injectable formulation of florfenicol was approved for the treatment of bovine respiratory disease in the United States. It has not yet been approved for poultry, and, in fact, an animal feed formulation is not available. Florfenicol is bacteriostatic, and its mechanism of action is similar to that of chloramphenicol [10]. The mechanism of resistance to florfenicol is unknown but is associated with theflo determinant, a highly conserved gene sequence detected in *Salmonella entericaserovar Typhimurium* DT104 [11, 12] and in the fish pathogen *Pasteurellapiscicida* (*Photobacterium damsela*) [13]. The flogene confers resistance to both chloramphenicol and florfenicol [13]. The aim of present study was to compare of biochemical and hematological parameters after administration of sulfonamide, florfenicol and Baytril antibiotics in poultry with colibacillosis.

MATERIALS AND METHODS

In present study, 6 broiler farms with colibacillosis were selected in which vaccination program, nourishment conditions and quality of day old chickens were the same. Animals were fed based on their physiological and culturing demands and were fed with different formulated feed. In farms with colibacillosis, 20 blood samples before and 20 blood samples after administration of drugs were obtained and some biochemical and hematological factors such as total protein, ALP, Uric acid, Albumin, glucose, RBS, heterophils and hematocrit were measured. It must be noted that sulfonamides was administrated in 3 farms with colibacillosis at the dose of 300cc per 1000 liter drinking water for 4 days and florfenicol was administrated in 3 farms with colibacillosis at the dose of 1000cc per 1000 liter drinking water for 4 days. Baytril also was administrated at the dose of 0.25 ml or cc of 10% liquid per day for average 5-lb. chicken.

Data were analyzed using SPSS ver. 18. ANOVA was used to compare groups and Tukey's Post Hoc Test and t-test were used to show accurate difference among groups. $P < 0.05$ considered as significant difference.

RESULTS

Comparison data showed that administration of drugs in chickens with colibacillosis decreases the level of ALP non-significantly. It has been shown that drugs decrease blood glucose significantly in compared to two other groups which no received drugs. Administration of sulfonamides and florfenicol increase levels of uric acid significantly.

As well as, Administration of sulfonamides and florfenicol increase the low levels of serum total protein and albumin in compared to groups. Hematological data showed that Administration of sulfonamides and florfenicol not affects value and number of eosinophil, hematocrit and heterophil while the amounts of RBC and lymphocytes decreased significantly. Also, monocytes were increased significantly subsequent use of sulfonamides and florfenicol.

Data showed that administration of Baytril increased amounts of ALP and Glc and decreased Uric acid but made no changes on Total protein and albumin values. In hematological assay, there was no different between Baytril and two other antibiotics ($P < 0.05$).

Table 1: Comparison Data Obtained From Biochemical Factors

Parameter Group Sample No.	ALP (U/l)					Glucose (mg/dl)					Uric acid (mg/dl)					Total protein (g/dl)					Albumin (g/dl)				
	C	P.t	S	F	B	C	P.t	S	F	B	C	P.t	S	F	B	C	P.t	S	F	B	C	P.t	S	F	B
1	40	180	150	100	200	240	228	141	150	158	4	2.3	5.6	5.6	3.7	3.2	4.7	4	4	3.7	2	2.2	2.5	2.4	2.3
2	60	220	200	123	123	228	157	125	145	145	4.3	2.3	4.3	8.1	12	2.8	3.9	4	4.2	3.7	1.8	2.1	2.5	2.4	2.3
3	70	160	200	165	190	229	155	129	105	137	4.5	2.5	3.1	12	6.8	2.9	3.1	4.4	4.6	3.5	1.9	2.3	2.6	2.7	2.2
4	80	110	170	133	175	229	175	132	136	152	6	2.4	4.6	9	8	3.1	3.1	4.2	4	3.5	2	2	2.4	2.2	2.3
5	90	160	180	125	165	217	170	130	130	140	4	2.3	4	8	7	3	2.6	4	4.4	3.7	2	2.1	2.3	2.5	2.3
6	80	206	-	-	-	200	178	-	-	-	4.3	2.1	-	-	-	3.1	3.1	-	-	-	2	2.2	-	-	-
7	100	220	-	-	-	205	171	-	-	-	4.4	2.1	-	-	-	2.9	3.1	-	-	-	1.8	2.1	-	-	-
8	80	206	-	-	-	147	189	-	-	-	4.5	2.3	-	-	-	2.9	3.6	-	-	-	1.9	1.7	-	-	-
9	70	233	-	-	-	164	210	-	-	-	4.8	2.3	-	-	-	3	3.4	-	-	-	2	2.3	-	-	-
10	60	233	-	-	-	217	192	-	-	-	4.9	2.3	-	-	-	2.9	2.9	-	-	-	1.8	2.1	-	-	-
11	80	220	-	-	-	235	143	-	-	-	4.2	5	-	-	-	3	3.4	-	-	-	2	2.2	-	-	-
12	85	203	-	-	-	200	214	-	-	-	5.2	2.5	-	-	-	3.1	2.6	-	-	-	1.9	2.1	-	-	-
13	90	180	-	-	-	205	200	-	-	-	4.3	2.3	-	-	-	3	3.7	-	-	-	1.9	1.8	-	-	-
14	95	233	-	-	-	211	228	-	-	-	3	2.2	-	-	-	3.1	2.6	-	-	-	2	1.8	-	-	-
15	100	195	-	-	-	205	186	-	-	-	3.3	2.5	-	-	-	3.3	3.1	-	-	-	2.1	2	-	-	-
16	60	204	-	-	-	200	187	-	-	-	3.3	2.4	-	-	-	3.2	3	-	-	-	2.1	2	-	-	-
17	65	190	-	-	-	223	177	-	-	-	2.7	2.3	-	-	-	3.1	3.4	-	-	-	2	1.9	-	-	-
18	68	199	-	-	-	194	182	-	-	-	2.7	2.7	-	-	-	3	3.1	-	-	-	2	2.1	-	-	-
19	70	194	-	-	-	205	195	-	-	-	3.6	2.4	-	-	-	3	3.3	-	-	-	1.9	1.9	-	-	-
20	75	200	-	-	-	211	190	-	-	-	2.9	2.6	-	-	-	3.1	3.2	-	-	-	2	2.1	-	-	-

C: Control Group, P.t: Pretreatment, S: Sulfonamide, F: Florfenicol, B: Baytril

Table 2: Comparison Data Obtained From Hematological Factors

Parameter Group Sample No.	HCT (%)					Eosinophil					Monocyte					Lymphocyte					RBC				
	C	P.t	S	F	B	C	P.t	S	F	B	C	P.t	S	F	B	C	P.t	S	F	B	C	P.t	S	F	B
1	35	30	35	31	30	2	2	3	3	4	2	2	4	3	2	74	56	73	66	68	19000	29000	10500	10800	12900
2	31	25	34	31	35	2	2	2	1	3	1	3	5	2	3	65	62	63	69	66	25000	24000	9600	10900	11600
3	34	31	37	33	33	2	2	2	2	4	3	4	3	3	4	75	60	65	66	64	22500	20000	10000	10600	11300
4	30	20	36	30	31	3	1	3	3	3	3	2	3	4	2	74	67	70	65	66	21000	23000	10100	10700	12000
5	30	32	34	30	33	2	1	2	3	3	2	2	2	4	4	78	65	71	66	68	19500	28800	10200	10800	11800
6	30	25	-	-	-	3	1	-	-	-	2	1	-	-	-	70	63	-	-	-	25000	19500	-	-	-
7	30	25	-	-	-	2	2	-	-	-	2	1	-	-	-	73	60	-	-	-	23000	21000	-	-	-
8	33	21	-	-	-	1	2	-	-	-	3	3	-	-	-	68	56	-	-	-	20000	22500	-	-	-
9	28	30	-	-	-	2	3	-	-	-	3	2	-	-	-	70	64	-	-	-	15000	25000	-	-	-
10	29	30	-	-	-	1	2	-	-	-	3	1	-	-	-	70	65	-	-	-	12000	19000	-	-	-
11	25	30	-	-	-	3	3	-	-	-	4	3	-	-	-	67	59	-	-	-	11000	29000	-	-	-
12	38	24	-	-	-	3	1	-	-	-	1	4	-	-	-	68	61	-	-	-	13000	21000	-	-	-
13	29	24	-	-	-	4	2	-	-	-	4	5	-	-	-	62	54	-	-	-	14000	21500	-	-	-
14	30	25	-	-	-	2	3	-	-	-	3	2	-	-	-	63	63	-	-	-	12000	30000	-	-	-
15	22	25	-	-	-	2	1	-	-	-	5	2	-	-	-	62	66	-	-	-	11500	26000	-	-	-
16	32	25	-	-	-	1	2	-	-	-	2	1	-	-	-	72	68	-	-	-	13000	29000	-	-	-
17	29	23	-	-	-	1	3	-	-	-	2	2	-	-	-	73	67	-	-	-	12000	26000	-	-	-
18	30	23	-	-	-	2	1	-	-	-	2	2	-	-	-	73	67	-	-	-	12700	20000	-	-	-
19	25	26	-	-	-	1	1	-	-	-	1	1	-	-	-	76	70	-	-	-	12000	22000	-	-	-
20	29	28	-	-	-	2	2	-	-	-	1	2	-	-	-	77	65	-	-	-	12200	30000	-	-	-

C: Control Group, P.t: Pretreatment, S: Sulfonamide, F:Florfenicol, B: Baytril

DISCUSSION AND CONCLUSION

Florfenicol is a broad-spectrum bacteriostatic antibacterial that belongs to amphenicol family, with a wide range of activity against different types of Gram-negative and Gram-positive organisms including: *Mannheimiahaemolytica*, *Pasteurellamultocida*, *Haemophilussomnus*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiellapneumoniae*, *Salmonella typhi*, *Shigelladysenteriae* and *Staphylococcus aureus* [14]. In addition, florfenicol is active at lower concentrations than its structural analogs, thiamphenicol and chloramphenicol, against a number of bacterial pathogens and against many chloramphenicol or thiamphenicol-resistant strains [15]. Florfenicol is approved in the European Union for use in cattle, sheep, pigs and chickens.

The efficacy of florfenicol has been demonstrated against many diseases of domestic animals [16]. However, to date, studies on the efficacy of florfenicol using pharmacokinetic/ pharmacodynamic (PK/PD) approaches have not been carried out in poultry. Nevertheless, the pharmacokinetics and bioavailability of florfenicol have been investigated in broiler chickens [17], turkeys [18] and ducks [19]. Most of these studies used the same original preparation of

florfenicol. There is therefore little information available regarding the differences between formulations of florfenicol used in poultry.

Florfenicol has been approved and become a valuable antibacterial in the treatment of serious bacterial infections in farm animals [20]. In poultry, florfenicol is used extensively for the treatment of respiratory and gastrointestinal bacterial infections, administered via drinking water [18]. It has been reported that florfenicol showed greater activity than chloramphenicol and thiamphenicol, especially against *Pasteurella*, *Salmonella*, *E. coli* and *Staphylococcus aureus* [21]. Moreover, Florfenicol has superior pharmacological and pharmacokinetics features over some other antimicrobials used in chicken industry [19]. This drug is characterized by high bioavailability ($F > 80\%$), good tissue penetration and rapid elimination, which are important for the systemic treatment of domestic animals [18].

Several commercial local and international pharmaceutical preparations of florfenicol oral solution are currently available. In this respect, generic pharmaceutical preparations of florfenicol seeking approval to enter the market should demonstrate their ability to achieve C_{max} and AUC values that are

equivalent to that of the original preparation. Inability to maintain high enough concentrations for sufficient periods of time may lead to therapeutic failure and may encourage the proliferation of resistant microorganisms [22].

Sulfonamides are a group of synthetic antibiotics with broad spectrum effects against most Gram positive, Gram negative bacteria and protozoa [7]. They are frequently used in the poultry industry for therapeutic, prophylactic, or growth-promoting purposes. Sulfonamides are also used to treat various types of infections in digestive and respiratory tracts [23].

The widespread use of sulfonamides as a result of their availability and low cost has resulted in considerable increase in resistant bacteria strains for these compounds [24]. Also the extensive application of this antimicrobial agent in chicken production have resulted in residues being detected in poultry products (eggs and meat) when adequate withdrawal periods have not been observed [8]. It is well established that consumption of animal products containing sulphamide residues poses potential human health risks which include hypersensitivity or anaphylactic shock [25], cancer [26, 27] and induction of bacterial resistance to the antimicrobials, amongst other risks.

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