Original Research Article

THE EFFECTS OF PROLONGED CHLORAMPHNICOL ADMINISTRATION ON HEAMATOLOGICAL PARAMETERS AND HISTOPHATOLOGY OF LIVER, KIDNEY, AND SPLEEN IN BROILER CHICKEN

Abstract

Chloramphenicol a broad spectrum antibiotic was tested on broiler birds to evaluate the effect of its prolonged administration on heamatological parameters, identification of histopathological changes on organs (Liver, Spleen and Kidneys) and to determine if prolonged effect has effects on weight gain and mortality rate.

One hundred and twenty day old chicks from Kamadex Ibadan were used for the experiment. The birds were assign to two (2) treatments and control group each replicated in a Complete Randomized Design (CRD), birds in treatment one (1) were administered normal dose of Chloramphenicol (250mg/Kg), while treatment two (2) were on triple dose in medicated water served ad-lib for seven weeks, while the control were served with un-medicated water ad-lib. Samples (blood, liver, kidney and spleen) were collected and analyzed after 8 weeks of the experiment.

Birds showed significant variations in heamatological values across treatments. Lymphocysts count: treatment two (2) was higher than the treatment one (1) whereas that of control was found to be less, compared to those of treatment 1 and 2. A lower value was observed in weight gain with birds on medicated water with triple dose chloramphenicol. The liver of birds on medicated water with normal and triple dose chloramphenicol were significantly larger than those on control. High mortality was recorded in birds on triples dosed medicated water compared to those in the normal dose and control.

The histopathological pictures of the liver, kidney and the Spleen depict a varying degree of necrosis and hemorrhagic foci on all the organs.

INTRODUCTION

Poultry are several species of birds read or hunted for several purposes mostly importantly for food and other uses. Poultry means domestic fowls, ducks, geese and certain other avian species,

which are kept throughout the world. Poultry and in particular chickens is commonly kept by 90–95% of the households in the rural areas. The number usually ranges from 2 to 5 hens per family unit. The purpose of raising chickens is to provide protein for the family and sale for cash income. Chickens raising is very popular among rural people because of the small investment and short time to income. However, chickens raising faces many problems and farmers rarely get the benefit that they expect. The constraints of chicken production are diseases, feed and feeding and husbandry practices. In fact, it is believed that if vaccination is applied against the common diseases (Newcastle, Infectious bursitis, Fowl typhoid, Fowl cholera and etc), farmers could benefit from 60–70% of the total chickens hatched in comparison to 20–30% without interventions.

Chickens can provide a good source of income to the rural villagers, particularly the poorest families with limited resources like land and capital. Women - and they constitute more than 50% of the total adult population - have direct benefit from chicken raising as they are working mainly at home. According to interviews with farmers at the Special Program for Food Security (SPFS) pilot sites, the income from chickens enables them to buy most of the materials needed for children to go to school. At the same time, chickens also provide protein for the family and high value food at occasional festivities, Khiew Borin, (1998).

Oluyemi and Robert (2000) classified poultry industry into two (2) main branches, namely; eggs and table meat production. The other branch includes; production of Chicks, point of lay pullets or already laying birds and of poultry feeds; the manufacturing of poultry for food.

Eggs are also used in various food industries like the manufacturing of confectionary. They are also used for producing cosmetics and vaccines, while feathers may be used for making pillows.

Some species of poultry are suitable for genetics, nutrition and physiological studies because of their relatively low cost of maintenance prolificacy and short generation intervals.

Despite all these silent contributions, poultry like any other livestock is confronted with the problem of disease thus; hindering profitable poultry production, which bring huge lose to the poultry farmers. Poultry just like Dogs and Cats may become ill from many causes. There are few categories of disease that commonly occur in small poultry flocks. These include external and internal parasites, respiratory diseases, nutritional problems, reproductive diseases, Bacteria (e.g fowl typhoid, Salmonella), fungal (e.g Aspergillosis), viral (e.g Gamboro, new castle and e.t.c) and protozoan (e.g coccidiosis) disease (Donely, 2001). On other hand, Salmonella infection caused by a variety of salmonella species as one the most important bacterial diseases in poultry causing heavy economic losses through mortality and reduced productivity (Haider, *et al*.; 2004). Avian salmonellosis infection may occur in poultry as either acute or chronic form by one or more member of genus *salmonella* under the family *Enterobacteriaceae* (Hofsad, *et al*.; 1992). Besides motile Salmonella (paratyphoid group) infection cause salmonellosis in chicken and have zoonotic significancedisease of poultry are of significance because of their zoonotic nature (e.g certain Salmonella infections, Chlamydiosis and Erysipelas caused by E. insidiosa

Avian *salmonella* infections are important as both a cause of clinical disease and as a source of food-borne disease to humans. Under the family of *Enterobacteriaceae*, the genus of *salmonella* is a facultative intracellular pathogen causing localized or systemic infections as well as chronic asymptomatic carrier state (Shivaprashad, *et al*.; 1997). The etiological agent of fowl typhoid and pullorum disease is salmonella enterica subsp. Enterica serovar Gallinarum, which is divided into two distict biovars under the serogroup D1,Gallinarum and pullorum, which are denoted as S. *gallinarum* and S. *pullorum*, respectively Shivaprashad, *et al*.; 1997 and Manie *et al.;* 1998). In

addition to S. *gallinarum-pullorum*, other salmonellae such as S. *enteritidis*, S. panama and S. Dublin also belong to the sero group D1 (Manie *et al.;* 1998). The various motile and non host adaptive highly invasive serotypes such as *salmonella enteritidis* and*salmonella typhimurium* are commonly referred to as paratyphoid salmonellae (Gast, 1998). Age wise prevalence of avian salmonellosis showed highest infection rate in adult layers (53.25%) in comparison to brooding (14.55%), growing (16.10%) and pullet (16.10%) chicken (Rahman *et al*.; 2004)

Although more than 2,300 serotypes of *salmonella* have been identified, only about 10% of these have been isolated from poultry (Gast, 1998), Chickens are the natural hosts for the highly host adapted biovar S. *gallinarum* and S. pullorum , but natural outbreaks have also been reported in turkeys, guinea fowl quail and pheasants (Shivaprashad, *et al*.; 1997). Salmonella strains of avian origin are also often resistant to various antimicrobials approved for use in poultry medications including; tetracycline (Poppe, *et al*.; 1995 and Parveen, *et al.;* 2007), oxytetracycline (Sharma and Katock 1996), penicillin (Rahman *et al*.; 2004), aminoglycosides(Berrang *et al*.; 2006), suifisoxazole (Parveen, *et al.;* 2007) and fluoroquinolones (Herikstad et al,; 1997). On the other hand, Manie *et al.*, 1998, found several strains of multiple antibiotic-resistant *salmonella* strains in chicken

Among the drugs used to treat these conditions are Furazolisone, gentamycin sulfate, and sulfa drugs (Sulfadimethoxine, sulfamethaxine and sulfamerazane)

Frank *et al*.; 2017 reported that; Chlorampenicol is a broad spectrum antibiotic whose spectrum includes several gram positive and gram negative bacteria, spirochetes and Rikettsiae.

Chloramphenicol is a bacteriostatic antimicrobial originally derieved from the bacterium Streptomyces venezuelae, isolated by David Gortlieb, in 1947 and introduced into clinical practice in 1949, Guang-Zhong Wu and Wanda; 1992.

Chloramphenicol

An antibiotic first isolated from cultures of *Streptomyces venequelae* in 1947 but now produced synthetically. It has a relatively simple structure and was the first broad spectrum antibiotic to be discovered. It is mainly bacteriostatic but may be bactericidal when use in high concentrations or when used against highly susceptible organisms. Chloramphenicol is effective against a wide range of microorganisms. It acts by stopping bacterial growth by binding to the bacteria ribosome there by blocking (peptidyl tranferase) and inhibiting protein synthesis (Guang-Zhong Wu and Wanda; 1992). Chloramphenicol is lipid soluble, allowing it to diffuse through the bacterial cell membrane. It then reversibly binds to the L16 protein of the 50S subunit of bacterial ribosome, where transfer of amino acids to growing peptide chains is prevented (perhaps by suppression of peptidyl tranferase activity), thus inhibiting peptide bond formation and subsequent protein synthesis, (Guang-Zhong Wu and Wanda; 1992). Blood and Radostis (1989) reported that chloramphenicol has advantages over other antimicrobial agents. It has a broad spectrum of activity in combination with excellent penetrability into body tissues and its use in large animals has not been associated with any degree of the toxic side activity.

Three common forms are used for systematic therapy depending on the rout of administration, a free base form of chloramphenicol, chloramphenicol palmitate and chloramphenicol succinate other formulations are also available for topical use (Parfit, 1999). Chloramphenicol in animals is well absorbed by both oral and parenteral routes (Plumb 2002). The usual dose of

chloramphenicol is 5mg/kg/day in four divided doses. It is available as 25mg capsule or as a liquid (125mg/5ml) (Parker and Shaw, 1988). Chloramphenicol is metabolized by the liver to chloramphenicol glucoronate (which is active) and the dose must be reduced in liver Impairement. Majority of chloramphenicol is excreted by the kidney as the inactive metabolite, chloramphenicol glucoronate. Only a tiny fraction of the chloramphenicol is excreted by the kidney unchanged (Adam, 1995)

Heamatology profiles

Blood plays an important role in the transportation of nutrients, metabolic waste products and gasses around the body (Zhou *et al*.; 1999). Moreover, blood represents a means of assessing clinical and nutritional health status of animals (Olorade and Longe 2000). Heamatological profiles both in both in human and in animal science is an important index of the physiological state of an individual. The ability to interpret the state of blood profile in normal and diseased conditions is among its primary tasks. The full blood count examines mostly the cellular component of blood whereas biochemical testing focuses on its chemical constituents (Hrubec *et al*.; 2002). It has been shown that data from blood profiles could be exploited in the improvement of chicken (Ladokun *et al*.; 2008). In addition, blood parameters helps greatly in diagnosis of specific poultry hen pathologies and might serve as basic knowledge for studies in immunology and comparative avian pathology (Bonadiman, 2009). Flactuations or varriations in heamo-biochemical profiles have been reported in chickens of the same age and sex and reared under the same conditions but sampled at different times of the day (Azeez *et al*.; 2004). It was observed that there is definite change in the profiles of the blood cells throughout life. Blood picture changes with the advancement in age, certain condition as stress, bacterial infections, viral infections and intoxication

Blood is a combination of plasma and cells that circulate through the entire body. It is a specialized bodily fluid that supplies essential substance around the body such as Sugars, Oxygen and hormones. Plasma makes up to 55 percent of blood content. The other 45 percent consist mainly of red blood and white blood cells and platelets. Each of these has a vital role to play in keeping the blood functioning effectively (Debra, 2017). The blood of the domestic fowl contains erythrocytes, thrombocytes, granulated and agranulated leucocytes suspended in plasma.

MATERIALS AND METHODS

The following materials were employed in order to carry out this experiment:

Materials

1. One hundred and twenty (120) day – old broiler birds (F-from Kamadex)
2. Brooding materials:, wood shavings, lighting material (light bulbs, lanterns, bush lamp and etc), heating materials (Warmers, Stoves and etc), Saw dust, Newspapers and magazines and Ceiling boards.
3. Feeds: Broiler starter (commercial feed vital) was used from day old to four weeks, while broiler finisher was used from five (5) weeks to eight (8) weeks.
4. Drugs: Chloramphenicol 100%, Multivitamin (Vitalyte powder), Anti coccidian (Amprollium) and Antiseptic (Morigad)
5. Vaccines: Infectious bursal disease vaccine (IBDV), Newcastle Disease vaccine Lasota (NDVL)
6. Sample containers: Sample bottles, EDTA bottles, Formalin, Cotton wool, Cold box, Syringe and Needle and Digital scale.

7. Scalpel blades, Scissors, Disposable hand gloves, Forsceps, Collection tray and Polyethane bags.
8. Miscellaneous equipment: Manual and Digital weighing scale, Syringes and needles, Teaspoon, Graduated cup, Bucket, Broom, Chart paper and marker.
9. **Pen**: Three pens were constructed; each pen has a dimension of 6.0 m^2 capable of stocking fourty birds.
10. Feeders and Drinkers: Plastic drinkers (Chick tray) were used to serve feed to the birds from day old to four weeks and were replaced with metal feeders from five weeks of age up to 8 weeks. A plastic drinker of four-liter capacity was used to serve water to the birds

Methods

Study area

The study was conducted at College of agriculture and animal science, Ahmadu Bello University, Mando Road – Kaduna at the students experimental pen located at (11^0, 10^2 07^2 38'E) in the Northen Guinea Savannah Zone of Nigeria.

Treatment and Sample Techniques

The birds were stabilized for seven days using; Enrofloxacin and multivitamin for three (3) and four (4) days respectively, they were fed and watered ad-libitum using broiler starter fed and clean water. They were vaccinated against Gamboro (infectious bursal) disease at seven (7) and twenty one days and Newcastle disease at fourteen (14) and twenty eight days (28) respectively. Anti stress was given after each vaccination. The birds were assigned to two (2) treatments and control each containing twenty (20) birds. Each treatment was replicated; Completely Randomized Design (CRD) was used for the experiment.

T_1 ---------- (i.e 250mg/kg. bdw)

T_2---------- =Triple dose of the drug (i.e 750mg/kg.bdw)

Oral preparation of chloramphenicol (normal dose 250mg capsule) was used as the treatment. The dosage was determined based on body weight, which was obtained by taking the average weight three (3) times weekly. This procedure lasted for eight (8) weeks.

Data Collection and Handling

The weight of the birds were measured on the weekly basis and tabulated. The mortalities were also recorded from each treatment and control as they occurred. At the end of the experiment eight (8) weeks, three (3) birds were randomly picked from each replicate and blood samples were collected using the wing vain and emptied into EDTA (ethyl di-tetra Acetic acid) container/bottles for preservation and the bottles were immediately arranged inside a cold box containing ice parks and cotton wool.

The birds were finally slaughtered and the livers, spleens and kidneys were carefully cut and weighed using a digital scale, portion of each organs were swiftly immersed in a labeled bottle containing 75% concentration of formalin and were also arranged inside the cold box. The samples (blood, livers, spleens, and kidneys) were finally histopathologically analyzed.

RESULT AND DISCUSSION

The results of this experiment are highlighted under the following:

Effects of prolonged chloramphenicol administration on hematological parameters.

Effects of prolonged chloramphenicol administration on weights of various organs.

Effects of prolonged chloramphenicol administration on mortality rate

Effects of prolonged chloramphenicol administration on histopathology of various organs.

Table 1: Effects of Prolonged Chloramphenicol Administration on Heamatological Parameters.

Parameters	**T1**	**T2**	**T3**
PCV	29.2± 0.2	30.4±0.2	31.2±0.5
Hb	7.3±1.2	8.1±0.3	8.4±0.1
RBC	1.9±0.1	2.0±0.1	2.1±0.0
LYMPHOCYTES	26.9 ± 0.5^{b}	28.0 ± 0.6^{a}	25.0 ± 0.4^{b}
MONOCYTES	9.2±0.7	9.4±0.5	8.8±0.3
HETEROPHILS	62.4 ± 0.8^{a}	60.9 ± 1.2^{a}	65.0 ± 0.3^{b}
EOSINOPHILES	1.9±0.7	1.5±0.2	1.3±0.2
BASOPHILS	1.0 ± 0.2^{b}	0.0 ± 0.0^{a}	0.8 ± 0.0^{b}

Note: Mean Values with the same superscript are not significantly different ($P<0.05$) across the same row.

From the above table (1), the PCV value agrees with Ali and Jalal (2004), which falls between 29 – 30.5, while the hemoglobin value is relatively higher between 6 and 8. The RBC value closely related with Ali and Jalal (2004), which falls between 2.0 and 3.0 for the leucocyte components, there is slight differences between the treatments (especially, treatment two (2) and control), which can be seen in lymphocytes, heterophils and basophil values.

Table 2: Effects of Prolonged Chloramphenicol Administration on Weight Gains

	Initial live Weight (Kg)	Final Weight Weight (Kg)	Weight Gain (Kg)
T1	0.13±0.1	1.9±0.1	1.8±0.0

T2	0.13±0.1[b]	1.6±0.1[b]	1.5±0.0
C	0.13±0.1	1.7±0.1	1.6±0.0

Note: Mean Values with the same superscript are not significantly different (P< 0.05) across the same row.

Most of the values obtained are similar to the value of streptomycin (1.65kg) obtained by Taiwo et al., (2003). Also, there were significant differences between the values obtained in the result with treatment two (2) having less weight gain. Treatment one (1) has more weight gain compared to treatment two (2) and control.

Table 3: Effects of Prolonged Chloramphenicol Administration on Weight of Various Organs

ORGANS	T1	T2	C
Liver	43.3±1.0[b]	43.6±0.6[a]	37.1±0.5[b]
Spleen	1.5±0.4	1.6±0.3	1.4±0.1
Kidney	12.7±0.1	13.3±0.1	12.4±0.1

Note: Main Values with the same superscript are not significantly different (P< 0.05) across the same row.

The values obtained above disagrees with the values obtained by Taiwo *et al*., (2003) possibly because they were pullets and the treatment given was *Lablab purpureus* beans. For the liver, the control has lesser values compared to the two (2) treatments whereas, for the spleen, there is significant difference among the treatments and control. The kidney shows significant difference in treatment two (2) only.

Effects of Prolonged Chloramphenicol Administration on Mortality Rate

The mortality rates were as follows; Normal dose had no mortality, triple dose had three (3) mortalities and control had a single mortality.

The triple dose showed a higher significant different mortality across treatments.

Effects of Prolonged Chloramphenicol Administration on Histopathology of Various Organs

The Liver

Based on the histopathological analysis, in treatment one (1), there were areas of coagulation necrosis characterized by varying degrees of karyohexis and pyknosis of hepatocytes. There was moderate congestion of Vessels and few hemorrhagic foci sparsely spread. Also there was disoriented architecture associated with massive hemorrhage where as in other samples there were no microscopic changes seen.

However treatment two (2), on the other hand multiple foci of hemorrhages with sinusoids while some portions are necrotic characterized by karyohexis and different degrees of pyknosis of hepatocytes. Also in one of the samples, there was a marked (severe), hemorrhage within the sinusoids and moderate congestion of vessels and hepatocytes very prominent but normal. Consequently, the control was having vascular congestion and cellular infiltration by mostly mononuclear cells and few heterophils. There was a definite circumscribed area heavily populated by microphages, lymphocytes and perivascular cuffing.

The spleen:

In the treatment one (1), there was no obvious microscopic change except for few foci of hemorrhages, whereas in treatment two (2) there was moderate proliferation of fibrous connective tissues around a blood vessel. The control was having widespread degeneration of connective tissues and marked increase in fibrous connective tissues around a few arteries with

closely parked concentric lamellae of collagen fibre surrounded by fragmented elastic lamellae and deposits of eosinophilic materials in the wall of the vessels – i.e “oion-skining” systemic lupus erythematosus.

The kidney:

In treatment one (1), there was generalized disintegration of tissues architecture characterized by loss of glomeruli and disappearance of renal tubules. There was a marked and diffused area of hemorrhages as well as few patches of coagulation necrosis showing varying degree of karyohexis of the tubular cells.

On the other hand, treatment two (2) depicts picture of foci of necrosis and disruption of capillary loops in the glomerulus as well as shrinking of glomerular material – a turf with swelling of endothelia cells. There was severe tubular damage with vacuolation of most of the epithelia cells and also replacement of epithelia cells by flattened cells – segmented glomerulonephritis.

The control contains few patches of hemorrhages diffusely dispersed and condensation of glomerular materials while there was a sharp area of demarcation in apparently encapsulated reminiscent to coagulation necrosis. There was thinning of tubular wall leading to enlargement of tubules and compaction of interstitial tissue.

CONCLUSION

From the foregoing, it was concluded that chloramphenicol which is a broad spectrum antibiotic has significant effects when overdosed on the hematological parameters and histopathology of visceral organs, so, it should not be overdosed for prolonged period.

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