Some biochemical and histopathological alterations after amikacin treatment in healthy and colisepticemic broiler chickens

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A B S T R A C T

The aim of the present study was to determine the changes in some blood biochemical parameters and the histopathological alterations in both kidney and liver after a 3-day intramuscular injection (IM) of amikacin (10 mg/kg b.wt.) in broiler chickens. Forty-eight broiler chickens were used in that experiment and divided into four groups (each of 12 chickens). Group (1) served as control (non-infected non treated; group (2) infected by *E. coli* and non-treated; group (3) infected by *E. coli* and treated by amikacin and group (4) non infected and treated by amikacin. The results indicated that, *E. coli* infection caused elevation in creatinine, uric acid, total bilirubin, AST, ALT levels and decreases the levels of glucose, total protein and albumin. Amikacin treatment caused alterations in biochemical parameters, there was a tendency toward a rise in serum creatinine, uric acid, glucose, AST, ALT and total bilirubin levels. Also, amikacin induced decreases in serum total protein and albumin concentrations. Histopathological changes were observed in kidney and liver of chickens and these changes returned towards normal after 21 days. On conclusion; amikacin altered the biochemical values and made some histopathological changes after its use at therapeutic dose for 3 consecutive days in broiler chickens. Since amikacin was used for treatment of infections that also cause changes in some blood biochemical parameters, if the physician or veterinarian does not take into account the possible alterations caused by aminoglycosides (amikacin), an improper medication could be administered.

Keywords: Amikacin, Biochemical, Histopathological, Alterations, Chickens.

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1. INTRODUCTION

Escherichia coli (*E. coli*) is a member of Gram negative bacteria. Avian pathogenic *E. coli* (APEC) frequently infects broiler chickens inducing severe diseased conditions with great economic losses (Chansiripornchai and Sasipreeyajan, 2002). All ages of poultry are susceptible to APEC infection, however, the birds are mostly infected at 4-5 weeks old (Chansiripornchai et al., 1995). *E. coli* infection (colibacillosis) is considered one of the most serious problems responsible for economic losses to poultry industry. It includes several forms of infections as colisepticaemia, air sac disease, peritonitis, salpingitis, synovitis, omphalitis, coligranuloma and enteritis (Calnek et al., 1997). Administration of antibiotics is the most common and fast way for treating of APEC infection in broiler chickens, but the major problem associated with the treatment is the development of drug resistant strains to the most commonly used drugs (Vandemaele et al., 2002). Hence, it's necessary to search for new therapeutic agents to control this infection and to define the most effective route of administration.

Aminoglycosides have long been touted as beneficial antibiotics in preventing Gram-negative infections. Despite all their beneficial effects, such as high antibacterial efficacy, rapid onset of action, low rate of true resistance, and low cost (Begg and Barclay, 1995). Amikacin, an aminoglycoside antibiotic, is recommended in the treatment of several bacterial infections such as *Escherichia coli, Klebsiella, Enterobacter, Staphylococcus aureus, Proteus mirabilis, Serratia, Mycobacterium, Corynebacterium equi, Streptococcus zooepidermicus* and *Actinobacillus* in various animal species (Huber, 1984). Aminoglycosides have considerable nephrotoxic side effects that have been documented in numerous species of experimental animals (Ibrahim et al., 1994; Klein et al., 1992). One mechanism of this toxicity from aminoglycosides

is believed to involve the generation of reactive oxygen radical species; these agents likely account for the pathophysiology of aminoglycoside-induced nephrotoxicity (Naidu et al., 2000; Parlakpinar et al., 2005).

The aim of the current study was to investigate, the effect of amikacin on some biochemical parameters and histopathological changes in both kidney and liver following IM injection once daily for 3 consecutive days in healthy and colisepticemic broiler chickens.

2. MATERIALS AND METHODS

2.1. Drug (Amikacin :

Amikacin (Amigasol®), as injectable solution containing amikacin sulphate at a concentration of 250 mg/ml. It was manufactured by (ATCO Pharma Trading Co.), Egypt.

2.2. Experimental chickens:

Forty eight clinically healthy Hubbard chickens of 3 weeks of age weighing about 600 to 800 g each chosen randomly from Qaliobiya poultry farm were used in this investigation. Chicken were fed on a balanced ration free from antibiotics. Chickens were divided into four groups (each of 12 chickens). Group (1) served as control (non infected non treated; group (2) infected by *E. coli* and non-treated; group (3) infected by *E. coli* and treated by amikacin once daily for 3 days and group (4) non infected and treated by amikacin (IM injection of 10 mg/kg b.wt. of amikacin once daily for 3 consecutive days). The experiment was performed in accordance with the guidelines set by the Ethical Committee of Faculty of Veterinary Medicine, Benha University, Egypt.

2.3. Experimental infection:

E. coli strain O_{78} serotype of poultry origin was obtained from Poultry Department, Animal Health Research Institute, Dokki, Giza, Egypt. The preparation of the infecting dose was performed according to Chansiripornchai and Sasipreeyajan (2002), where it was 0.1 ml from a concentration of 1×10^6 c.f.u/ml. The infected chicken group was injected subcutaneously in the tissue of infra orbital sinuses. This group was left two days after infection until symptoms were observed (chickens suffering from severe diarrhoea, lack of appetite and ruffled feathers).

2.4. Blood samples:

Blood samples were taken from each slaughtered chicken at 1, 7, 14, 21 days post last dose of amikacin injection. All blood samples were collected in sterilized tubes and allowed to clot. Serum was separated by centrifugation for 10 minutes at 3000 r.p.m. Sera were kept frozen at -20°C until assayed.

2.5. Biochemical assay:

The determination of serum biochemical constituents was performed by using ready-made kits from Diamond diagnostics company (Egypt). The biochemical measurements were performed for estimation of activities of serum creatinine, uric acid, glucose, total protein, albumin, total bilirubin, aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT).

2.6. Histopathological study :

Small fresh specimens from kidney and liver were collected from slaughtered chickens and rapidly fixed in 10% formalin solution for at least 24 hrs. Histopathology was performed according to the method described by Harries (1989).

2.7. Statistical analysis:

All data were expressed as means±SEM and statistically analyzed using Statistical Package for Social Science program (SPSS. 16), using one-way analysis of variance (ANOVA) followed by Duncan's Multiple Range Test to examine the difference among the experimental groups, at significance level of $P\leq0.05$.

3. RESULTS

The serum analysis of untreated, *E. coli*-infected broiler chickens denoted a significant increase in the activity of liver enzymes including, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and serum level of total bilirubin as well as significant increase the kidney parameters considering serum levels of creatinine and uric acid, all of these findings indicating dysfunction of both liver and kidney. On the other hand, the above mentioned parameters in infected-treated broiler chickens of groups (3) decreased significantly toward the values that recorded in uninfected-untreated birds indicating the good therapeutic effect of amikacin against *E. coli* and its safety on liver and kidney function when clinically used at the recommended dose and duration. The biochemical parameters in different groups were recorded in tables (1, 2, 3, 4). The histopathological changes in both kidney and liver were shown in figures (1 to 8).

Table (1): Effect of intramuscular injection of amikacin at a dose of 10 mg/kg bwt once daily for three consecutive days on creatinine (mg/dl) and uric acid concentrations (mg/dl) in broiler chicken (n=3).

Parameters	Creatinine				Uric acid			
	Days post treatment				Days post treatment			
Groups	1st day	7th day	14th day	21st day	1st day	7th day	14th day	21st day
Group 1	1.81 ± 0.01 ^{Ad}	1.87 ± 0.02 ^{Ad}	1.84 ± 0.01 ^{Ad}	1.80 ± 0.04 ^{Ad}	5.23 ± 0.05 ^{Ad}	5.20 ± 0.01 ^{Ad}	5.23 ± 0.06 ^{Ac}	5.17 ± 0.09 ^{Ab}
Group 2	3.95 ± 0.01 ^{Ab}	3.92 ± 0.03 ^{Ab}	3.76 ± 0.07 ^{ABb}	3.68 ± 0.10 ^{Ba}	7.22 ± 0.05 ^{Ab}	6.83 ± 0.15 ^{ABb}	6.53 ± 0.17 ^{Ba}	6.43 ± 0.18 ^{Ba}
Group 3	4.95 ± 0.05 ^{Aa}	4.41 ± 0.11 ^{Aa}	4.02 ± 0.09 ^{Ba}	3.81 ± 0.08 ^{Ba}	7.64 ± 0.10 ^{Aa}	7.45 ± 0.12 ^{Aa}	6.79 ± 0.08 ^{Ba}	6.62 ± 0.18 ^{Ba}
Group 4	2.80 ± 0.09 ^{ABc}	2.95 ± 0.05 ^{Ac}	2.54 ± 0.06 ^{BCc}	2.47 ± 0.14 ^{Cb}	6.06± 0.10 ^{Ac}	5.99 ± 0.13 ^{Ac}	5.98 ± 0.12 ^{Ab}	5.43 ± 0.18 ^{Bb}

Values are mean ± SE. Means with different alphabets as superscripts differ significantly (P<0.05). Capital alphabets (horizontal comparison between days of experiment), small alphabets (vertical comparison between groups).

Table (2): Effect of intramuscular injection of amikacin at a dose of 10 mg/kg bwt once daily for three consecutive days on glucose (mg/dl) and total protein concentrations (g/dl) in broiler chicken (n=3).

Parameters	Glucose				Total protein			
	Days post treatment				Days post treatment			
Groups	1st day	7th day	14th day	21st day	1st day	7th day	14th day	21st day
Group 1	106.6 ± 1.45 ^{Ab}	111.6± 6.35 ^{Ab}	105.67 ± 9.52 ^{Ab}	115.67± 9.70 ^{Aa}	5.23 ± 0.05 ^{Ad}	5.20 ± 0.01 ^{Ad}	5.23 ± 0.06 ^{Ac}	5.17 ± 0.09 ^{Ab}
Group 2	87.6 ± 1.33 ^{Ac}	88.33± 0.88 ^{Ab}	79.67 ± 7.51 ^{Ac}	73.33 ± 6.64 ^{Ab}	7.22 ± 0.05 ^{Ab}	6.83 ± 0.15 ^{ABb}	6.53 ± 0.17 ^{Ba}	6.43 ± 0.18 ^{Ba}
Group 3	99.3 ± 7.79 ^{Abc}	90.67± 8.37 ^{Ab}	94.33 ± 4.91 ^{Abc}	86.67 ± 4.91 ^{Ab}	7.64 ± 0.10 ^{Aa}	7.45 ± 0.12 ^{Aa}	6.79 ± 0.08 ^{Ba}	6.62 ± 0.18 ^{Ba}
Group 4	127.6 ± 2.96 ^{Aa}	147.67± 9.82 ^{Aa}	131.33 ± 6.06 ^{Aa}	129.33± 2.90 ^{Aa}	6.06± 0.10 ^{Ac}	5.99 ± 0.13 ^{Ac}	5.98 ± 0.12 ^{Ab}	5.43 ± 0.18 ^{Bb}

Values are mean ± SE. Means with different alphabets as superscripts differ significantly (P<0.05). Capital alphabets (horizontal comparison between days of experiment), small alphabets (vertical comparison between groups).

Table (3): Effect of intramuscular injection of amikacin at a dose of 10 mg/kg bwt once daily for three consecutive days on albumin (g/dl) and total bilirubin concentrations (mg/dl) in broiler chicken (n=3).

Parameters	Albumin				Total bilirubin			
	Days post treatment				Days post treatment			
Groups	1st day	7th day	14th day	21st day	1st day	7th day	14th day	21st day
Group 1	2.27 ± 0.15 ^{Aa}	2.18 ± 0.09 ^{Aa}	2.21 ± 0.09 ^{Aa}	2.24 ± 0.05 ^{Aa}	0.36 ± 0.01 ^{Ac}	0.37 ± 0.01 ^{Ab}	0.35 ± 0.02 ^{Ab}	0.35 ± 0.01 ^{Ab}
Group 2	1.16 ± 0.09 ^{Ac}	1.38 ± 0.09 ^{Abc}	1.37 ± 0.21 ^{Ab}	1.48 ± 0.21 ^{Ac}	0.55 ± 0.02 ^{Ab}	0.54 ± 0.02 ^{Aa}	0.51 ± 0.02 ^{Aa}	0.50 ± 0.03 ^{Aa}
Group 3	1.03 ± 0.03 ^{Bc}	1.09 ± 0.05 ^{Bc}	1.59 ± 0.15 ^{Ab}	1.72 ± 0.11 ^{Abc}	0.67 ± 0.02 ^{Aa}	0.59 ± 0.04 ^{ABa}	0.48 ± 0.04 ^{BCa}	0.45 ± 0.03 ^{Cab}
Group 4	1.61 ± 0.16 ^{Ab}	1.71 ± 0.16 ^{Ab}	1.83 ± 0.10 ^{Aab}	1.98 ± 0.08 ^{Aab}	0.42 ± 0.03 ^{Ac}	0.49 ± 0.05 ^{Aab}	0.41 ± 0.03 ^{Aab}	0.39 ± 0.04 ^{Ab}

Values are mean ± SE. Means with different alphabets as superscripts differ significantly (P<0.05). Capital alphabets (horizontal comparison between days of experiment), small alphabets (vertical comparison between groups).

Table (4): Effect of intramuscular injection of amikacin at a dose of 10 mg/kg bwt once daily for three consecutive days on AST (U/L) and ALT concentrations (U/L) in broiler chicken (n=3).

Parameters	AST				ALT			
	Days post treatment				Days post treatment			
Groups	1st day	7th day	14th day	21st day	1st day	7th day	14th day	21st day
Group 1	165. 7 ± 12.13 ^{Ad}	154. 7± 13.3 ^{Ac}	162.7 ± 15.3 ^{Ac}	159.3± 9.52 ^{Ac}	64.7 ± 6.4 ^{Ac}	63.3 ± 6.56 ^{Ac}	61.7 ± 8.08 ^{Ac}	62.3 ± 5.48 ^{Ac}
Group 2	301.3 ± 2.33 ^{ABb}	307.7± 19.7 ^{Ac}	276.3 ± 12.4 ^{ABb}	256.3± 16.2 ^{Bb}	134.7± 6.6 ^{Aa}	138.7± 5.5 ^{Aa}	121.3 ± 6.1 ^{ABa}	111.7± 6.35 ^{Ba}
Group 3	396.3 ± 15.9 ^{Aa}	406 ± 15.6 ^{Aa}	388.7 ± 6.9 ^{ABa}	362 ± 17.3 ^{Ba}	112 ± 6.4 ^{Ab}	107.3± 6.8 ^{ABb}	96.3 ± 8.7 ^{ABab}	87.7 ± 5.20 ^{Bb}
Group 4	236.7 ± 15 ^{Ac}	255.7± 18.8 ^{Ab}	203.7 ± 15.6 ^{ABc}	173.7± 13.1 ^{Bc}	93.3 ± 3.5 ^{Ab}	82.7 ± 5.2 ^{ABc}	87.3 ± 10.7 ^{ABbc}	69.3 ± 5.5 ^{Bbc}

Values are mean ± SE. Means with different alphabets as superscripts differ significantly (P<0.05). Capital alphabets (horizontal comparison between days of experiment), small alphabets (vertical comparison between groups).

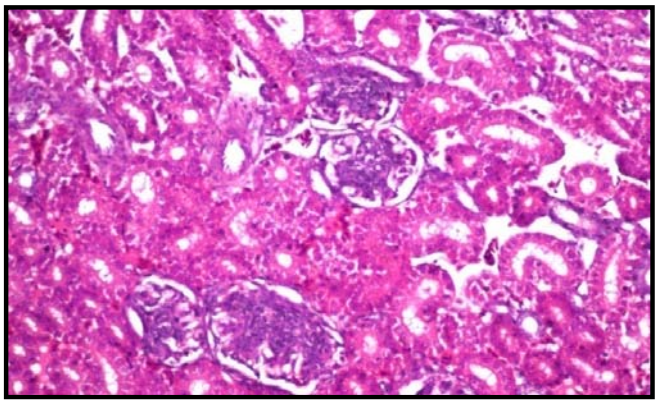

Figure (1): Kidney of control healthy broiler chickens, there was no histopathological alteration and the normal histological structure of the glomeruli and tubules were recorded.

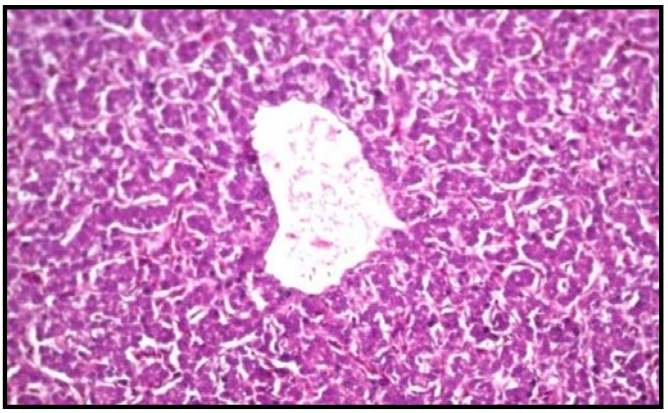

Figure (2): Liver of control healthy broiler chickens, there was no histopathological alteration and the normal histological structure of the central vein and surrounding hepatocytes in the hepatic lacunae.

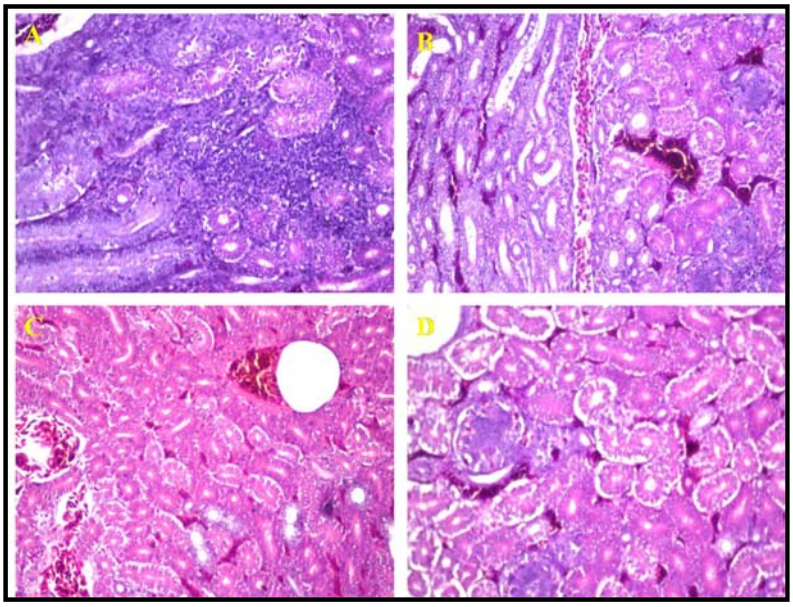

Figure (3): Kidney of experimentally *E. coli* infected broiler chickens (Stain was H&E); A: Focal inflammatory cells aggregations were detected in between the tubules. B: Congestion in the blood vessels. C: There was congestion in the blood vessels between the tubules associated with swelling in the tubular lining epithelium. D: Congestion was observed in the blood vessels between the tubules.

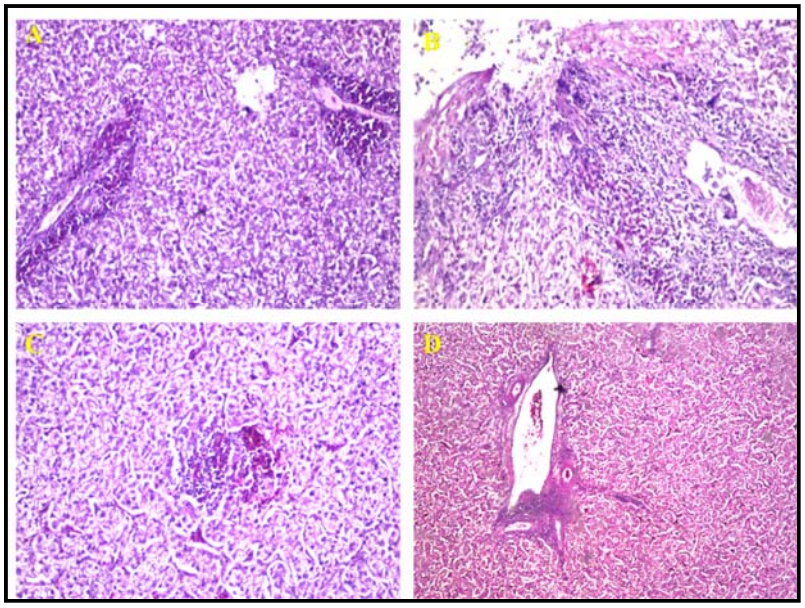

Figure (4): Liver of experimentally *E. coli* infected broiler chickens (Stain was H&E); A: Massive inflammatory cells infiltration was detected in the portal area. B: sever dilatation and congestion were detected in the portal veins associated with massive inflammatory cells aggregation in the portal area as well as degeneration in the hepatocytes in the parenchyma. C: There was focal necrosis in the hepatic parenchyma. D: The portal area showed, sever congestion in the portal vein associated with fibrosis and inflammatory cells infiltration.

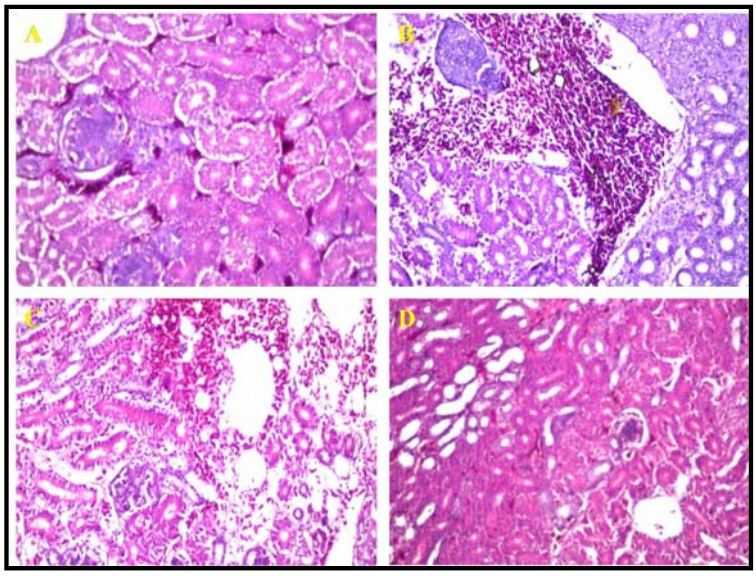

Figure (5): Kidney of experimentally *E. coli* infected broiler chickens and treated by IM injection of amikacin at a dose of 10 mg/kg bwt, for 3 consecutive days (Stain was H&E); A: After 1st day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, there was congestion in the blood vessels between the tubules associated with swelling in the tubular lining epithelium. B: After 7th day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, focal hemorrhage between tubules were detected. C: After 14th day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, there was focal hemorrhage in between the degenerated tubules. D: After 21st day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, there was no histopathological alteration.

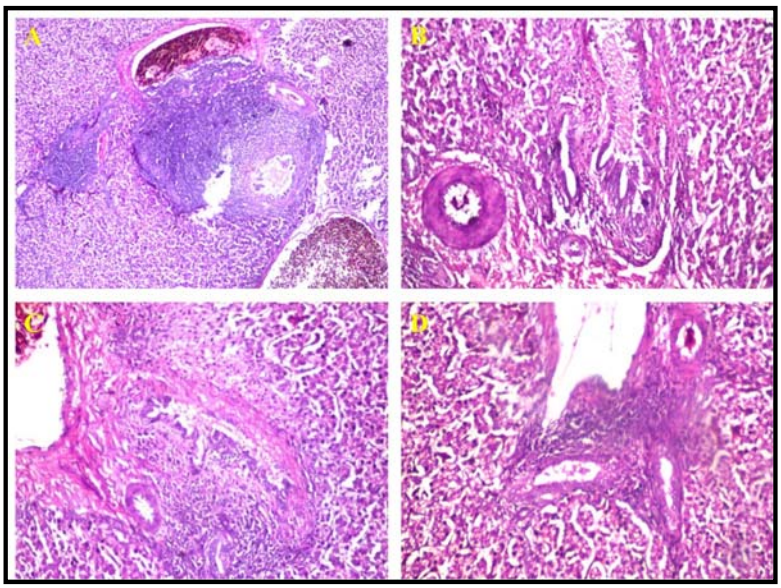

Figure (6): Liver of experimentally *E. coli* infected broiler chickens and treated by IM injection of amikacin at a dose of 10 mg/kg bwt, for 3 consecutive days (Stain was H&E); A: After 1st day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, sever congestion was observed in the portal vein associated with inflammatory cells infiltration in the portal area surrounding the bile duct. B: After 7th day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, the portal area showed sever congestion in the portal vein associated with fibrosis and inflammatory cells infiltration. C: After 14th day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, dilatation in the portal vein with hyperplasia in the bile ducts as well as inflammatory cells infiltration with

fibrosis were detected in the portal area. D: After 21st day following last dose of amikacin injection in experimentally *E. coli* infected broiler chickens, the portal area showed mild hyperplasia in the bile ducts.

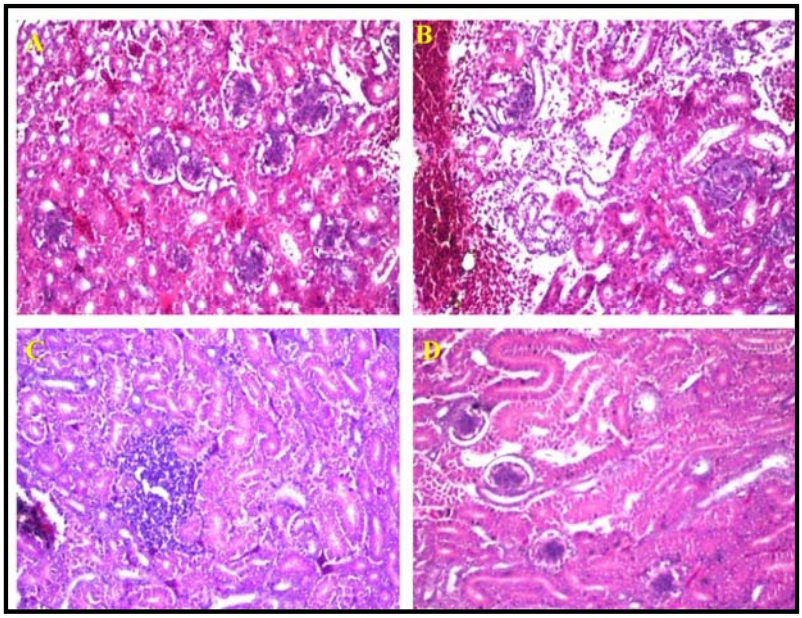

Figure (7): Kidney of healthy broiler chickens after IM injection of amikacin at a dose of 10 mg/kg bwt, for 3 consecutive days (Stain was H&E); A: After 1st day following last dose of amikacin injection in healthy broiler chickens, there was no histopathological alteration were recorded. B: After 7th day following last dose of amikacin injection in healthy broiler chickens, focal hemorrhage was detected in between the glomeruli and tubules. C: After 14th day following last dose of amikacin injection in healthy broiler chickens, focal lymphoid cells aggregation was detected in between the tubules. D: After 21st day following last dose of amikacin injection in healthy broiler chickens, there was no histopathological alteration were recorded.

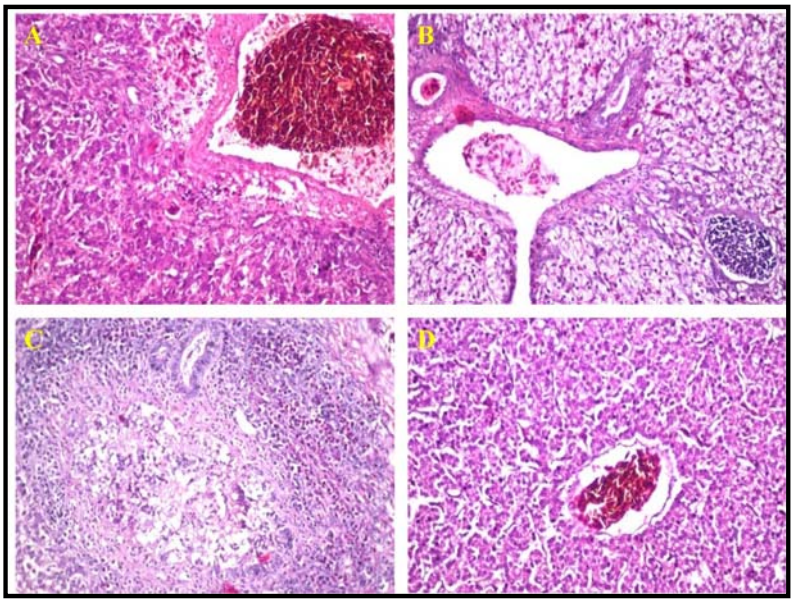

Figure (8): Liver of healthy broiler chickens after IM injection of amikacin at a dose of 10 mg/kg bwt, for 3 consecutive days (Stain was H&E); A: After 1st day following last dose of amikacin injection in healthy broiler chickens, congestion was observed in the portal vein associated with focal hemorrhage in the adjacent hepatic parenchyma. B: After 7th day following last dose of amikacin injection in healthy broiler chickens, congestion in the portal vein associated with focal circumscribed round aggregation of lymphoid cells in the degenerated hepatocytes of the hepatic parenchyma. C: After 14th day following last dose of amikacin injection in healthy

broiler chickens, central and portal veins showed sever dilatation and congestion associated with edema in the portal area and focal necrosis, as well as focal inflammatory cells infiltration in the degenerated hepatic parenchyma. D: After 21st day following last dose of amikacin injection in healthy broiler chickens, there was mild congestion in the central vein.

4. DISCUSSION

Clinical chemical analysis is a fundamental tool used in human and veterinary medicine to diagnose and predict the outcome of disease and to monitor the effect of therapeutic, nutritional, and environmental management (Smith and Reynard, 1992).

The serum analysis of untreated, *E. coli*-infected broiler chickens denoted a significant increase in the activity of liver enzymes including, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and serum level of total bilirubin as well as significant increase the kidney parameters considering serum levels of creatinine and uric acid, all of these findings indicating dysfunction of both liver and kidney. On the other hand, the above mentioned parameters in infected-treated broiler chickens of groups (3) decreased significantly toward the values that recorded in uninfected-untreated birds indicating the good therapeutic effect of amikacin against *E. coli* and its safety on liver and kidney function when clinically used at the recommended dose and duration.

Results of serum creatinine and uric acid showed significant increases in *E. coli* infected chickens. These increases may be attributed to occurrences of a renal disease resulted from *E. coli* infection (Kaneko et al., 1997). Aminoglycoside antibiotics have long been used as antibacterial therapy. Despite their beneficial effects, aminoglycosides have considerable oto and nephro-toxic side effects (Yazar et al., 2003). It has been reported that amikacin may induce free radical production which implicates a variety of pathological processes (Chaudhary et al., 2008; Parlakpinar et al., 2003). In this study the marked elevation of the levels of both serum creatinine and urea in healthy broiler chickens following amikacin administration. This gives an indication to the reduction in the glomerular filtration. Since serum creatinine and urea are waste products of protein metabolism that need to be excreted by the kidney; therefore, such increase of serum creatinine and urea as reported in this study confirm an indication of functional damage of the kidney and these results were in consistent with other studies (Al-Attar and Al-Taisan, 2010; Yazar et al., 2003). The nephrotoxicity of aminoglycoside (represented by acute tubular necrosis) usually appeared 5 to 10 days after a toxic insult and may be seen even after discontinuation of aminoglycosides therapy. The elevation of the serum creatinine and urea may be seen in association with hyponatremia and hyperkalemia. In general, aminoglycosides induced acute kidney injury results in non oliguric renal failure (Bentley et al., 2010; Parlakpinar et al., 2003).

Significant hypoglycemia was observed in *E. coli* infected chicken. These decreases could be suggestive of septicemia and hepatic affection which resulted in decreased hepatic gluconeogenesis and glycogenolysis (Thrall, 2004). These results were proved by the observed hepatic necrosis, congestion were detected in the portal veins and degeneration in the hepatocytes in the parenchyma. There was focal necrosis in the hepatic parenchyma in groups (2) and (3) as a result of *E. coli* infection. There was a significant increase in levels of serum glucose levels following amikacin injection as compared to control group. These results similar to that obtained after gentamicin injection in rats (Elkomy et al., 2015).

Significant hypoproteinemia and hypoalbuminemia were seen in *E. coli* infected group throughout the experiment. These hypoproteinemia and hypoalbuminemia could be suggestive of hepatic affection which confirmed histopathologically by the observed congestion in portal veins and degeneration in hepatocytes as a result of *E. coli* infection. The protein profile of *E. coli* infected broiler chickens and treated by amikacin returned to normal probably due to the liver returned to its physiological function. In this study the marked reduction of the levels of both serum total protein and albumin in healthy broiler chickens following amikacin injection. Similar results were obtained following IM injection of amikacin (80 mg/kg bwt) daily for the period of 15 days to rabbits which caused a significant decrease in concentration of albumin and total protein (Ahmad and Al-Tai, 2013).

Hepatic enzymes (AST, ALT and ALP) activities showed significant increases in *E. coli* infected group. These increases could be suggestive of hepatic affection as ALT and AST are indicators of hepatocellular damage (Harr, 2002). ALT and AST are cytosolic enzymes and their activities increase with the changes in hepatocellular permeability as in hepatic necrosis (Harr, 2002). Histopathological examination supported these results by demonstrating marked dilatation and congestion in the portal veins

associated with massive inflammatory cells aggregation in the portal area as well as degeneration in the hepatocytes in the parenchyma. There was focal necrosis in the hepatic parenchyma in liver of *E. coli* infected chicken.

Also, Campell and Coles (1986) concluded that the increased activity of liver enzymes has been associated with hepatocellular damage in birds infected with *E. coli* as well as increase in creatinine and uric acid (kidney function parameters) may be attributed to septicemia caused by *E. coli* and also due to effect of its toxin on kidney (Pai et al., 1984; Tizipori et al., 1987). Significant increase in serum levels of liver enzymes, creatinine and uric acid in chickens infected with *E. coli* and referred that increase to liver and kidney damage associated with bacterial infection (Mona and Osfor, 2002; Omaima, 1987). Administration of hepatotoxic agent caused a significant elevation of enzymes level such as AST, ALT and bilirubin level has been attributed to the damage structural integrity of liver indicating development of hepatotoxicity (Gutiérrez and Solis, 2009). In this study, amikacin causes elevation in AST, ALT and bilirubin level. This finding correlates with previous reports by Noorani et al. (2010) who also showed that gentamicin induces hepatotoxicity evidenced by elevated levels of serum enzymes.

Alteration observed in kidney following *E. coli* infection, congestion was observed in the blood vessels between the tubules. Focal inflammatory cells aggregations were detected in between the tubules. Following amikacin injection in the present study, congestion was observed in the intertubular blood vessels associated with swelling in the tubular lining epithelium. Focal haemorrhage was detected between the glomeruli and tubules. Focal lymphoid cells aggregation was detected in between the tubules. And after 21 days of amikacin administration in healthy broiler chickens, there was no histopathological alteration were recorded.

Aminoglycosides induced nephrotoxicity is characterized by tubular necrosis, basal membrane disruption, mesangial cell contraction, proliferation and apoptosis, indicated by a decrease in glomerular filtration and alteration in intraglomerular dynamics (Bennett et al., 1986).

Histopathological alteration observed in liver following amikacin injection in the present study included, congestion was observed in the portal vein associated with focal hemorrhage in the adjacent hepatic parenchyma. The portal area showed congestion in the portal vein and inflammatory cells infiltration while the parenchyma showed degeneration in the hepatocytes. Congestion in the portal vein associated with focal circumscribed round aggregation of lymphoid cells in the degenerated hepatocytes of the hepatic parenchyma. After 21 days of amikacin administration in healthy broiler chickens, there was mild congestion in the central vein. Similar results obtained following gentamicin injection to rats, severe congestion of portal blood vessels with fibrin emboli were recorded (Aboubakr and Abdelazem, 2016). Following *E. coli* infection, sever dilatation and congestion were detected in the portal veins associated with massive inflammatory cells aggregation in the portal area as well as degeneration in the hepatocytes in the parenchyma. There was focal necrosis in the hepatic parenchyma.

5. CONCLUSIONS

From the above-mentioned results in this study, it could be concluded that IM injection of amikacin, (10 mg/kg) for three successive days is very effective in controlling of colisepticemia in broiler chickens. Also, the possible side effects due to amikacin injection are short-term as the most of the parameters went back to normal after three weeks post amikacin injection.

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