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Research Article

The Effect of Kanamycin on Biochemical Parameters Following Repeated Intramuscular Administrations in Chukar Partridges (*Alectoris Chukar*)

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ABSTRACT

Kanamycin is an aminoglycoside antibiotic widely used to treat infections caused by aerobic gram-negative bacteria in animals. The chukar partridge plays an important role in the nutrition and hunting industries. The study aimed to determine the effect of repeated intramuscular administration of kanamycin at doses of 15 and 100 mg/kg on biochemical parameters in chukar partridge. A total of 18 partridges were randomly divided into three equal groups: control (n=6) and kanamycin groups. Saline solution was administered to the control group. In the other groups, 15 and 100 mg/kg of kanamycin were administered intramuscularly, respectively. Kanamycin was administered once daily for 5 days, and blood samples were taken at 24, 72, and 120 hours. Kanamycin at a 15 mg/kg dose increased albumin (ALB) at 120 h and aspartate transaminase (AST) at all sampling times. The administration of kanamycin at a 100 mg/kg dosage resulted in a notable elevation in ALB, AST, alkaline phosphatase, and cholesterol levels. No difference was observed in other parameters at both dose levels. The results show that kanamycin, at a dose of 100 mg/kg, can cause liver and lipid metabolism damage in chukar partridges. In the future, further studies on histopathological and molecular techniques are required to delineate the organ damage caused by kanamycin.

Keywords: *Alectoris Chukar*, Biochemical parameters, Kanamycin

INTRODUCTION

Aminoglycosides are bactericidal antibiotics, especially against gram-negative bacteria and some gram-positive bacteria. They show their effects by binding irreversibly to the 30S subunit of the bacterial ribosome and inhibiting protein synthesis (1). Aminoglycosides have the advantages of being cheap and having a long post-antibiotic effect. Still, they have the disadvantages of having a narrow therapeutic index and causing adverse effects such as nephrotoxicity, ototoxicity, and neurotoxicity (1,2). Kanamycin is an aminoglycoside antibiotic obtained from *Streptomyces kanamyceticus*. It is effective against gram-negative bacteria such as *Escherichia coli, Salmonella enteriditis, Pseudomonas aeruginosa, Helicobacter pylori, Moraxella, Proteus mirabilis, Enterobacter, Klebsiella pneumoniae,* and *Serratia marcescens.* Kanamycin is frequently used parenterally and orally in veterinary medicine. However, as with other aminoglycosides, kanamycin is a polar and cationic compound, so its oral bioavailability is very low (1%), and it should only be used orally in digestive system diseases (3,4,5).

Partridge is a medium-sized, short-winged, and short-tailed bird species in the Phasianidae family, well-known in Anatolia. One of the most important partridge species is the chukar partridge (*Alectoris chukar*) (6). It is produced for partridge meat or hobby purposes in special hunting grounds. To meet the increasing demand, partridge production on farms has become widespread. However, poor maintenance conditions and stock density on farms have led to the spread of bacterial infections. Bacterial infections in poultry are caused by gram-negative bacteria, especially *E. coli, Klebsiella, Pseudomonas, Salmonella, Citrobacter, Proteus,* and *Serratia* species (7,8). Antibiotics such as enrofloxacin, trimethoprim/sulfamethoxazole, and amoxicillin/clavulanate are commonly used in infections caused by gram-negative bacteria in poultry (7). However, it has been reported that resistance to these antibiotics has developed, and alternative antibiotic options are needed (9). Therefore, kanamycin can be used in infections caused by gram-negative bacteria in chukar partridges.

No research was found on the usage and safety of kanamycin in partridges. Assessing the safety of pharmaceuticals in the target species is crucial for the efficacy of the treatment. Kanamycin can be used in bacterial infections caused by gram-negative bacteria in partridges; therefore, establishing its reliability is essential for widespread use. The aim of this study was to determine the effects of repeated (every 24 hours for 5 days) intramuscular administration of kanamycin at 15 and 100 mg/kg doses to chukar partridges on biochemical parameters.

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MATERIAL AND METHODS

Animals

The study utilized eighteen chukar partridges (*Alectoris chukar*) with weights ranging from 0.4 to 0.6 kg, which had not been administered any medication in the prior two months. The partridges were evaluated as healthy based on physical examination, starvation, and behavior, and housed in groups of three within stainless steel cages. The birds were fitted with numbered rings on their feet for better identification. They were provided with a drug-free diet, and water was made available ad libitum. The research was performed following a two-week acclimatization phase. All study protocols were approved (2017/71) by the Ethics Committee of the Faculty of Veterinary Medicine (University of Selcuk, Konya, Türkiye).

Experimental design

A total of 18 partridges were divided into three equal groups to receive different doses of kanamycin and a control. The control group received intramuscular injections of sterile saline solution. The other two groups were administered kanamycin intramuscularly at 15 and 100 mg/kg, respectively. Drug administration to partridges continued every 24 hours for 5 days. Following drug administration, 0.5 ml blood samples were collected from the jugular vein at 24, 72, and 120 hours. Serum samples were obtained by centrifuging blood samples at 4000 x g for 10 minutes and stored at -80 °C until analysis.

Biochemical analysis

The measurements of albumin (ALB), alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), blood urea nitrogen (BUN), cholesterol (CHOL), creatinine (CRE), gamma glutamyl transpeptidase (GGT), total bilirubin (TBIL), total protein (TP) and triglyceride (TRIG) values from serum samples were performed on an auto-analyzer using commercial kits.

Statistical analysis

Biochemical parameters were presented as mean±SD. Analyses were performed using the SPSS program (22.0 software; IBM). Statistical comparison of biochemical parameters was performed using one-way analysis of variance (ANOVA) and post-hoc Tukey test. Statistical significance was accepted as $P<0.05$.

RESULTS

No differences were observed in the behavior, appetite, and movement of partridges after intramuscular administration of kanamycin at doses of 15 and 100 mg/kg once daily for 5 days. The effects of repeated administration of kanamycin to chukar partridges on biochemical parameters are presented in Table 1. The administration of kanamycin at a dosage of 15 mg/kg resulted in elevated ALB levels at 120 hours and increased AST levels at 24, 72, and 120 hours. In contrast, a 100 mg/kg caused increased levels of ALB, AST, ALP, and CHOL. No difference was observed in the values of ALP, ALT, BUN, CREA, GGT, TBIL, TP, TRIG, and CHOL at the 15 mg/kg dose and in the values of ALT, BUN, CREA, GGT, TBIL, TP, and TRIG at the 100 mg/kg dose.

DISCUSSION

For the first time, this study established the effects of repeated intramuscular kanamycin treatment at doses of 15 and 100 mg/kg on biochemical parameters in Chukar partridges. Notable hepatic and lipid metabolism alterations were seen in the 100 mg/kg dose group relative to the 15 mg/kg dose. The information obtained in this study is important for the safe use of kanamycin in chukar partridges.

While kanamycin applications to chukar partridges did not cause any difference in ALP, ALT, BUN, CREA, GGT, TBIL, TP, and TRIG values, differences were observed in ALB and AST levels in the 15 mg/kg dose group and ALB, AST, ALP, and CHOL levels in the 100 mg/kg dose group. Surprisingly, despite repeated application of kanamycin, no difference was observed between the groups in BUN and CRE values, which are indicators of kidney damage. There may be more than one reason underlying this situation. The physiological and functional structure of the poultry kidney is quite different from that of the mammalian kidney. While the perfusion of the kidneys of mammals, where nephrotoxic effects are seen at the same doses, is provided by a single renal artery, there are three renal arteries feeding the poultry kidneys (10). The kidneys of poultry possess a renal-portal system that improves their blood flow (11). These perfusion differences between the mammalian and avian kidneys may have provided a better blood supply to the avian kidneys and thus facilitated the rapid removal of kanamycin from the kidneys before damage occurs. Another reason might be that the 100 mg/kg dose cannot cause nephrotoxic effects. This conclusion is supported by the fact that kanamycin causes toxic effects at doses >200 mg/kg in other species (12,13,14,15).

Aminoglycosides cause nephrotoxic effects because they accumulate in the kidney tissue. These drugs accumulate in the liver tissue and the kidneys (16). Aminoglycosides can bind to cell membranes and intracellular organelle membranes, such as lysosomes/mitochondria. Aminoglycosides have a very high affinity for lysosomes and inhibit phospholipase A1 and sphingomyelinase enzymes, preventing intracellular reactions and stopping intracellular events, leading to cellular damage (17,18,19). In addition, histopathological examinations have shown that aminoglycosides cause damage to the liver (20).

Both kanamycin doses in chukar partridges caused elevated ALB and AST, but the 100 mg/kg dose increased ALP. ALB is produced by the liver and is the most common protein found in the blood, and it plays a vital role in body development and tissue repair (21). ALB may be elevated as a defense mechanism to repair damage to the liver. Additionally, aminoglycosides may increase or decrease urination frequency to varying degrees between individuals (3). Therefore, the increased serum ALB levels may be due to the blood's reduced fluid. ALP is a protein enzyme found in various tissues in the body, including the liver, bone, intestines, and kidneys, but 95% of its measured amount in the blood comes from the liver and bone. High ALP levels generally indicate liver and bone damage. AST is an enzyme found in different tissues in the body, such as the liver, heart, muscle, kidney, and brain. Although its specificity for liver damage is lower than other parameters, it is generally accepted as a parameter indicating liver damage with the increase in the enzymes found in the liver in the blood (22). When all these results are evaluated, it can be said that repeated administration of kanamycin may cause liver damage in chukar partridges. Previous studies have also reported liver injury due to aminoglycosides (23,24,25).

CHOL is an enzyme produced by the liver, plays a role in synthesizing some hormones and vitamins D and E, and contributes to synthesizing bile acids with cell/organelle membranes (26). It has been reported that oral administration of aminoglycosides (kanamycin, neomycin, paramomycin) reduces the blood's CHOL level in humans (27). However, parenteral administration to rats and rabbits did not cause any change in CHOL levels (28,29). In this study, the CHOL value increased after intramuscular application of kanamycin. These results indicate that the effect of kanamycin on CHOL varies depending on the route of administration.

Table 1: Effect of kanamycin (15 or 100 mg/kg, intramuscular, every 24 h for 5 days) in chukar partridge on biochemical parameters (n = 6, mean ± SD)

Parameters	Groups	Sampling time (Mean ± SD)		
		24 hours	72 hours	120 hours
ALB (g/dL)	Control	0.85±0.13	0.88±0.10b	0.90±0.08b
	15 mg/kg	1.00±0.16	1.23±0.33ab	1.30±0.24a
	100 mg/kg	1.28±0.43	1.33±0.17a	1.38±0.21a
ALP (U/L)	Control	140.00±30.16b	170.25±60.98b	149.75±46.00b
	15 mg/kg	260.75±78.13ab	259.50±92.41ab	436.25±177.24ab
	100 mg/kg	344.25±96.00a	566.50±79.24a	624.75±242.34a
ALT (U/L)	Control	2.00±0.82	1.50±0.48	1.50±0.58
	15 mg/kg	1.75±0.96	1.50±0.58	2.50±0.58
	100 mg/kg	1.75±0.96	1.50±0.58	1.50±0.58
AST (U/L)	Control	201.75±29.90b	212.00±25.07b	208.75±17.76b
	15 mg/kg	515.25±132.77a	772.25±148.50a	787.75±83.84a
	100 mg/kg	617.50±147.84a	809.50±138.90a	881.50±94.04a
BUN (mg/dL)	Control	2.15±0.85	2.14±0.33	2.02±0.50
	15 mg/kg	2.30±0.82	2.33±0.38	2.22±1.04
	100 mg/kg	2.45±1.03	2.21±0.45	2.10±0.27
CHOL (mg/dL)	Control	94.00±21.15	96.50±21.27b	103.00±21.95b
	15 mg/kg	109.00±19.25	133.00±24.64ab	132.50±22.84ab
	100 mg/kg	151.75±48.02	167.75±24.74a	174.00±21.18a
CRE (mg/dL)	Control	0.44±0.04	0.49±0.05	0.47±0.03
	15 mg/kg	0.42±0.05	0.46±0.13	0.50±0.05
	100 mg/kg	0.40±0.07	0.48±0.07	0.48±0.04
GGT (U/L)	Control	4.75±0.96	5.00±1.41	5.75±1.71
	15 mg/kg	4.25±0.50	5.75±1.26	5.50±1.29
	100 mg/kg	5.00±0.82	6.00±1.41	6.25±1.26
TBIL (mg/dL)	Control	0.08±0.03	0.08±0.01	0.09±0.04
	15 mg/kg	0.12±0.03	0.08±0.02	0.08±0.02
	100 mg/kg	0.11±0.02	0.10±0.04	0.09±0.01
TP (g/dL)	Control	3.90±0.89	4.15±0.93	4.33±0.56
	15 mg/kg	3.70±0.48	4.43±0.79	4.63±0.78
	100 mg/kg	4.18±1.19	4.35±0.64	4.48±0.81
TRIG (mg/dL)	Control	106.00±30.14	118.50±9.38	113.75±32.38
	15 mg/kg	150.25±40.61	178.00±83.36	152.50±38.92
	100 mg/kg	161.00±64.22	182.00±65.63	165.00±27.65

Different letters (a, b) in the same column are statistically significant ($P<0.05$).
ALB; albumin, ALP; alkaline phosphatase, ALT; alanine aminotransferase, AST; aspartate aminotransferase, BUN; blood urea nitrogen, CHOL; cholesterol, CRE; creatinine, GGT; gamma-glutamyltransferase, TBIL; total bilirubin, TP; total protein, TRIG; triglyceride.

In conclusion, repeated intramuscular administration of kanamycin to chukar partridges at doses of 15 and 100 mg/kg did not cause any difference in markers of kidney damage but caused liver damage. The liver adverse effects of kanamycin were dose-dependent. Therefore, observing the adverse effects of repeated intramuscular application of kanamycin at a dose of 100 mg/kg in partridges is necessary. In addition, further studies with histopathological and molecular techniques are needed to understand better the damage caused by kanamycin to organs.

DECLARATIONS

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author (O.A.).

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Ethical Statement: The experiment was approved (2017/71) by the Local Ethics Committee of the Faculty of Veterinary Medicine (University of Selcuk, Konya, Türkiye).

Competing Interests: The authors declare that there is no competing of interest regarding the publication of this article.

Declaration of Generative Artificial Intelligence: The authors of the current study declare that the article and/or tables and figures were not written/created by AI and AI-assisted technologies.

Authors' Contributions: All authors contributed to this present work. Experimental design (O.A, O.C, K.U, F.A), Laboratory studies (D.D.C, B.E), Drafted the manuscript (O.A, O.C, K.U), Provided final approval (O.A, O.C, K.U, F.A, D.D.C, B.E).

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