Effects of increasing doses of enrofloxacin on biochemical parameters in ducks

ABSTRACT

This research aims to determine the effect of oral single-dose administration of 10, 50, and 100 mg/kg of enrofloxacin on ducks on biochemical parameters. The research was carried out on eighteen ducks. Ducks were divided into 3 equal groups to receive 10, 50, and 100 mg/kg doses. Blood samples were taken at 0, 6, 12, 24 and 48 hours. No clinical side effects were observed in ducks after enrofloxacin administration. When dose groups were compared, significant differences were observed in aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), albumin (ALB), cholesterol (CHOL), total protein (TP) and creatinine (CRE) values ($p<0.05$). However, these differences returned to normal at the 48 hour. When the dose groups were evaluated within themselves, ALT, GGT, CHOL, triglyceride, and urea values did not differ ($p>0.05$). However, there were significant differences in AST, ALP, ALB, and CRE values at 10 mg/kg, AST at 50 mg/kg, and TP at 100 mg/kg ($p<0.05$). In conclusion, it was determined that oral administration of enrofloxacin to ducks at doses of 10, 50, and 100 mg/kg caused temporary changes in biochemical parameters. In this study, enrofloxacin was administered as a single dose. However, considering the repeated use of enrofloxacin in case of bacterial infection, attention should be paid to possible adverse effects that may occur in ducks.

Keywords: Ascending dose, biochemical, duck, enrofloxacin.

INTRODUCTION

Enrofloxacin is a fluoroquinolone group antibiotic approved for the treatment of infections caused by susceptible microorganisms in many animal species including cattle, pigs, cats, dogs, and poultry (EMA, 2001). It exhibits its antibacterial effect by inhibiting the bacterial DNA gyrase and topoisomerase IV enzymes. Enrofloxacin is extensively utilized in veterinary medicine because of its broad spectrum of activity, superior pharmacokinetic properties, and few adverse effects (Corum et al., 2019; Uney et al., 2021). Enrofloxacin is used in the treatment of respiratory, digestive, and soft tissue infections caused by Gram-negative and Gram-positive bacteria as well as mycoplasma-type bacteria and secondary bacterial infections accompanying viral infections (EMA, 2001). Enrofloxacin is used in the treatment of respiratory and digestive system diseases caused by *Mycoplasma gallisepticum, M. synoviae, Avibacterium paragallinarum, Clostridium perfringens, Escherichia coli, Pseudomonas aeruginosa* and *Salmonella spp.* in poultry (Bonassa et al., 2021; Cerda et al., 2002).

Duck is an important poultry species cultivated in many parts of the world for its meat and eggs (Corum et al., 2024; Coskun et al., 2023). The use of enrofloxacin is recommended for infections caused by Gram-negative bacteria such as *Salmonella spp., Campylobacter spp., E. coli, Vibrio spp.*, and *Yersinia spp.* in ducks (Aggad et al., 2010; EMA, 2001;

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Research Article

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Patil et al., 2021). It has also been reported that enrofloxacin can be used in the prevention and treatment of secondary infections that may occur during viral infection in ducks (EMA, 2001; Patil et al., 2021).

Fluoroquinolone group antibiotics show their effect in a concentration-dependent manner and their efficacy increases as the dose increases (Corum et al., 2019; Coskun et al., 2020). The traditional dose of enrofloxacin in poultry is 10 mg/kg. However, recent efficacy studies have recommended a dose of 50-100 mg/kg against *Salmonella* and *Clostridial* spp. bacteria in chickens (Kang et al., 2019; Li et al., 2017a; Li et al., 2017b; Maślanka et al., 2009). However, increasing the dose of drugs may cause undesirable effects on the body and these undesirable effects may differ between poultry species (Coskun et al., 2023). Side effects of drugs can be classified as pharmacological, biochemical, pathological, genotoxic, and allergic reactions. Therefore, biochemical parameters can be utilized in the evaluation of adverse effects in organs and tissues (Corum et al., 2015; Coskun et al., 2018). There is no information on the safety of enrofloxacin in ducks. This study aimed to determine the effect of enrofloxacin on biochemical parameters following oral administration of 10, 50, and 100 mg/kg single dose to ducks.

MATERIALS AND METHODS

Animals

The study was carried out on eighteen male ducks (8-12 months old) with a body weight of 1.8-2.5 kg. Ducks that were determined to be healthy by general clinical examination and had not received any medication in the last eight weeks before the study were included in the study. Ten days before the start of the study, the animals were taken to the pens where the study would be conducted and acclimatized to the environment. The animals were given ad-libitum access to water and fed concentrate feed twice a day. Animals were fasted 6 hours before the drug administration to prevent the effect of nutrients on the absorption of enrofloxacin. All procedures were approved by the ethics committee of Hatay Mustafa Kemal University, Faculty of Veterinary Medicine, Experimental Animal Production and Research Center (2022/06-03).

Experimental design

Eighteen ducks used in the study were divided into three equal dose groups. A single dose of enrofloxacin (Enrocure 10% oral solution, Teknovet, Istanbul/Türkiye) was administered orally to the first group (n=6) 10 mg/kg, to the second group (n=6) 50 mg/kg, and to the third group (n=6) 100 mg/kg. Drug administration was performed by gastric gavage. Blood samples (3 mL) were collected in anticoagulant-free tubes from the the brachial vein by venepuncture for biochemical analyses before (0 hour, control) and at 6, 12, 24, and 48 hours after enrofloxacin administration. Blood samples were centrifuged at 4000 x g for 10 minutes and the serum samples were stored at -80 ºC until analysis.

Analysis of biochemical parameters

Albumin (ALB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), cholesterol (CHOL), alkaline phosphatase (ALP), total protein (TP), triglycerides (TG), creatinine (CRE) and urea levels were measured in serum samples using an autoanalyzer (Abbott architect c8000, Abbott Core Laboratory, USA).

Statistical analysis

Biochemical parameters were presented as mean ± standard deviation (SD). The homogeneity of variance was evaluated using Levene's test, and the normality of the data distribution was assessed using the Shapiro-Wilk criterion. Intra- and inter-group statistical analysis of the obtained data was performed using one-way analysis of variance (ANOVA) and post-hoc Tukey tests in SPSS software (22.0 software; IBM). $p < 0.05$ was accepted as the limit of statistical significance.

RESULTS

Oral administration of enrofloxacin at doses of 10, 50, and 100 mg/kg did not cause any abnormalities in the duck's behavior, feed and water consumption, frequency, and consistency of defecation. Changes in biochemical parameters after oral administration of 10, 50, and 100 mg/kg single dose of enrofloxacin to ducks are presented in Table 1.

Table 1. Biochemical parameters in ducks following oral single-dose administration of enrofloxacin 10, 50, and 100 mg/kg (n=6, Mean ± SD).

Parameters	Group	Sampling time (hour)				
		0	6	12	24	48
AST	10 mg/kg	14.33 ± 5.89^{b}	$^{x}35.33\pm12.75^{a}$	22.67 ± 15.68^{ab}	11.67 ± 3.14^{b}	16.83 ± 5.23^{b}
	50 mg/kg	15.00 ± 4.38^{b}	$^{xy}23.83\pm5.81^{a}$	16.33 ± 5.24^{ab}	11.67 ± 3.83^{b}	10.67 ± 4.18^{b}
	100 mg/kg	14.50 ± 6.28	$^{y}14.00\pm6.51$	11.17 ± 5.74	8.67 ± 4.46	11.00 ± 5.37
ALT	10 mg/kg	26.33 ± 8.29	32.83 ± 10.61	33.83 ± 9.91	30.83 ± 8.91	25.83 ± 8.16
	50 mg/kg	28.17 ± 6.52	31.33 ± 10.97	33.17 ± 11.62	26.50 ± 8.41	21.50 ± 8.64
	100 mg/kg	26.00 ± 8.10	29.33 ± 7.15	28.50 ± 10.60	22.33 ± 5.50	20.17 ± 4.12
ALP	10 mg/kg	28.50 ± 8.31^{b}	$^{x}60.67\pm24.55^{ab}$	63.83 ± 22.41^{ab}	$^{x}83.33\pm29.21^{a}$	94.83 ± 32.26^{a}
	50 mg/kg	27.33 ± 6.98^{c}	$^{xy}35.00\pm15.47^{bc}$	64.83 ± 25.10^{ab}	$^{xy}60.17\pm18.65^{ab}$	72.17 ± 24.03^{a}
	100 mg/kg	28.33 ± 9.52	$^{y}32.50\pm10.01$	38.67 ± 17.21	$^{y}47.83\pm14.77$	61.67 ± 35.31
GGT	10 mg/kg	1.00 ± 0.63	$^{x}2.00\pm1.10$	$^{x}2.33\pm1.37$	$^{x}2.33\pm1.03$	2.00 ± 0.63
	50 mg/kg	1.33 ± 0.52	$^{y}0.83\pm0.41$	$^{y}0.67\pm0.52$	$^{y}0.83\pm0.75$	1.00 ± 0.89
	100 mg/kg	1.50 ± 0.55	$^{y}0.50\pm0.55$	$^{y}0.67\pm0.52$	$^{y}0.67\pm0.82$	1.33 ± 1.03
ALB	10 mg/kg	12.33 ± 1.37^{b}	$^{x}15.67\pm3.39^{a}$	12.17 ± 1.47^{b}	$^{x}14.00\pm1.41^{ab}$	11.67 ± 1.03^{b}
	50 mg/kg	12.83 ± 1.33	$^{y}11.50\pm1.97$	13.33 ± 2.66	$^{xy}11.67\pm1.37$	12.33 ± 1.37
	100 mg/kg	12.67 ± 1.63	$^{y}11.33\pm0.82$	11.83 ± 1.33	$^{y}9.17\pm4.45$	11.67 ± 1.37
TP	10 mg/kg	40.33 ± 2.76	40.65 ± 7.32	39.23 ± 4.41	$^{x}42.82\pm3.39$	39.92 ± 3.03
	50 mg/kg	40.70 ± 2.84	34.48 ± 3.27	40.08 ± 10.01	$^{y}35.52\pm2.83$	36.23 ± 4.48
	100 mg/kg	40.08 ± 3.83^{a}	33.95 ± 3.74^{b}	35.68 ± 1.80^{ab}	$^{y}36.24\pm3.34^{ab}$	36.48 ± 4.42^{ab}
CHOL	10 mg/kg	127.78 ± 19.00	$^{x}147.20\pm40.47$	134.67 ± 24.34	$^{x}152.94\pm28.93$	141.20 ± 27.00
	50 mg/kg	129.62 ± 18.50	$^{y}109.01\pm7.44$	127.07 ± 19.39	$^{y}120.15\pm11.13$	122.78 ± 17.18
	100 mg/kg	127.83 ± 28.92	$^{xy}110.84\pm11.29$	124.54 ± 10.09	$^{xy}127.80\pm15.62$	122.62 ± 18.66
TG	10 mg/kg	113.35 ± 20.66	101.80 ± 33.81	118.43 ± 44.99	117.66 ± 26.84	132.00 ± 57.52
	50 mg/kg	116.24 ± 18.96	96.83 ± 22.74	133.52 ± 31.29	102.55 ± 31.09	122.95 ± 25.61
	100 mg/kg	115.55 ± 17.65^{ab}	82.88 ± 8.68^{b}	137.56 ± 38.93^{a}	112.95 ± 35.47^{ab}	117.95 ± 27.65^{ab}
Urea	10 mg/kg	3.53 ± 1.68	4.33 ± 1.09	2.61 ± 0.91	3.37 ± 1.62	2.61 ± 1.34
	50 mg/kg	3.56 ± 1.44	4.15 ± 1.29	2.55 ± 1.34	2.51 ± 0.91	2.35 ± 0.83
	100 mg/kg	3.60 ± 1.70	3.59 ± 0.98	2.35 ± 0.75	2.45 ± 0.67	1.89 ± 0.56
CRE	10 mg/kg	0.06 ± 0.03^{b}	$^{x}0.20\pm0.08^{a}$	0.08 ± 0.02^{b}	0.09 ± 0.05^{b}	0.13 ± 0.06^{ab}
	50 mg/kg	0.06 ± 0.02	$^{xy}0.13\pm0.10$	0.15 ± 0.06	0.12 ± 0.08	0.13 ± 0.09
	100 mg/kg	0.07 ± 0.02	$^{y}0.07\pm0.04$	0.10 ± 0.06	0.11 ± 0.06	0.16 ± 0.09

^{x,y}; Indicates statistical difference between groups ($p<0.05$). ^{a,b,c}; Indicates statistical difference within the group ($p<0.05$)
AST; aspartate aminotransferase, ALT; alanine aminotransferase, ALP; alkaline phosphatase, GGT; gamma glutamyltransferase, ALB; albumin, TP; total protein, CHOL; cholesterol, TG; triglyceride, CRE; creatinine.

When the different dose groups were compared, significant changes were observed in AST, ALP, GGT, ALB, CHOL, and CRE at 6 hour, GGT at 12 hour, and ALP, GGT, ALB, CHOL, and TP at 24 hour ($p<0.05$). However, no difference was observed between dose groups at 48 hour ($p>0.05$). When the dose groups were evaluated within themselves, no difference was observed in ALT, GGT, CHOL, TG, and urea levels ($p>0.05$). In comparison to the 0 hour, significant increases in AST levels were observed at the 6 hour in the 10 mg/kg and 50

mg/kg dose groups. ALP levels showed significant increases at 24 and 48 hours in the 10 mg/kg dose group, and at 12, 24, and 48 hours in the 50 mg/kg dose group. Additionally, ALB and CRE levels increased significantly at the 6 hour in the 10 mg/kg dose group, while TP levels decreased at the 6 hour in the 100 mg/kg dose group ($p<0.05$).

DISCUSSION

Duck farming is an important part of industrial and rural poultry farming. Duck meat and eggs are crucial economic resources for the rural economy. Duck farming has increased significantly worldwide in recent years. It is very important to reduce the losses and deaths that will occur with the effective treatment of bacterial infections that occur with this increase (Adzitey & Adzitey, 2011). Enrofloxacin is widely used in the treatment of bacterial infections in poultry. Enrofloxacin is more effective than amoxicillin, colistin, erythromycin, oxytetracycline, and chlortetracycline against agents causing salmonellosis and colibacillosis in ducks (Aggad et al., 2010), and *Staphylococcus aureus* isolated from ducks was resistant to erythromycin, streptomycin and chloramphenicol, while it showed high sensitivity to enrofloxacin and ciprofloxacin (Amen et al., 2019). The antibacterial effect of enrofloxacin is concentration dependent, and increasing the dose increases its effectiveness (Bonassa et al., 2021; Coskun et al., 2020; Riviere & Papich, 2018). Although the traditional dose of enrofloxacin in bacterial infections is 10 mg/kg, it is recommended to use higher doses in infections caused by microorganisms such as *Salmonella enteritidis* and *Clostridium* spp. (Kang et al., 2019; Temmerman et al., 2021). Use of medicines in high doses may cause adverse effects (Coskun et al., 2018). In this study, the effect of increasing doses of enrofloxacin on biochemical parameters in ducks was demonstrated for the first time. Although some significant changes were observed in biochemical parameters due to the increase in enrofloxacin dose, it was determined that these changes were transient and that enrofloxacin was generally well tolerated in ducks.

In this study, after oral administration of enrofloxacin to ducks at doses of 10, 50 and 100 mg/kg, significant changes were observed in AST, ALP, GGT, ALB, CHOL and CRE at 6 hour, GGT at 12 hour and ALP, GGT, ALB, CHOL, and TP at 24 hour. However, no difference was detected between dose groups in biochemical parameters at the 48 hour. In the intra-group evaluation, changes were observed in AST and ALP levels at a dose of 10 mg/kg, in AST, ALB, and CRE levels at a dose of 50 mg/kg, and in TP levels at a dose of 100 mg/kg. After oral administration of enrofloxacin to broiler chickens at doses of 10 and 100 mg/kg for 5 days, an increase in serum ALT and AST levels and histopathological changes in the liver associated with these increases were observed in the high-dose group (Ellakany et al., 2008); in another study, administration of 100 and 200 mg/kg doses to broiler chickens for 30 days caused anemia and leukopenia by changing hematological parameters (Ibrahim et al., 2011). It was stated that it did not cause any changes in cartilage formation and structure when applied to chickens at doses of 10, 50, and 100 mg/kg, while it caused significant changes at doses of 300 and 600 mg/kg (Maślanka et al., 2009). It has been reported that it does not affect biochemical parameters (AST, creatinine kinase, LDH, ALB, ALT, glucose, TP, uric acid, and CHOL) when given intramuscularly (15 mg/kg) and orally (3, 15, and 30 mg/kg) to African gray parrots (Flammer et al., 1991).

The effect of enrofloxacin on biochemical parameters has been demonstrated in other animal species as well as poultry. Administration of enrofloxacin to lambs at a dose of 35 mg/kg for 15 days (Khazaeil et al., 2012) and to rams at a dose of 10 mg/kg for 14 days did not cause chondrotoxic effects (Coskun et al., 2018). It has also been reported that it caused significant

changes in ALP, ALT, AST, TP, BUN, and CRE values in rams, but these changes were within reference limits (Coskun et al., 2018). Enrofloxacin was administered orally to dogs for 3 days (18-20 mg/kg) and intramuscularly for 5 days (2.5 mg/kg) and administered to cats intramuscularly for 7 days (5, 15, and 25 mg/kg) not cause any changes in biochemical parameters (Shoorijeh et al., 2012; Vinay et al., 2017; Westropp et al., 2012). However, it has been stated that oral administration to rats at doses of 5 and 10 mg/kg for 28 days increased ALT, AST, GGT, ALP, ALB, bilirubin, BUN, and CRE levels and that these effects were due to oxidative stress in the kidney and liver (Khan et al., 2017; Mishra et al., 2021; Srinivasu et al., 2022).

CONCLUSION

It was determined that oral administration of enrofloxacin at 10, 50, and 100 mg/kg single doses to ducks caused temporary changes in AST, ALP, GGT, CHOL, TP, ALB, and CRE values. Although enrofloxacin was administered as a single dose in this study, repeated use is recommended in case of bacterial infection. Therefore, the safety of enrofloxacin after repeated use in ducks needs to be demonstrated hematologically.

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Conflict of interest: The authors declare no conflicts of interest.

Ethical statement or informed consent: The experiment was approved (2022/06-03) by the Local Ethics Committee for Animal Research Studies at Hatay Mustafa Kemal University (Hatay/Türkiye) and carried out by the European Directive (2010/63/EU).

Author contributions: *Conceptualization; investigation; methodology; project administration; resources; supervision; writing – original draft; writing – review and editing*: Duygu Durna Corum, Devran Coskun, Orhan Corum. *Writing – review and editing; project administration:* Feray Altan, Zafer Bulut.

Availability of data and materials: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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