The therapeutic effect of bromocriptine as mesylate and estradiol valerate on serum and blood biochemistry of common quails

Zain ul- Abideen,[*] Hafiz Ishfaq Ahmad,[†] Muhammad Nadeem,[*] Aleem Ahmad Khan,[‡] Muhammad Imran,[§] Tanveer Majeed,[#] Shouqun Jiang,[‖,1] and Abdelmotaleb Elokil[¶]

[*]*Department of Zoology, Ghazi University, D G Khan, Pakistan;* [†]*Department of Animal Breeding and Genetics, University of Veterinary and Animal Sciences, Lahore, Pakistan;* [‡]*Department of Zoology, Bahauddin Zakariya University, Multan, Pakistan;* [§]*Department of Veterinary Surgery and Pet Science, University of Veterinary and Animal Sciences, Lahore, Pakistan;* [#]*Department of Biotechnology, Kinnaird College for Women, Lahore, Pakistan;* [‖]*Institute of Animal Science, Guangdong Academy of Agricultural Sciences, State Key Laboratory of Livestock and Poultry Breeding, Key Laboratory of Animal Nutrition and Feed Science in South China, Ministry of Agriculture and Rural Affairs, Guangdong Provincial Key Laboratory of Animal Breeding and Nutrition, Guangzhou 510640, P. R. China; and* [¶]*Animal Production Department, Faculty of Agriculture, Benha University, Moshtohor 13736, Egypt*

ABSTRACT Hematology and serum biochemistry study may provide antique knowledge about the physical status of individuals, making them a valuable tool to differentiate healthy animals from affected animals. We aimed to investigate Steroid safety levels in birds through ex-situ studies at regular therapeutic doses. A total of 100 birds were used for hematology and serum biochemistry. This study was designed into 2 trials over the summer and winter, each comprised 5, 10, 15, and 20 d. Each study group was based on 5 control group birds and 20 experimental group birds. A sum of 2 groups representing 2 different steroids trial groups was treated with therapeutic doses to the stretch of 5, 10, 15, and 20 d each season. A therapeutic dose of each of the steroids was given at the rate of 3 drops 2 times a day to each bird. Analysis of data reveals that steroids had severe effects on bird's (Coturnix coturnix) hematological parameters. In most trials, the hematological effects of bromocriptine as mesylate showed an increase in red blood cell count and white blood cell count. On the other hand, steroid estradiol valerate showed a decrease in these parameters. Effect of steroids on serum biochemistry profile indicate acute damage to vital organs, especially to liver and kidney, indicating an increase in cholesterol, total protein, albumin, urea, and uric acid. The overall effect of steroids on the bird's serum and biochemistry of quails were nearly similar but different only in their intensity.

Key words: brotin, estradiol valerate, hematology, quail, serum biochemistry

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INTRODUCTION

Steroids are essential in biology, medicine, and chemistry (Covey, 2006). Steroid includes all adrenal cortical hormone bile acids, sex hormones, moulting hormones of insects, and active hormone of animals and plants (Sultan and Raza, 2015). The steroid has a peculiar molecular configuration with 4 fused rings. The steroid has performed 2 primary functions: an essential constituent of the cell and modifies the cell's fluidity, and the other is signaling molecule (Shahidi, 2001). Bromocriptine is a semi-synthetic chemical compound obtains artificially or naturally from plant and ergot fungi (Tauchen, 2020). Bromocriptine ergoline is a diverse group of chemical compounds used for vasoconstriction and dopamine agonistic receptor D2 ergoline cause convulsive and gangrenous symptom (Van Weenen et al., 2010). In 1965, a scientist called Sandoz was discovered and first published in 1968 under the brand name of Parlodel (Beekman and Barrow, 2014).

The total bioavailability of oral administration of bromocriptine is 28% (Scranton and Cincotta, 2010). The half-life of bromocriptine is 12 to 14 h after this eliminate from the body by urine (Oshige et al., 2020). Bromocriptine is used to treat acromegaly (is a disease due to pituitary gland abnormal secretion), also used to prolactin level (hyperprolactinemia) like the absence of menstrual periods in women of reproductive age (Amenorrhea) (Aroda et al., 2017). Bromocriptine is used to treat infertility, hypogonadism, and ovarian hyperstimulation

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[1]Corresponding authors: jiangshouqun@gdaas.cn

syndrome, benign tumors produced in the pituitary gland, adrenal gland, and thyroid gland. In reviewing 2014, it was shown that bromocriptine used to suppress milk production after birth cause severe cardiovascular and neurological effects (Elkhier et al., 2017). Previous studies reported bromocriptine (0.2 or 0.6 mg rat-1 d-1) was injected daily during the last 5 or 12 d of estrogen treatment. Data were compared with those obtained for intact control rats. Administration of both doses of estrogen increased serum prolactin levels. No difference in the number of prolactin cells in rats treated with 50 μg estradiol valerate was observed compared to intact adult animals.

In contrast, rats treated with 300 μg estradiol valerate showed a significant increase in the number of prolactin cells ($P < 0.05$) (Ribeiro et al., 1997). Estradiol valerate is a naturally or synthetically produced steroid and sold in brand names like Prygnova, Delestrogen, Prygnon depot (Di Paolo et al., 1982). Estradiol valerate was initially reported in 1940 and commercialised for medicinal use in 1954. Estradiol valerate is medically used in hormone therapy like transgender women, hormonal birth control, menopausal symptoms, and low estrogen levels (Hruska, 1986). It is also used in the treatment of prostate cancer in men. Estradiol valerate is used in Canada, Europe, United States, and throughout the world. For more than 50 yr worldwide, women are used estradiol valerate to prevent pregnancy (Hruska, 1986). According to the Control Center of Disease, 10.5 million people used estradiol valerate by oral contraceptives in 2006 and 2008 for modality and birth control (Johnson, 2010). Estradiol valerate stops the pregnancy by suppressing the ovulation and with its hormone. The change in cervical mucus and integrity of endometrium resulting creates unfavorable conditions for penetrating the sperm (Craig and Stitzel, 2004). The present study was designed to assess the effects of bromocriptine as mesylate and Estradiol valerate on the serum and blood biochemistry of common quails subacutely or chronically stimulated with estrogen to validate an experimental model for the study of the interaction between Bromocriptine as mesylate and estradiol valerate. Data were compared with those obtained for intact or control groups.

MATERIALS AND METHODS

Sample Collection

Up to 100 quail (Coturnix coturnix) were obtained from Bazar, a pheasant family market (Pakistani chowk, DGK). The weight of the birds was nearly from 60 to 80 g, and after purchasing, they were bringing to the zoological laboratory at Ghazi University Dera Ghazi Khan.

Experimental Method

Birds were placed in a wooden box that had bronze wires. Birds were placed from 1 wk to 3 wk in this situation. Physically all the birds were looking mature. Birds were divided into 5 major groups; each had 5 birds. There were 4 experimental groups and one control group for each experimental group. Two steroids, "bromocriptine as mesylate and estradiol valerate," are used in this project. All the birds were orally given the drugs that were prepared in an up-to-date and fresh solution. Birds were weighed from the start day, and their homeostatic conditions, including their temperature, were checked consistently. The procedure started with the slaughtering and cutting of birds of every group from 5 d to 20 d. The overall experiment was performed 2 times, in a different environment, including the climate of the winter season and weather of the summer season. Steroids were given to every bird according to their physical condition regarding their body weight. Bromocriptine as mesylate and estradiol valerate 3 drops to each bird 2 times a day.

Hematological Parameters Collection

Blood was assembled by cutting and dissecting the birds and gathered in the specific tubes used in the labs for safe and secure sample collections cells containing Ethylenediaminetetraacetic acid. The blood obtained by the particular method was used to study and examine the overall parameters, including the biochemical composition of blood and its other characters. For example, we can observe the level of mean corpuscle volume and count the total number of different blood cells and creatinine, urea and uric acids, etc.

Observations of Blood Parameters

Some different characters and ingredients present in the blood were studied by examining the blood in the laboratory. All the characteristics, including every component, were considered, for example, blood cells, cholesterol, etc. The complete blood volume of the cell also contains red blood cells. By utilizing the advanced gadgets, tube-like hematocrit is expressed with the help of a robotic investigatorthat is an electronic device and is not measured with any direct source or method.

Observations of Serological Parameters

The serum was obtained from blood samples and taken in the tubes that are labeled for safe use. This transferred serum was utilized to observe the different ingredients, including the total protein level, urea, uric acid, AST, ALT, cholesterol, total albumin, total creatinine, and creatine kinase values through the laboratory test examination.

Statistical Analysis

All the data were analyzed by statistical methods as Mean ± Standard deviation in version 11 of Pennsylvania. *t*-Tests were applied to find out the relationships between different parameters. The common quails were treated with steroids in the experimental group and

control birds for 5, 10, 15, and 20 d experimental conditions. Statistical method ANOVA was used to find out the relationships between different blood parameters of common quails, including serum and blood parameters.

RESULTS

While the observations during the experimental work, there are following signs and symptoms were observed. There was seen highly blackish color of eyes in some birds treated with prygnova drug, and birds scratch their legs with beaks that also show some allergic reactions within the body. The birds became aggressive, and their hunger increased. The birds that were given the drug Brotin show bloody waste and some symptoms of diarrhea. These pathological signs, that is, body swelling, roughly skin, abnormality in the proximal part of heart, enlarged stomach, air-fill in the intestine, the black color of the intestine, and pale liver, have been observed (Figure 1). The treatments were compared with the healthy control group.

Hematological and Serological Parameters

We collected blood samples from treatment and control groups to analyze the hematological parameters at different treatment days' intervals. We observed the hematological parameters at d 5, 10, 15, and 20 post-treatments. In the first 5 days' summer trial, urea, total protein, mean corpuscle volume, and cholesterol highly decreased and indicated the severe effects of Bromocriptine as mesylate on hematology and serum of common quails. The level of creatinine, ALT, and AST highly increased and showed more significant effects of steroids. All other remaining hematological parameters remain unchanged except for minor variations (Figure 2). While in the first 5 d experiment, by using Prygnova, an increase in urea and uric acid concentration was observed. The creatinine shows a significant decrease in intensity as compared to the standard group. ALT increases to some extent, and there is a decrease in AST concentration in the first 5 d trial. There is no change in the concentration of cholesterol level in the first 5 d of the trial. The remaining parameters show slight change by decreasing the values (Figure 2). These remaining parameters are total protein, albumins, total red blood, and white blood cells. Mean corpuscles volume increased significantly. Overall the behavior of birds was slightly changed as they showed aggressive behavior, and specific spots were seen on the eyes.

While on 10 d post-treatment of Brotin, the creatinine, AST, total proteins, albumin, and mean corpuscle volume remains unchanged. They are unchanged in terms of their values. The number of packed cells, urea, uric acid, and ALT in the blood rose dramatically. The levels of the other hematological parameters have decreased somewhat. The overall metrics of hematology show variations in values, and there is a decrease in some parameters include creatinine, uric acid, cholesterol, and packed cell volume (**PCV**) on Prygnova treatment. These parameters show decreased consistently. The other parameters show an increase in values (Figure 3).

Figure 1. Observed treatment signs in dissected birds. (A) Brotin treated birds; (B) prygnova treated birds; (C) swelling of the small intestine in brotin treated birds; (D) brotin treated birds swelling of testes; (E) body swelling Brotin treated birds; (F) control bird.

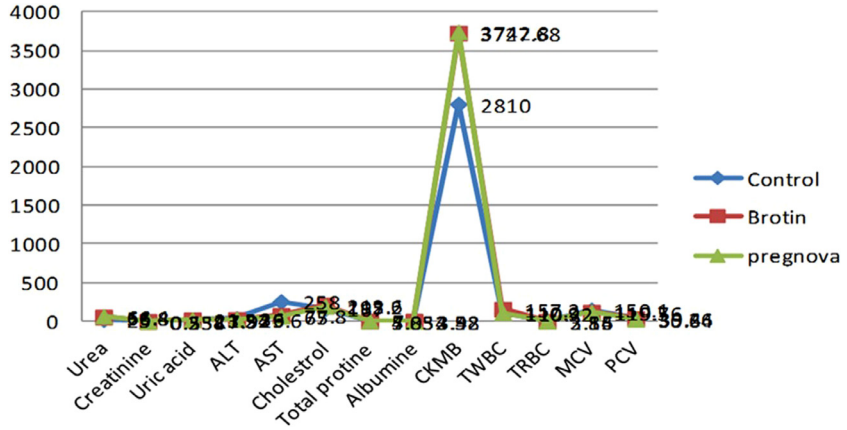

Figure 2. Hematological and serological parameters were observed in the treatment and control group 5 d post-treatment of brotin and prygnova in common quails.

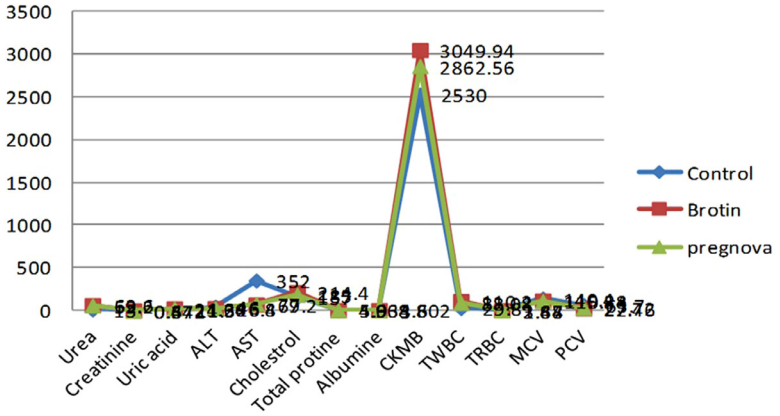

Figure 3. Hematological and serological parameters were observed in the treatment and control group 10 d post-treatment of brotin and prygnova in common quails.

On 15 d post-treatment, we observed that urea, ALT, and AST increased significantly, showing the severe effect of steroids on hematological parameters. The remaining parameters, including cholesterol, total proteins, albumins, whole blood cells, and mean corpuscle volume, decrease. Creatine remained unchanged on Brotin treatment. While on Prygnova treatment, we observed that the urea, uric acid, and cholesterol increased compared to the control group of 15 d. Except given above, all the other parameters, including total protein and albumin, remain unchanged except for minor variance (Figure 4). These steroids affect sexual behaviors in quail. Steroids are used to evaluate the effects of testosterone. To assess the testosterone effects on the copulation and cloacal glands in birds. When administered testosterone in females, the female fails to copulate and reduces the cloacal glands.

On 20 d post-treatment, we observed that all the hematological parameters increased greatly and consistently. Only total red blood cells show no change and

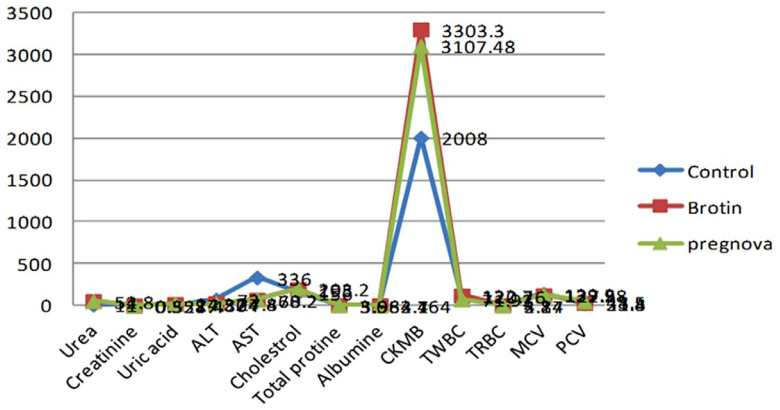

Figure 4. Hematological and serological parameters were observed in the treatment and control group 15 d post-treatment brotin and prygnova in common quails.

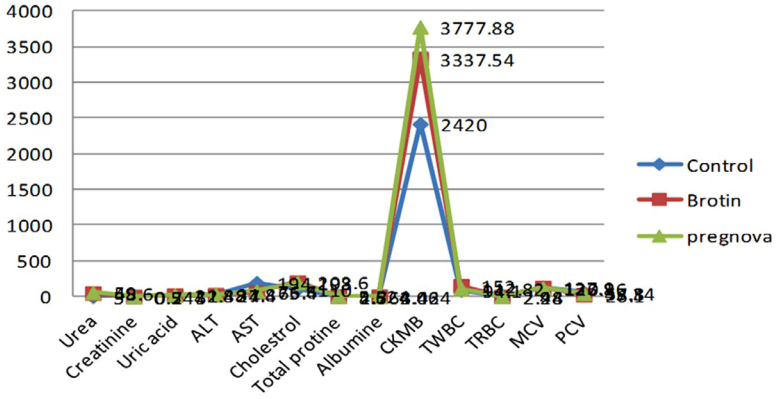

Figure 5. Hematological and serological parameters were observed in the treatment and control group 20 d post-treatment of brotin and prygnova in common quails.

remain the same as in the control group. AST, uric acid, and urea levels increase greatly. All the other parameters, including blood cells, total protein, and albumin, were changed by decreasing values on Brotein treatment. While urea, uric acid, and cholesterol decrease greatly to a great extent. These parameters show the effects of the steroid Prygnova greatly. All the other parameters, including PCV and blood cells, total protein, and albumin, remain unchanged except for little change (Figure 5). The Prygnova administration in healthy birds with different dosage changes in the blood pressure, body weight, adrenal gland size, and blood serum. The dose rate 2 mg/kg/d for 2 wk, 1 mg/kg/d for 4 wk and 0.4 mg/kg/d in 3 wk. The change was mild but not significantly different from baseline values.

DISCUSSION

The current research was objected to finding out the impact on the hematology of common quail. For this purpose, data were obtained through experimental work on common quail. The results of the current study follow the previous empirical literature on the hematology of common quail. First, the behavior of the common quail was affected by the utilization of steroids—lengthened use of a large dose of steroid results in several side effects. The use of Bromocriptine as mesylate shows severe effects on physiology and morphology (Nongonierma and FitzGerald, 2015). In this trial, the morphological and physical behavior of the birds were changed enormously. Some birds form a blackish spot that looks like tumors on their eyes, and their skin becomes roughly in appearance. The aggressive behavior of all birds was also increased clearly.

They show clear aggression during the feeding procedure and try to escape from the stainless-steel cages by making noise and pinching the wires of cages aggressively (Nirenberg, 2013).

Moreover, their hunger has also been increased. In the first 5 d summer trial, urea, total protein, mean corpuscle volume, and cholesterol highly decreased and indicated the severe effects of bromocriptine as mesylate on hematology and serum of common quails. The level of creatinine, ALT, and AST highly increased and showed more significant effects of steroids. All other remaining hematological parameters remained unchanged except for minor variations (Figure 2). In stress conditions, the endocrine system secretes the glucocorticoids that help in emergency conditions (Garbacz et al., 2017). During prenatal increase, the glucocorticoids concentration in body serum was modulated in body weight. Brotin consumption in pregnant women significantly increased body weight and leptin in serum (Al-Shboul et al., 2019). They were drinking one μg/ml of dexamethasone with water from 13d of pregnancy until delivery modulates the body temperature (Mizejewski and Butterstein, 2006). The results showed that long-lasting glucocorticoids consumption during prenatal periods increases body weight (Hayashi et al., 2004; Afzal et al., 2019). In 10 d, trial, creatinine, AST, total proteins, albumin, and mean corpuscle volume remains unchanged. They remain the same without any change in values.

PCV, urea, uric acid, and ALT level increased highly. The other hematological parameters show a slight decrease in the values (Figure 4). Ergosterols and phytosterol are found respectively in animals and plants cells (Ito et al., 2017). The 100 g dry weight of mushroom consists of 10 to 100 milligrams of ergosterols, and oxygen is utilized to synthesize ergosterols (Wani et al., 2019). In 15 d trial, the level of urea, ALT, and AST increased significantly, which shows the severe effect of steroids on hematological parameters. The remaining parameters, including cholesterol, total proteins, albumins, total blood cells, and mean corpuscle volume, decrease. Creatine remained unchanged. In 20 d, summer trials, all the hematological parameters increased significantly and consistently. Only total red blood cells show no change and remain the same as the control group (Figure 5).

We used prygnova in the current experimental investigation at the same time as brotin. We used prygnova and observed different fluctuations in hematological and serum parameters, including total protein, cholesterol, urea, uric acid, and Astatine transferase in the experimental group and its relation with the control group. In the first 5 d experiment, by using prygnova, an increase

in urea and uric acid concentration was observed. The creatinine shows a more significant decrease in the concentration as compared to the standard group. ALT increases to some extent, and there is a decrease in AST concentration in the first 5 d trial. There is no change in the concentration of cholesterol level in the first 5 d trial (Figure 2). By lowering the settings, the remaining parameters exhibit a slight difference. Total protein, albumins, total red blood cells, and white blood cells are the remaining criteria. The number of mean corpuscles rose dramatically. Overall the behavior of birds was slightly changed as they showed aggressive behavior, and specific spots were seen on the eyes. Also, birds start scratching their legs by pinching their beaks (Kindler et al., 1991; Afzal et al., 2021). It was clarified that if there is an increase in enzyme quantities in the blood chemistry with particular reference to serum, it may severely affect the level of heat-stable alkalis that are very helpful in examining hematopathology and other characters. The increased values or concentration of alanine amino corticosteroid-produce that alkaline phosphatase (Sagir et al., 2008; Afzal et al., 2021). In 10 d, trials, the overall parameters of hematology show variations in values, and there is a decrease in some parameters include creatinine, uric acid, cholesterol, and PCV. These parameters show it decreased consistently in these 10 d trials. The other parameters show an increase in values during the experiment, 17 B-estradiol transduction, and with or without vaginal progesterone infusion in 6 postmenopausal women (Stachenfeld et al., 2000).

The infusion of naloxone into 2 d consecutive in 4 h in postmenopausal women (Cagnacci et al., 1990). Thermistor placed in rectum and measures the variation of body temperature. The administration of 17 B-estradiol body temperature variation records (P less than 0.01), the infusion records of naloxone body temperature variation (P less than 0.01), and the administration of progesterone body temperature variation records (P less than 0) were all found to be statistically significant (Cagnacci et al., 1990). The administration of naloxone induced a decrease body temperature was more significant than during 17 Bestradiol administration than before treatment (P less than 0.02)—the progesterone to 17 Bestradiol administration increased body temperature 0.4° from the baseline value. In recent study reveals that the use of steroids was widespread in the general population. The use of steroids is most common in obese people than nonobese people. The steroids administration rate for obese persons was 27.0%, and for nonobese people was 11.9% (Savas et al., 2017). There was a large difference in the use of corticosteroids in obese and nonobese people. Reporting was that the users of corticosteroids increase the body weight in obese persons by 10.5% (Savas et al., 2017). When administered testosterone in females, the female fails to copulate and reduces the cloacal glands.

Indeed, the use of estradiol-17β applies to male quail, activates the copulation, and 5α dihydrotestosterone activates the development of cloacal glands (Balthazart and Ball, 2018). In this study, 41 castrated male and female quail were implanted with 2 steroids like estradiol-11β and 5α dihydrotestosterone. There is a small change in the morphology and behaviors of quail. In 20 d, summer trial, urea, uric acid, and cholesterol decrease greatly to a great extent. These parameters show the effects of the steroid prygnova greatly. All the other parameters, including PCV and blood cells, total protein, and albumin, remain unchanged except for little change (Figure 5). The Prednisolone administration in healthy doges with different dosage changes in blood pressure, body weight, adrenal gland size, and blood serum (Park et al., 2011). The dose rate 2 mg/kg/d for 2 wk, 1 mg/kg/d for 4 wk and 0.4 mg/kg/d in 3 wk. The change was mild but not significantly different from baseline values. They show some minimal effect with a low dosage of prednisolone (Park et al., 2011). The study indicates that some steroids modulate the temperature of the body. Steroids are thermogenic substances in rats, birds, and hibernators. Progesterone in rats demonstrated the thermogenic effects. The steroids used in the experimental analysis have a greater effect on their homeostatic activity (Sparkman et al., 2011). The enzymes present in the birds show a response to these steroids that can affect their temperature. Estradiol effects were investigated on the thermoregulatory responses induced by methanol in ovariectomized rats.

CONCLUSIONS

The overall effect of steroids on the bird's serum and biochemistry of quails were nearly similar but different only in their intensity. The present study suggests that Bromocriptine as mesylate has less severe adverse hematology and blood biochemistry impacts on common quails than Estradiol valerate. Bromocriptine as mesylate can cause pulmonary fibrosis, skin rashes, swelling of tongue and throat, and Extreme tiredness in birds. The Estradiol valerate can cause ovarian cancer, Eye disorder, cardiac disorder, hepatobiliary disorders in birds. The long-term use of steroids can cause severe complications by affecting various body organs like the liver, kidney, heart, etc.

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DISCLOSURES

The authors declare no conflict of interest.

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