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Studies on the Effects of Enrofloxacin Overdose on Different Health Parameters in Broiler Chickens

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The effect of 10 times (10x) overdose of enrofloxacin was studied in broiler chickens. One hundred and eighty chicks were classified in 3 equal groups. The first group received normal theurapeutic dose of enrofloxacin (1x) in drinking water for the first 5 consecutive days of age and repeated again at 24th -28th day of age. The second group received 10x (overdose) at the same ages. The third group was left non-medicated as a control group. Blood samples were taken on the 6th, 14th, 29th and 34th day of age for different laboratory tests. Enrofloxacin at 10x caused a decrease in the value of the following parameters: HI antibody titers to NDV vaccine at the 14th and the 34th day of age, serum albumin at the 10th day of age, hemoglobin at the 29th and the 34th day, lymphocytic count and IBDV ELISA titers at 29th day of age, uric acid at 29th day, phagocytic activity at 34th day, Lactobacillus spp. count in duodenum, feed conversion efficiency and body weight gain. The 10x (overdose) increased serum urea and creatinine at 29th day of age, serum AST and ALT at 29th and 34th day of age, and heterophilic count. Histopathological degeneration in liver, spleen, kidneys, bursa of Fabricius and thymus were demonstrated by 10x (overdose) of enrofloxacin. Challenge with vNDV caused 66.6% mortality in birds received the 10x (overdose) compared with 33.3% in the vaccinated non treated control group.

Enrofloxacin belongs to fluoroquinolones. It was developed in 1983 for controlling Gram negative, Mycoplasma and some Gram positive bacteria and was the first fluoroquinolone approved for use in animals (Martinez *et al.,* 2005). Enrofloxacin was first synthesized after series of chemical modifications of nalidixic acid. The antibacterial properties and absorption of the molecule were increased and its adverse effects were reduced (Albercht, 1977; Wolfson and Hooper, 1985; Walker *et al.,* 2000).

Chloramphenicol, Nitrofurans, Erythromycin, Tylosin and Chlorotetracycline were said to lower the hemagglutination inhibiting (HI) titers to NDV and impaired phagocytosis (Paningrahy *et al.,* 1979; Nagi *et al.,* 1984; Afifi, 1987; Rzedzicki *et al.,* 1991). Gentamicin and Oxytetracycline decreased IgA, IgM, IgG and Ig bearing cells in large intestine and cecal tonsils and interfered with cell mediated immunity (Grondel *et al.,* 1985). Nalidixic acid caused hemolytic anemia, leukopenia and thrombocytopenia (Baulter, 1969; Gilbersto and Jones, 1972).

Tokarzewski (2002) mentioned that enrofloxacin and chloramphenicol decreased the level of IgG after vaccination with *Salmonella enteritidis*, and NDV). Fleischer *et al.,* (2000) added that enrofloxacin decreased lymphocytes starting from 17th till 35th day of age when chickens were fed a diet supplemented with enrofloxacin, while increased leukocytic count; and neutrophils. The humoral immune response following Newcastle disease vaccination was not reduced by treatment with enrofloxacin (Behr *et al.,* 1988). El–Mosallamy (1995) mentioned that enrofloxacin had a slight depressant effect on the HI titer and decreased the protective power of NDV vaccine, suppressed the lymphocyte stimulation index to concavalin–A, pokeweed and phytohemagglutinin.

Perdigon *et al.,* (1998); Nemcova *et al.,* (1999); Mokhbatly and Asawy (2003) concluded that addition of probiotics in feed or drinking water of broilers improved the host defense against infection, and confirmed the immunostimulating effects on cell mediated immunity and initiated the induction of lymphokinase and immunoglobulins.

During the oral administration of fluoroquinolones, aerobic fecal flora were almost entirely abolished, but the count of Lactobacillus

spp. in the intestine returned back 7 days after stop of treatment (Bramfitt *et al.,* 1984; Sainsbury, 1992; El–Sayed and Ahmed, 1997).

Because of the large-scale usage of enrofloxacin in poultry for treatment of complicated chronic respiratory disease (CCRD), Colibacillosis, Salmonellosis, and Fowl Cholera, a detailed knowledge should be known in case of mistaken overdosing. This study was designed to investigate the effect of 10 times overdose (10x) of enrofloxacin on different biochemical, hematological, immunological and histopathological parameters in broiler chickens.

Material and methods

Chickens. 180, one-day old, Hubbard, broiler chicks were obtained from a local hatchery in Alexandria. They were divided randomly on the first day of age into 3 equal groups, whereas each group was subdivided into 3 replicates of 20 birds, housed separately on floor pens under the same conditions. The treatments were as follows:

Group (1) received enrofloxacin at a usual therapeutic dose, 1x (50 ppm in drinking water, equavalent to 10 mg/kg B.wt.(Scheer, 1987) for the first five consecutive days of age. They were treated again with enrofloxacin from day 24^{th} - 28^{th} of age at a dose of 10 mg/kg B.wt.

Group (2) received enrofloxacin as 10x overdose (500 ppm in drinking water, equavalent to 100 mg/kg B.wt.) for the first five consecutive days of age. They were treated again with enrofloxacin from day 24^{th} -28^{th} of age at a dose of 100 mg/kg B.wt.

Group (3) was left without treatment and fed a basal diet as a negative control.

All the birds in groups 1,2 and 2 replicates of group 3 were vaccinated against NDV, but one replicate of group 3 was left unvaccinated as a control for challenge with vNDV at the end of the experiment. The birds were vaccinated with Hitchner B1 (eye drop) at 7^{th} day of age, with Bivalent NDV + IBDV killed oil adjuvant vaccine (i.m.) at 12^{th} day, Gumboro live intermediate (eye drop) at both 14^{th} and 28^{th} day, La Sota (eye drop) at 17^{th} and 30^{th} day of age.

Ration. The chicks were fed non medicated balanced commercial starter ration (basal diet) with 23% protein, 2950 k calorie/kg bought from Cairo Company for Poultry®.

Drug. The generic name is Enrofloxacin 10% (Baytril®, Bayer, Germany), while the chemical name is 1–cyclopropyl-7-(4–ethyl–1–piperazinyl)–6–fluoro–1.4–dihydro–4–oxo–3-quinolone carboxylic acid. The molecular formula is $C19H22FN_3O_3$ and the molecular weight: is 359.4.

Sampling. Heparinized as well as non–heparinized blood samples were collected at the 6^{th}, 10^{th} , 14^{th} , 29^{th} and 34^{th} day of age from 6 birds from each replicate (18 birds per group).. The heparinized blood samples were used for red blood cells count, differential leukocytic count (Schalm *et al.,* 1975) and phagocytic activity for *Candida albicans* (Woldehiwat and Rowan, 1990). The non–heparinized samples were used to determine total serum proteins (Henry, 1964), albumin (Young *et al.,* 1975), liver function tests (ALT, alanine aminotransferase and AST, aspartate aminotransferase according to Reitman and Frankel, 1957) and kidney function tests: creatinine, uric acid, urea according to Fossatti and Prencipe (1980) from 6 birds from each replicate (18 birds per group). Other non-heparinized blood samples were taken at 6^{th}, 14^{th} and 34^{th} day of age and used for hemagglutination inhibition for NDV vaccine (Anon, 1971). Other blood samples taken at 29^{th} and 34^{th} day of age were used to for testing antibodies to Gumboro in ELISA (Cosgrove, 1962). At the age of 29^{th} day, 9 birds per group were killed and their livers, spleens, thymus and bursa of Fabricius were weighed and their relative weight to body weight ratios were calculated according to Rizvi and Anjum (1999). For Lactobacillus spp. count, the duodenal loops from the same 9 birds from each group, on the 29^{th} day of age, were split opened and one gram of the contents was collected and put in 10cc Rogosa broth and incubated for 2 hrs. at 37 C, tubes were then diluted in sterile PBS, and transfered onto Rogosa agar. Cultures were incubated for 24 hrs in candle jar at 37 C, and colonies were counted per gram of the duodenal contents (Buratto, 1983).

Also from these 9 birds, samples from the internal organs (liver, spleen, kidneys, thymus and bursa of Fabricius) were taken and processed for histopathological examination according to Bancroft and Stevens (1990).

Body weight gain and feed consumption were recorded weekly and at the end of the experiment (34^{th} day of age) for determination of feed conversion ratio.

Challenge with velogenic Newcastle disease virus. Fifteen chicks from each group 1,2,3 that were vaccinated with NDV vaccines, in addition to 15 non–vaccinated chickens from group 3, were kept for challenge with vNDV at the age of 34^{th} day. Chicks were inoculated (i.m.) with 0.2

ml of allantoic fluid previously titrated to contain 10^6 LD_{50}/bird of velogenic NDV (kindly supplied by the Dept. of Poultry and Fish Diseases, Faculty of Vet. Med., Alexandria Univ.). Mortality and signs were observed for 10 days PI.

Results and Discussion

In (Table 1), the haemoglobin concentration at 29th and 34th day of age in group 2 (10x, overdose) was significantly lower than the other two groups (1 and 3). Gilbersto and Jones (1972). admitted the relationship between nalidixic acid (mother nucleus of enrofloxacin) and the incidence of anaemia and leukopenia. No significant effect of the 10x (overdose) on RBCs count or haematocrit was seen.

In group (2) (overdose, 10x), the lymphocytic count also decreased significantly at 34th day of age (Table 2). This may be a reflection for the histopathological alterations in both thymus and bursa of Fabricius which showed dispersion and depletion of the lymphocytic contents with several areas of lymphoblastic degeneration (Fig. 3,4,5). These changes might be attributed to the inhibition of RNA and protein synthesis by enrofloxacin (David *et al.,* 1988). But in group (1) (therapeutic dose, 1x) enrofloxacin had non–significantl effect on lymphocytic count. This was also noticed by El–Mosallamy (1995) when dosed enrofloxacin at 10 mg/kg for broilers for 3 successive days with no effect on the lymphocytic count.

In group (2) (overdose, 10x) a transient decrease in leukocytic count at 6th day of age (after the first dose) was seen, which may be explained by the higher susceptibility of the haemopiotic system of the baby chick to the drung at young age. Also transient and significant decreases in basophilic count were seen at 29th day of age (after the second dose) in the same group.

Allover the experiment, heterophils were significantly higher in both 1x and 10x treatments than the control group 3 (Table 2). This result agrees with Fleischer *et al.,* (2000) who mentioned that enrofloxacin treatment increased heterophils. This may explain the inflammatory process in thymus, bursa, and spleen (Fig. 2,3,4,5). The 10x overdose decreased lymphocytes, basophils and esinophils almost allover the experiment, which may have an effect on immune response.

Regarding serum proteins (Table 3), only a significant decrease in the level of serum albumin was noticed on day 10 (4 days after the first treatment) in group 2 (10x overdose). Albumin is the major protein constituent of serum which regulates the distribution of extracellular fluid and transport of many substances. It is synthesized in the liver. Low levels are associated with liver diseases (Doumas and Biggs, 1976). We noticed that the 10x overdose in group 2 significantly decreased the albumin at 10 days of age (after the first dose) reflecting the transient adverse effect on liver function, especially in young age. Our finding agrees with Shawky *et al.,* (1998) who reported that high dose of enrofloxacin caused hypoalbuminaemia.

Higher doses of enrofloxacin was said to cause a dose-dependent histopathological changes in liver, lung, heart and kidney (Shawky *et al.,* 1998).

Serum ALT enzyme is a specific and indicative for liver destruction. The only elevation of serum ALT was only in the 10x overdose group at 29th days of age (72.9 vs. 67.3) but after 6 days of withdrwal of treament the values of ALT returned to nearly the same value as the control (88.0 vs. 87.3, respectively) (Table 4). This correlated the results of histopathology of liver (taken on the 29th day of age, just after the last dose of enrofloxacin) where noticeable hepatocytic vacuolation and hydropic degeneration, associated with vascular congestion and degeneration of lymphoid foci were seen (Fig 1). Our findings were supported by Shawky *et al.,* (1998) who found that enrofloxacin at 400 ppm given for 6 weeks had histopathological effect on liver.

The serum AST enzyme is not a specific parameter for liver health as it measures the degeneration in heart and somatic muscles as well. AST enzyme was found to be higher than the control group in those receiving 10x or 1x enrofloxacin (but not significantly), at both 29th and 34th days of age.

There was an increase in the serum AST on the 6th day of age (just after the first course) in the 10x overdose group compared with the control non treated group 3 (155.3 vs. 122, respectively), then decreased afterwards and increased again after the second course on the 29th day compared with the control (194.7 vs. 168.7, respectively), then decreased again after withdrwal of the treament till the end of the experiment at 34th day of age.

The kidney function tests (Table 5) showed a transient significant increase in values of serum

urea and creatinine after the first course at 6 day in group 1 (normal dose, 1x) and at 29th day in group 2 (overdose, 10x). These biochemical changes were parallel to histopathological alterations in kidneys which showed congestion, tubular degeneration, and area of hemorrhages (Fig. 6).

At the 34th day of age, the phagocytic activity (Table 6) was lower in groups (1) and (2) than the control group (3). The decrease in phagocytosis and in leukocytic count (especially basophils, lymphocytes and esinophils) in young age and also at 34th day may be associated with the decrease in the HI titer for NDV and ELISA titer for IBDV.

Regarding the effect of enrofloxacin on the humoral immune response, at 14th day, the HI titer for NDV vaccines in group 2 was lower than the control group 3. Table (7) shows that no significant effect of normal dose on HI titers for NDV. This was in agreement with Behr *et al.,* (1988); Rzedzicki *et al.,* (1991); Shojadoost *et al.,* (1999) who reported that enrofloxacin treatment (10 mg/kg B.Wt.) caused a slight decrease or caused no changes in HI titers to NDV. Also, ELISA titers for IBDV, were decreased on 29th and 34th day (Table 8). The decrease in antibody titers may be attributed to the adverse effect on phagocytic activity, decreased lymphocytes basophils, esinophils and the adverse histopathological effect on bursa of Fabricius, thymus and spleen tissues and to the inhibitory effect of enrofloxacin on the lactobacillus spp. in the gut.

Table (9) shows that enrofloxacin overdose (10x, group 2) decreased the count of Lactobacillus spp. to the least value in the duodenum. Also, the normal dose (1x) led to moderate decrease of Lactobacillus spp. count. The same notice was taken by El–Sayed and Ahmed (1997) who added that Lactobacillus spp. count returned to normal level after 7 days. Enrofloxacin inhibits Lactobacillus spp. may be in the same mechanism of action on pathogenic bacteria.

Regarding the relative organs weight to body weight ratio, our results (Table 10) indicated that there was no significant effect of treatment of relative weight of bursa of Fabricius. The bursa of Fabricius was twice in weight as the spleen in group (2) received 10x enrofloxacin which was similar to observation of Enrique (1999) who said that in normal broiler life, bursa should be always larger than spleen during the first 35 days of age. There was no significant difference in liver relative weights among different groups. Sakar *et al.,* (2004) also mentioned that relative liver weight was not affected by enrofloxacin treatment.

Body weight gain and feed conversion ratio in group (1) (Table 11) treated by normal dose, were not different from the non–treated control group (3), which correlates with El–Sayed and Ahmed (1997) who gave one course of enrofloxacin from 10–15 days of age at normal dose and found no effect on the body weight. Body weight gain and feed conversion ratio in 10x overdose was significantly the worst among other 2 groups (Table 11). Suppression of Lactobacillus spp. by 10x overdose of enrofloxacin may had led also to a reduction in body weight of this group (2) received 10x dose. Brander *et al.,* (1993); Ellakany *et al.,* (2004) concluded that Lactobacillus spp. enhanced production and growth through increased metabolizing energy, growth promoting factors as vitamin B complex, vitamin A, trace elements, proteases, amylases and lipases.

Gross examination of the internal organs of 9 birds at the 29th day old from each group (slaughtered for histopathological examination) showed that no detectable lesions in the organs of birds in group (1) (1x). Whereas birds of group (2) (10x) had congested and enlarged livers, besides small sized bursa of Fabricius and thymus, and congested spleens. This finding was in accordance with the results of histopathology (Fig. 1, 6). Even the relative weight of bursa and thymus which were not different from the control, but the absolute weights were clinically reduced than the control, because the body weight was also reduced with the overdose (10x) treatment.

The mortality after challenge with vNDV (Table 12) was 95% in non–vaccinated, non-treated birds, 66.6% in both vaccinated and treated groups 1 (1x) and group 2 (10x), and 33.3% in vaccinated non–treated control group (3). This means that both the normal and the overdose of enrofloxacin had decreased equally the rate of protection against vNDV challenge. These findings were in consistence with El–Mosallamy (1995) who recorded that the mortality after challenge with vNDV in vaccinated treated group was 10% versus 50% in vaccinated non–treated group. The low protection against vNDV challenge may be due to the adverse effect of enrofloxacin on phagocytosis, Lactobacillus spp. count in intestine, low HI antibody titers, low serum

proteins, and histopathological deformities in the lymphoid organs. After challenge with vNDV, birds of group 2 (overdose, 10x) showed respiratory signs that were much milder than in group 1 (1x). This difference in severity of respiratory signs might be due to bactericidal effect of high level of enrofloxacin in the blood of birds in group 2, which might had suppressed the *E. coli* and *Mycoplasma* in their respiratory tract which usually aggrevate the infection with vNDV.

Conclusion

Enrofloxacin at overdose (10x), had an adverse effect on an *in-vitro* phagocytosis of *Candida albicans*, the lymphocytic count, HI antibody titers to NDV vaccines and protection rate after challenge with velogenic NDV. There was a correlation between reduction in the size of bursa of Fabricius and thymus, decreased lymphocytic count, increased heterophil count, and the histopathological alterations in both thymus and bursa of Fabricius which showed a dispersion and depletion of the lymphocytic contents with several areas of lymphoblastic degeneration. Allover the experiment, heterophils were significantly increased. These adverse effects on host might be attributed to the inhibition of RNA and protein synthesis by enrofloxacin.

The overdose of enrofloxacin increased the levels of both serum ALT and AST enzymes, which correlated the histopathological changes in the liver in the form of congestion with dilated vein and hydropic degeneration. Overdose of enrofloxacin (10x) decreased drastically the count of Lactobacillus spp. in the duodenum, which in combination with other factors as alterations in liver and spleen, and adverse effect on immune parameters had an adverse effect on the body weight gain, and subsequently the feed conversion. It was noticed from the results that young chicks (under 2 weeks of age) were relatively more susceptible to enrofloxacin than older ages (4-5 weeks).

Table (1): Values of haematological parameters at different testing intervals.

Groups	RBCs (10^6/cmm)	Haemoglobin (g/dl)	Haematocrit (%)	WBCS (10^3/cmm)
at 6th day of age				
1 (1x)	2.3 ± 0.1 a	13.5 ± 1.2 a	22.9 ± 4.1 a	17.2 ± 0.2 b
2 (10x)	2.4 ± 0.1 a	14.3 ± 0.7 a	27.2 ± 3.6 a	17.9 ± 0.2 b
3 (control)	2.3 ± 0.1 a	12.6 ± 0.7 a	24.8 ± 1.1 a	20.9 ± 0.5 a
at 10th day of age				
1 (1x)	2.6 ± 0.1 a	16.1 ± 0.4 a	36.5 ± 0.6 a	18.8 ± 0.4 a
2 (10x)	2.3 ± 0.1 b	13.9 ± 0.9 b	31.5 ± 0.3 b	18.2 ± 0.1 a
3 (control)	2.3 ± 0.03 b	12.7 ± 0.3 b	30.1 ± 0.9 b	19.4 ± 0.9 a
at 29th day of age				
1 (1x)	3.8 ± 0.1 a	13.3 ± 0.3 b	35.8 ± 1.9 a	22.2 ± 0.7 a
2 (10x)	3.4 ± 0.2 a	13.4 ± 0.2 b	29.0 ± 2.8 a	22.5 ± 0.3 a
3 (control)	3.6 ± 0.2 a	14.6 ± 0.2 a	29.0 ± 2.4 a	21.9 ± 0.8 a
at 34th day of age				
1 (1x)	3.7 ± 0.2 a	14.7 ± 0.4 ab	—	20.7 ± 0.9 a
2 (10x)	3.4 ± 0.3 a	14.0 ± 0.2 b	—	22.2 ± 0.7 a
3 (control)	3.3 ± 0.2 a	15.9 ± 0.7 a	—	20.8 ± 1.3 a

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 18 birds.
Values were adjusted to one decimal number.

Table (2): Values of differential leukocytic counts of chicks at different intervals

Groups	Lymphocytes (%)	Monocytes (%)	Basophils (%)	Eosinophils (%)	Heterophils (%)
at 6th day of age					
1 (1x)	55.7 ± 0.8 a	1.8 ± 0.3 a	7.8 ± 0.4 a	10.0 ± 0.4 a	24.8 ± 1.1 a
2 (10x)	56.3 ± 1.0 a	1.9 ± 0.3 a	8.3 ± 0.5 a	10.2 ± 0.8 a	23.3 ± 1.5 a
3 (control)	58.4 ± 1.5 a	2.6 ± 0.7 a	9.0 ± 0.5 a	11.0 ± 0.8 a	19.0 ± 1.9 b
at 10th day of age					
1 (1x)	60.7 ± 1.2 a	1.6 ± 0.3 a	8.3 ± 0.5 a	8.8 ± 0.5 a	20.7 ± 1.6 a
2 (10x)	60.4 ± 1.0 a	1.9 ± 0.4 a	8.4 ± 0.5 a	10.2 ± 0.6 a	19.1 ± 1.4 a
3 (control)	60.6 ± 1.5 a	2.2 ± 0.4 a	8.8 ± 0.6 a	10.0 ± 0.5 a	18.5 ± 1.6 a
at 29th day of age					
1 (1x)	51.4 ± 0.8 ab	1.3 ± 0.2 a	7.4 ± 0.4 ab	9.6 ± 0.3 a	30.2 ± 1.0 a
2 (10x)	52.9 ± 0.8 a	1.8 ± 0.3 a	6.9 ± 0.4 b	9.8 ± 0.4 a	28.4 ± 1.2 a
3 (control)	50.2 ± 1.1 b	1.1 ± 0.2 a	8.2 ± 0.4 a	10.0 ± 0.4 a	30.6 ± 1.1 a
at 34th day of age					
1 (1x)	46.8 ± 0.5 ab	1.3 ± 0.2 a	8.4 ± 0.4a	8.6 ± 0.5 a	34.8 ± 0.8 ab
2 (10x)	45.7 ± 0.7 b	1.7 ± 0.2 a	7.5 ± 0.4 a	8.4 ± 0.5 a	36.7 ± 1.4 a
3 (control)	47.9 ± 0.7 a	1.1 ± 0.2 a	8.1 ± 0.5 a	9.5 ± 0.4 a	33.4 ± 0.8 b

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 18 birds.

Table (3): Values of total protein, albumin, and globulin

Groups	Total protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)
at 6th day of age			
1(1x)	3.2 ± 0.3 a	0.3 ± 0.11 ab	2.9 ± 0.3 a
2(10x)	2.6 ± 0.2 ab	0.5 ± 0.1 a	2.1 ± 0.1 b
3(control)	2.2 ± 0.1 b	0.2 ± 0.1 b	2.0 ± 0.1 b
at 10th day of age			
1(1x)	5.6 ± 0.2 a	0.2 ± 0.01 ab	5.4 ± 0.2 a
2(10x)	5.1 ± 0.3 a	0.1 ± 0.01 b	5.0 ± 0.3 a
3(control)	5. ± 0.2 a	0.2 ± 0.02 a	5.2 ± 0.3 a
at 29th day of age			
1(1x)	4.3 ± 0.3 a	2.4 ± 0.4 a	1.9 ± 0.1 a
2(10x)	4.6 ± 0.5 a	2.8 ± 0.4 a	1.8 ± 0.1 a
3(control)	4.2 ± 0.3 a	2.3 ± 0.4 a	1.9 ± 0.1 a
at 34th day of age			
1(1x)	5.0 ± 0.3 a	4.1 ± 0.3 a	0.9 ± 0.1 a
2(10x)	6.3 ± 0.3 a	4.9 ± 0.2 a	1.4 ± 0.3 a
3(control)	5.7 ± 0.4 ab	4.9 ± 0.5 a	0.9 ± 0.3 a

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 18 birds.
Values were adjusted to one decimal number.

Table (4): Values of liver function tests.

Groups	AST (U/l)	ALT (U/l)
at 6th day of age		
1 (1x)	128.0 ± 7.0 a	15.1 ± 1.4 a
2 (10x)	155.3 ± 15.0 a	16.7 ± 4.9 a
3 (control)	122.0 ± 8.6 a	18.1 ± 1.2 a
at 10th day of age		
1 (1x)	156.8 ± 9.3 a	17.0 ± 1.6 a
2 (10x)	133.7 ± 5.4 a	17.8 ± 3.2 a
3 (control)	161.5 ± 16.7 a	17.3 ± 2.5 a
at 29th day of age		
1 (1x)	202.0 ± 35.7 a	63.7 ± 5.2 a
2 (10x)	194.7 ± 2.5 a	72.9 ± 3.6 a
3 (control)	168.7 ± 23.2 a	67.3 ± 6.4 a
at 34th day of age		
1 (1x)	91.7 ± 2.1 a	82.8 ± 2.7 a
2 (10x)	94.8 ± 2.1 a	88.0 ± 2.7 a
3 (control)	92.3 ± 1.1 a	87.3 ± 3.5 a

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 18 birds. Values were adjusted to one decimal number.

Table (5): Values of kidney function tests.

Groups	Urea (mg/dl)	Creatinine (mg/dl)	Uric acid (mg/dl)
at 6th day of age			
1 (1x)	8.5 ± 0.6 b	0.4 ± 0.05 a	
2 (10x)	10.5 ± 0.6	0.2 ± 0.03 b	Not done
3 (control)	10. ± 0.2 a	0.2 ± 0.03 b	
at 10th day of age			
1 (1x)	8.2 ± 1.0 a	0.2 ± 0.02 b	
2 (10x)	6.7 ± 0.7 a	0.2 ± 0.04 ab	Not done
3 (control)	8.3 ± 1.7 a	0.3 ± 0.05 a	
at 29th day of age			
1 (1x)	8.1 ± 1.1 a	2.0 ± 0.25 a	6.5 ± 0.3 ab
2 (10x)	7.7 ± 0.5 a	2.2 ± 0.36 a	5.9 ± 0.2 b
3 (control)	7.0 ± 0.4 a	1.8 ± 0.18 a	7.3 ± 0.4 a
at 34th day of age			
1 (1x)	6.5 ± 0.8 a	2.5 ± 0.2 a	5.5 ± 0.2 b
2 (10x)	5.1 ± 1.0 a	2.5 ± 0.2 a	6.5 ± 0.4 a
3 (control)	6.2 ± 0.8 a	2.1 ± 0.2 a	6.8 ± 0.3 a

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 18 birds. Values were adjusted to one decimal number.

Table (6): Effect of enrofloxacin on phagocytic activity of chicks at different intervals.

Groups	Age (days)			
	6th	10th	29th	34th
	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
1 (1x)	25.17 ± 0.85 b	31.00 ± 1.00 a	21.06 ± 0.45 a	19.61 ± 0.57 b
2 (10x)	28.67 ± 0.74 a	30.08 ± 0.96 a	20.89 ± 0.67 a	19.83 ± 0.47 b
3 (control)	27.38 ± 1.61 ab	31.67 ± 1.08 a	21.33 ± 0.86 a	22.00 ± 0.57 a

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 18 birds.

Table (7): Values of HI titer to NDV vaccine at different intervals (means ± standard error).

Groups	Age (days)		
	6th	14th	34th
1 (1x)	2.75 ± 0.25 a	3.33 ± 0.16 c	7.25 ± 0.37 a
2 (10x)	2.58 ± 0.15 a	5.13 ± 0.19 b	6.73 ± 0.33 a
3 (control)	2.50 ± 0.19 a	5.80 ± 0.11 a	7.25 ± 0.22 a

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 18 birds.

Table (8): Values of ELISA titer of IBDV.

Groups	29th day	34th day
1 (1x)	$2.90 \times 10^4 \pm 3.30 \times 10^3$ a	$1.71 \times 10^4 \pm 3.89 \times 10^3$ b
2 (10x)	$2.47 \times 10^4 \pm 3.73 \times 10^3$ a	$3.11 \times 10^4 \pm 2.91 \times 10^3$ a
3 (control)	$3.07 \times 10^4 \pm 2.25 \times 10^3$ a	$3.36 \times 10^4 \pm 4.35 \times 10^2$ a

Means in the same column and the same age followed by similar letter do not differsignificantly (at P = 0.05). Each value is a representative of 18 birds.

Table (9): Effect of enrofloxacin on intestinal Lactobacillus count in the duodenum

Groups	Lactobacillus spp. count / g intestinal scrap
1 (1x)	70×10^6
2 (10x)	25×10^6
3 (control)	26×10^7

Table (10): Values of organ weights to body weigh (means ± standard error) at 29th day of age.

Groups	Bursa to body weight ratio (%)	Spleen to body weight ratio (%)	Thymus to body weight ratio (%)	Bursa to spleen ratio
1 (1x)	0.21±0.03 a	0.12±0.02 a	0.26±0.04 a	2.02±0.73 a
2 (10x)	0.17±0.04 a	0.08±0.01 a	0.22±0.06 a	2.14±0.63 a
3 (control)	0.18±0.02 a	0.08±0.01 a	0.22±0.02 a	2.20±0.12 a

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05). Each value is a representative of 9 birds.

Table (11): Values of body weight gain (7th -34th day) and feed conversion ratio (means ± standard error).

Groups	Body weight gain (g) (7th -34th day)	Feed conversion ratio
1 (1x)	671.33 ± 12.86 a	3.13 ± 0.16 b
2 (10x)	580.67 ± 21.18 b	3.93 ± 0.17 a
3 (control)	703.50 ± 6.50 a	2.96 ± 0.20 b

Means in the same column and the same age followed by similar letter do not differ significantly (at P = 0.05).

Table (12): Mortality within 10 days after challenge with velogenic NDV.

Groups	Mortality %
1 (1x)	66.6
2 (10x)	66.6
3 (vaccinated, non–treated control)	33.3
(non–vaccinated, non–treated control)	95.0

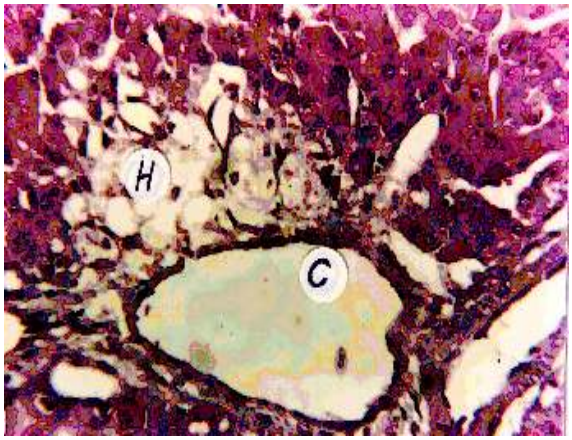

Fig. 1 Liver from a bird given 10x overdose of enrofloxacin: Congestionwith an extensively dilated vein (C) and one area of severe hydropic degenerated and ruptured hepatic cells (H). H&E (X4000).

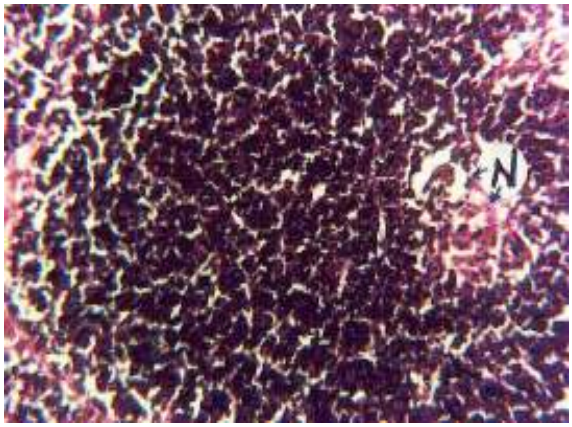

Fig. 2 Spleen from a bird given 10x overdose of enrofloxacin: One area of degenerated and necrotic lymphoblasts (N). H&E (X2500).

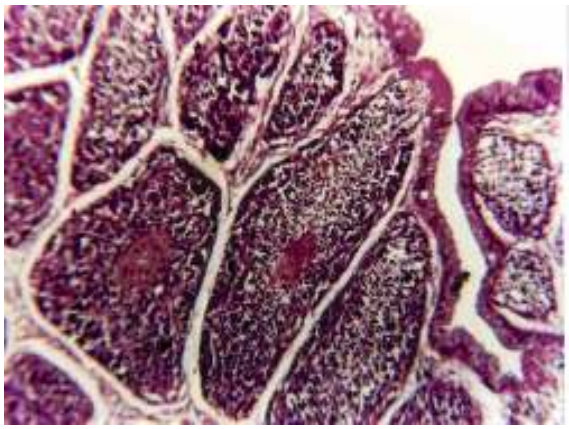

Fig. 3 Bursa of Fabricius from a bird given 10x overdose of enrofloxacin:Numerous central areas of lymphoblastic degeneration and necrosis with epithelial vacuolations. H&E (X1600).

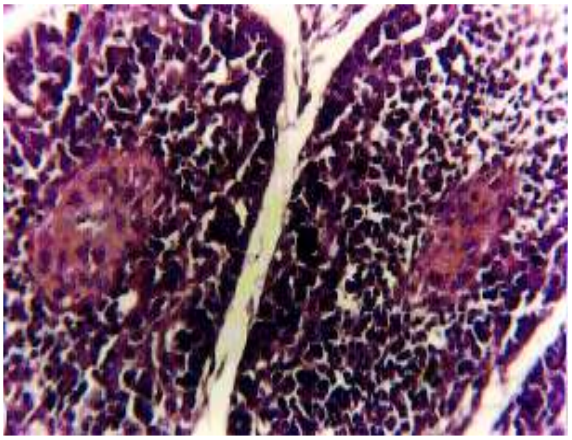

Fig. 4 Bursa of Fabricius from a bird given 10x overdose of enrofloxacin: Higher magnification of the previous Fig. 3, to show the central area of the lymphoblastic degeneration and necrosis. H&E (X4000).

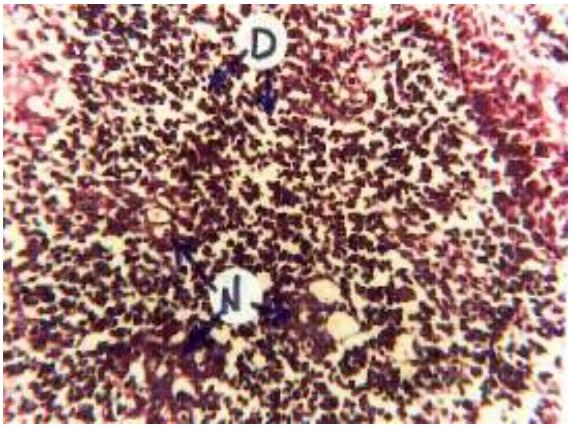

Fig. 5 Thymus from a bird given 10x overdose of enrofloxacin: Numerous areas of lymphoblastic degeneration and necrosis (N), dispersion and depletion of the lymphocytes (D). H&E (X2500)

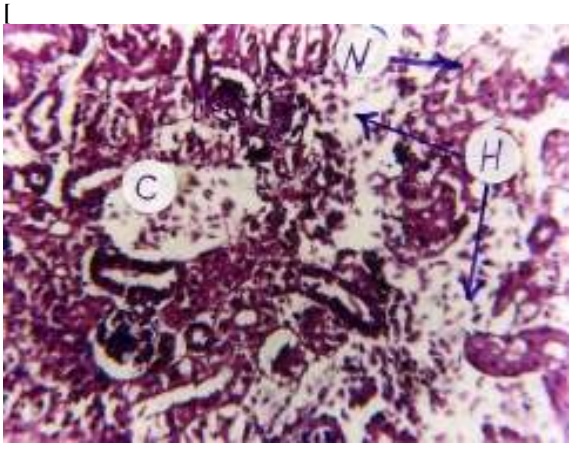

Fig.6 A kidney from a bird given 10x overdose of enrofloxacin showing: congestion (C), tubular degeneration (N), and wide area of hemorrhages (H). H&E (X250)

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دراسات على تأثيرالجرعة الزائدة للإنروفلوكساسين على القياسات الصحية المختلفة لدجاج التسمين

تمت الدراسة على ١٨٠ طائر تم تقسيمهم بالتساوى على ثلاث مجموعات كل مجموعة قسمت إلى ثلاث مكررات فى كل منها ٢٠ طائر . المجموعة الأولى (1x) تم إعطائها جرعة علاجية (٥٠ جزء في المليون من الانروفلوكساسين في مياه الشرب يعادل ١٠ مجم/كجم من وزن الطائر) لمدة خمسة أيام متتالية ابتداء من عمر يوم و تكررت نفس الجرعة العلاجية من عمر ٢٤ - ٢٨ يوم. المجموعة الثانية (10x) تم إعطائها عشرة أضعاف الجرعة العلاجية (٥٠٠ جزء في المليون في مياه الشرب يعادل ١٠٠ مجم/كجم من وزن الطائر) لمدة خمسة أيام متتالية ابتداء من اليوم ا لأول في العمر و تكررت نفس الجرعة من عمر ٢٤ - ٢٨ يوم فى مياه الشرب . المجموعة الثالثة ضابطة بدون معالجة. تم أخذ عينات الدم عند اعمار ٦،١٠،١٤،٢٩،٣٤ يوما وذلك لعمل مختلف التحليلات المعملية . وقد وجد أن أعطاء الإنروفلوكساسين بعشرة أضعاف الجرعة (10x) (١٠٠ مجم/كجم من وزن الطائر) أحدث إنخفاضاً معنوياً فى القياسات الأتية: (١) مستوى الأجسام المناعية لإختبار منع التلازن HI لمرض النيوكاسل عند عمر ١٤ يوم، (٢) مستوى الزلال فى مصل الدم عند عمر ١٠ أيام، (٣) نسبة الهيموجلوبين عند عمر ٢٩ و ٣٤ يوم، (٤) عدد كرات الدم البيضاء عند عمر ٦ أيام، (٥) حمض اليوريك عند عمر ٢٩ يوم، (٦) معامل تنشيط الخلايا الليمفاوية و الخلايا البلعمية عند عمر ٣٤ يوم، (٧) عدد البكتريا النافعة فى الأمعاء، (٨) وزن الجسم و معامل التحويل الغذائى. (٩) كما أحدث إنخفاضاً غير معنوياً فى معامل الإليزا الخاص بالجمبورو عند عمر ٢٩ يوم. بينما أحدث زيادة معنوية فى اليوريا و عدد الهيتروفيل . كما أحدث زيادة غير معنوية فى إنزيمات الكبد و الكرياتينين عند عمر ٢٩ و ٣٤ يوم. لم يؤثر الأنروفلوكساسين ب١٠ أضعاف الجرعة على عدد كرات الدم الحمراء، الهيماتوكريت و معامل وزن الأعضاء الليمفاوية بالنسبة لوزن الجسم. لوحظ تكسير فى أنسجة الكبد و الطحال والكليتين و حويصلة فابريشى و غدة الثايمس. بعد إختبار التحدى بعترة النيوكاسل الضارية كانت نسبة النفوق ٦٦,٦% فى هذه المجموعة (10x) مقارنة ب ٣٣,٣% فى المجموعة الثالثة الضابطة المحصنة و ٩٥% فى مكررة المجموعة الثالثة الغير محصنة.

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