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EFFECTS OF CEFTRIAXONE ON THE HEMATOLOGY AND LIPID PROFILE VALUES IN RATS

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ABSTRACT: *The present study aimed to determine the effects of ceftriaxone on hematological parameters and lipid profile in the normal and infected rat after treatment with ceftriaxone (1g) intramuscularly. Sixty male rats were randomly divided into five groups containing twelve rats per group. Group I as control were given feed and water, Group II was treated with 180mg/kg, Group III treated with 360mg/kg, Group IV was infected with E.coli and treated with 180mg/kg, and Group V was infected with E.coli and treated with 360mg/kg. Rats were treated at intervals of 24 hours for 5 consecutive days, thereafter blood samples for hematological and lipid profile examination were collected using EDTA and plain sample bottles, respectively, by sacrificing three rats from each group per day on the first, fourth, seventh, and fourteenth day after treatment. Hematology results showed a significant increase in PCV values, while Hb and RBC were significantly decreased. The mean corpuscular volume (MCV) was significantly increased while the Mean corpuscular hemoglobin was significantly decreased. The White blood cell (WBC), Neutrophils, and Lymphocyte counts were significantly decreased while the Eosinophil and Monocyte counts were significantly increased. Lipid profile results showed a significant in Cholesterol levels, while triglyceride levels were significantly increased. HDLC was significantly decreased. The results of this present study indicate that ceftriaxone can cause hypochromic macrocytic anemia, Leukocytopenia, Neutropenia, Lymphopenia, Eosinophilia, Monocytosis, and dyslipidemia. Therefore this drug may not be safe to administer in patients that have established cases of anemia and cardiac abnormalities*.

KEYWORD: anemia, dyslipidemia, immunosuppression

INTRODUCTION

Ceftriaxone is a third-generation cephalosporin antibiotic with a broad spectrum of activity which is extensively used for intravenous and intramuscular injections in hospitals for the treatment of skin and soft tissue infections, enteric fever, complicated urinary tract infections, community-acquired pneumonia, meningitis, abdominal sepsis, and septicemia (Borah *et al*, 2016). Over the years, the use of antibiotics has been associated with numerous adverse reactions and/or side effects. These side effects could be pharmacological, hematological, biochemical, pathological, genotoxic, or more frequent allergic reactions in different subjects (Ambili *et al*.,2013).

Hematological and serum biochemical parameters are vital indicators in clinical practice and biomedical research when confirming a diagnosis, an ongoing pathophysiological condition, or

monitoring the progress and/or effects of specific drugs or substances, which may be directly or indirectly related to organ function (Yu *et al*., 2019). Numerous studies on the adverse effects of the different classes of antibiotics on hematology and serum biochemistry have been carried out using different animal models. Sangunuwa (2006), studied the effects of ceftriaxone on hematological and biochemical parameters of turkey. The Effects of Metronidazole on the hematological parameters in male albino rats (Oyedeji and Bolarinwa, 2013). Effect of amoxicillin repeated administration on the hemogram and biochemical profile of sheep (Elmajdoub *et al*, 2014), Effects of repeated administration of Cefquinome on the biochemical and hematological parameters in buffalo calves (Mukesh and Suresh, 2015), The effects of Ceftazidime on hematological and biochemical parameters using albino Wistar rat was also reported by (Abhishek and Saumya, 2016) where numerous significant changes were documented depending on the dose used, duration of administration and animal species.

Lipids, represented by phospholipids, cholesterol, triglycerides, and fatty acids, are considered essential to the human body, both by making up the basic structure of cell membranes and by acting as a precursor to steroids hormones, bile salt, and vitamin D, as well as being a constituent of cell membranes, acting on the fluidity of the later and in the activation of the enzyme. Lipids are not only a central part of human metabolism but also play diverse and critical roles in the immune system. As such, they can act as ligands of lipid-activated nuclear receptors, control inflammatory signaling through bioactive lipids such as prostaglandins, leukotrienes, lipoxins, resolvins, protectins, and modulates immunity as intracellular phospholipids or sphingolipids-derived signaling mediators. Additionally, lipids serve as antigens and regulate immunity by activating lipid-reactive T cells (Dowds *et al*., 2014).

The use of antibiotics, particularly those that interfere with lipid metabolism. Despite the efficacy and wide range of clinical use of ceftriaxone, there is little information on its effects on blood and lipid parameters. This study was designed to determine the effects of ceftriaxone on the blood and lipid profile values in rats.

METHODOLOGY

Experimental Animals

Sixty male albino rats weighing between 110g ± 20g were procured from the National Veterinary Research Institute Vom Jos, Nigeria. They were housed under standard laboratory conditions with 12 hours daylight cycle and had free access to feed and water ad libitum, and they were acclimatized to laboratory conditions for two weeks before the commencement of the experiments.

Test drug

Ceftriaxone (Rocephin®) 1g injection for intramuscular or intravenous administration was purchased from a registered pharmacy.

Experimental organism

The pathogenic strain of *Escherichia coli* was procured from the National Veterinary Research Institute (NVRI.) Jos, Plateau State.

Experimental Design

Group I	Feed and Water
Group II	Ceftriaxone 180mg/kg IM
Group III	Ceftriaxone 360mg/kg IM
Group IV	Infected with *Escherichia coli* and treated with Ceftriaxone 180mg/kg IM
Group V	Infected with *Escherichia coli* and treated with Ceftriaxone 360mg/kg IM

Preparation and administration of Escherichia coli inoculum

The *E.coli* isolate was obtained from the Bacteriology Laboratory of the Department of Veterinary Microbiology, University of Maiduguri. The isolate was revived by subculturing in nutrient broth and incubated for 24hrs at 37ºC. The turbidity of the actively growing broth culture after 24hrs was adjusted with sterile distilled water to obtain turbidity optically comparable to that of the 0.5 Mc Farland standards. This resulted in a bacterial suspension to approximately 10^6 CFU/ml (Barenfangar *et al*., 1999). The weights of each rat were taken using a digital weighing balance before inoculation with the bacterial suspension and after the appearance of clinical signs and treatment. The rats in groups IV and V were subjected to oral administration of 0.3 ml/kg of *E.coli* suspension with the aid of cannula. Infected rats were observed for clinical signs of infection, and their stool samples were cultured to confirm *E.coli* infection.

Confirmation of Escherichia coli infection

Stool samples of experimental rats were collected on day 3 post-inoculation and cultured on MacConkey agar and Eosin Methylene Blue to establish *Escherichia coli* infection. Subsequently, the test was repeated after treatment with ceftriaxone. The stool sample was inoculated onto Selenite–F broth and incubated at 37ºC for 24 hours; it was then subcultured onto MacConkey agar and Eosin Methylene Blue agar incubated for 24 hours at 37ºC.

Blood sample collection

After the 5th day of treatment with ceftriaxone, 3 rats from each group were sacrificed on the 1st, 4th, 7^{th,} and 14th day, and blood samples were collected in two separate sample bottles, a plain sample bottle for biochemical parameters and one containing ethylenediaminetetraacetic acid (EDTA) for evaluation of hematological parameters. All the rats were handled according to the International Guiding Principles for Biomedical Research Involving Animals (CIOMS and ICLAS, 2012)

Determination of Hematological and Serum Protein Parameters

Hematological parameters determined include Pack cell volume (PCV), hemoglobin concentration (Hb), Red Blood Cell (RBC) count, Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), White Blood Cell (WBC), Lymphocyte, Neutrophils, Eosinophil, monocyte and Platelet counts. Hemoglobin count was done by using Sahli- Hellige Haemoglobinometer. RBC count was done using

Haemocytometer by red blood diluting pipette and by counting chamber. Similarly, the WBC count was done. Lymphocytes, neutrophils, eosinophils, and monocyte were counted on a slide by differential leukocyte counts with the help of a light Olympus microscope (Germany) (Carlson, 1996; Chineke, 2006). Platelet counts were done on Neubauer's hemocytometer as described by Coles (1986).

Blood samples for lipid profile were dispensed into clean plain glass test tubes and allowed to stand for 30 minutes at room temperature to clot. Serum for the assays was thereafter separated from the clot by centrifugation. All lipid profile value determinations were carried out immediately after centrifugation. Standard procedures were followed in all Serum lipid profile assays. Quimica Clinica Aplicada (QCA) test kits (Spain) and a digital colorimeter (Lab-Tech, India) were used for all the determinations. The serum Cholesterol and Triglycerides were determined by the enzymatic colorimetric method (Allain et al., 1974). HDLC was determined by the dextran sulfate-magnesium (II) precipitation method (Albers et al., 1978). The VLDLC was calculated by dividing the serum Triglyceride by 5, while the serum LDLC was calculated using the Friedewald formula (Friedewald et al., 1972; Warnick et al., 1990).

STATISTICAL ANALYSIS

The numerical data obtained from the study were expressed as the Mean ± Standard error of the mean (SEM). Statistical analysis was done using the GraphPad Prism Statistical Package Version 8.3.1.0 (GraphPad Software, inc USA). The differences between and within groups Means were analyzed using analysis of variance (ANOVA) followed by Bonferroni Post-hoc test to compare replicate means by row. ($p < 0.05$) was considered as statistically significant for all groups

RESULTS/FINDINGS

The results of hematology, Blood indices, Differential leucocyte counts, and serum protein are presented in Table 1, 2,3, and 4, respectively.

(Table.1) shows that the PCV of rats in group II (treated with 180mg/kg CTX) (42.0 ± 5.50) % on day 7 was significantly ($p<0.01$) higher than that of the normal control group (32.3 ± 0.90), there was a significant ($p<0.05$) increase in the PCV of rats in group III (treated with 360mg/kg CTX) on day 1 (39.3 ± 2.90 %) and a significant ($p<0.001$) decrease on day 4 (40.3 ± 2.00) % when compared to the control group (31.3 ± 0.90, 44.0 ±1.00) % respectively. There was a significant ($p<0.001$) increase in PCV of rats of group IV (infected with *E.coli*) on day 1 and 7 (44.3 ± 0.80, 42.0 ± 0.64) % as compared to the control group (31.3 ± 0.90, 32.3 ± 0.90) %. additionally, there was a significant ($p<0.001$) increase in the PCV of rats of group VI (infected with *E.coli* and treated with 360mg/kg CTX) on day 7 (42.3 ± 0.80) % as compared to the control group (32.3 ± 0.90) %. There was no significant change in PCV values of rats in group V (infected with *E.coli* and treated with 180mg/kg CTX) when compared to control groups.

Hemoglobin concentrations were observed to be significantly decreased ($p<0.05$) in rats of group II (treated with 180mg/kg CTX) (11.6 ± 0.40) g/dL and rats in group III (treated with 360mg/kg CTX) (12.1 ± 0.40) g/dL on day 14 post-treatment when compared to the control group (13.8 ± 0.50). Similarly, there was a significant($p<0.05$) decrease observed in rats of group VI (infected

with *E.coli* and treated with 360mg/kg CTX) on day 1(11.9± 0.70) g/dL compared to the control group(14.6 ± 0.30) g/dL.

The RBC counts were seen to be significantly ($p<0.05$) decreased in rats of group IV (infected with *E.coli*) on day 4 (4.40 ± 0.46) compared to the control group (6.10 ± 0.40). There were no significant changes observed in rats of group II (treated with 180mg/kg CTX), group III (Rats treated with 360mg/kg), group V (rats infected with *E.coli* and treated with 180mg/kg CTX) and group VI (rats infected with *E.coli* treated with 360mg/kg CTX) respectively.

The results of the hematological indices (Table.2) shows, there was a significant increase in MCV values of rats in group II (rats treated with 180mg/kg CTX) and group III (rats treated with 360mg/kg CTX) on day 1 (71.9 ± 5.90, 81.7 ± 1.50) fl and day 7 (71.9 ± 5.90, 83.7 ± 1.50) fl post-administration when compared to the control group (60.1 ± 1.90, 60.1 ± 1.90) fl. Similarly, there was a significant increase in MCV of rats infected with *E.coli* on day 1 (77.2 ± 5.06) fl and 4 (78.6 ± 3.93) fl as compared to the control group (60.1 ± 1.90) fl. Additionally, there was an increase on days 1 (77.2 ± 5.06) fl, 4 (100.6± 0.70) fl, and 7 (78.6 ± 3.93)fl in group V (rats infected with *E.coli* treated with 180mg/kg CTX) and group VI (rats infected with *E.coli* treated with 360mg/kg CTX) when compared to the control group.

There was a significant decline in MCH values noted in rats infected with *E.coli* day 1, 4, and 14, group II (rats infected with *E.coli* treated with 180mg/kg CTX) on day 1,4,7 and 14, and group III (rats infected with *E.coli* treated with 360mg/kg CTX) on day 1, 4,7 and 14 when compared to the control group. There was no significant change in MCHC valves observed in all groups.

Differential leucocyte counts results (Table.3) show a significant ($p<0.05$) decrease in the WBC counts in group II and group III on day 14 (3.60 ± 0.50, 4.27 ± 0.40) when compared to the control (6.90 ± 0.30).

Neutrophil counts was a significant ($p<0.05$) declined in rats of group II from day 1 to 14 (20.3 ± 0.81, 20.3 ± 0.80, 5.93 ± 0.10, 22.0 ± 0.10) %, Rats of group III on day 7 and 14 (5.53 ± 0.60, 27.6 ± 1.40) %. There was a significant increase in group IV and V on day 1,4 and 7 (33.3 ± 6.07, 40.0 ± 2.30, 50.3 ± 12.3) %, (56.0 ± 3.70, 58.0 ± 1.50, 53.0 ± 1.55) % when compared to the control for corresponding days (25.0 ± 2.30, 25.0 ± 2.01, 26.9 ± 0.50, 28.0 ± 0.60) %.

Eosinophils were significantly increased in group II and group III on day 14 (20.0 ± 0.81, 26.0 ± 0.71) % when compared against the control group (4.0 ± 0.61) %.

There was a significant ($p<0.005$) decline in lymphocyte counts of group II and group III on day 14 (17.3 ± 6.31, 16.0 ± 1.00) % respectively compared to the control group (65.3 ± 2.00) %. There was a significant ($p<0.05$) rise in lymphocyte count observed on day 14 in group IV (67.0 ± 2.17) % compared to the control group (65.3 ± 2.00) %. Lymphocyte counts of group V was significantly ($p<0.05$) decreased on 1, 4 and 7 (36.0 ± 0.06, 40.6 ± 1.30, 44.0 ± 2.60) % with a significantly ($p<0.01$) increased on day 14 (73.0 ± 1.50) % when compared to the control group (66.3 ± 1.70, 66.3 ± 1.70, 63.0 ± 1.50, 65.3 ± 2.00) %. Monocyte counts were significantly increased in rats of group II and III on day 14 (18.6 ± 6.30, 17.0 ± 2.82) % compared to the control (9.0 ± 0.60) %. There was no significant change in Platelet counts in all experimental groups when compared with the control group.

The results of the lipid profile as seen in table 4. Reveals that the Total cholesterol levels of rats in group II was significantly decreased on the 7th and 14th day post administration (1.8 ± 0.24, 1.6 ± 0.16) mmol/L when compared to the control group (2.0 ± 0.21, 2.3 ± 0.14) mmol/L. The Triglyceride levels was significantly increased in rats of group II on day 1,7 & 14 (1.4 ± 0.20, 1.6 ± 0.40, 1.5 ± 0.13) mmol/L and group III on day 14 (1.9 ± 0.50) mmol/L when compared to the control group (1.3 ± 0.23, 1.3 ± 0.14, 1.2 ± 0.22, 1.0 ± 0.15) mmol/L. Rats of group IV showed a significant rise in triglyceride levels on day 4 and 7 (1.5 ± 0.10, 1.6 ± 0.10) mmol/L with a significant decline on day 14 (0.4 ± 0.20) mmol/L, while rats of group V showed a significant decrease on day 4 (0.9 ± 0.18) mmol/L and a significant increase on day 7 (1.7 ± 0.10) mmol/L and 14 (2.0 ± 0.18) mmol/L when compared to the control. HDLC was significantly decreased in rats of group II and III on day 14 (1.0 ± 0.15, 0.8 ± 0.10) mg/L respectively. Similarly, rats of group IV and V from day 1 to 14 post administration (0.6 ± 0.18, 1.0 ± 0.01, 0.4 ± 0.05, 0.8 ± 0.01) mg/L, (0.7 ± 0.04, 0.7 ± 0.15, 0.15, 0.5 ± 0.03, 0.9 ± 0.02) mg/L when compared to the control group (1.4 ± 0.20, 1.5 ± 0.16, 1.4 ± 0.18, 1.5 ± 0.10) mg/L.

Table 1. Effects of Ceftriaxone on PCV, Hb, and RBC counts in normal rats and rats infected with *Escherichia coli*.

		Duration post-treatment with CTX			
Parameters	**Groups**	**1st Day**	**4th Day**	**7th Day**	**14th Day**
PCV (%)	Group I	31.3 ± 0.90	44.0 ±1.00	32.3 ± 0.90	45.0 ± 1.00
	Group II	35.6 ± 0.80	39.3 ± 3.70	42.0 ± 5.50 [a]	35.0 ± 1.20
	Group III	39.3 ± 2.90[a]	40.3 ± 2.00	46.0 ± 1.50 [a]	36.3 ± 1.40
	Group IV	38.6 ± 0.80	43.0 ± 0.65	37.3 ± 1.40	39.6 ± 0.82
	Group V	36.0 ± 2.10 [a]	39.0 ± 1.70	42.3 ± 0.80	39.3 ± 1.40
Hb (g/dL)	Group I	14.6 ± 0.30	14.8 ± 0.90	11.1 ± 0.80	13.8 ± 0.50
	Group II	15.6 ± 0.20	13.0 ± 1.40	13.0 ± 1.80	11.6 ± 0.40 [b]
	Group III	15.2 ± 0.30	12.4 ± 0.70	15.3 ± 0.50	12.1 ± 0.40 [b]
	Group IV	13.0 ± 0.60	14.3 ± 0.20	12.3 ± 0.50	13.4 ± 0.40
	Group V	11.9 ± 0.70 [b]	12.6 ± 0.30	13.7 ± 0.50	13.5 ± 0.35
Redblood cell count × 10^6/ul	Group I	5.21 ±0.10	6.10 ± 0.40	5.21 ± 0.10	6.10 ± 0.40
	Group II	5.66 ± 0.04	6.02 ± 0.40	6.39 ± 0.70	5.35 ± 0.35
	Group III	6.54 ± 0.50	6.50 ± 0.50	5.63 ± 0.20	5.28 ± 0.50
	Group IV	5.00 ± 0.10	6.00 ± 0.10	4.90 ± 0.20	5.80 ± 0.30
	Group V	4.90 ± 0.20	4.90 ± 0.20	5.60 ± 0.20	5.60 ± 0.20

PCV= Packed cell volume, Hb= Hemoglobin
Values are expressed as mean ± SEM (n= 3). ($p<0.05$)
a =significance increase in comparison normal control group
b =significance decrease in comparison with the normal control group

Table.2. Effects of ceftriaxone on Haematological Indices in normal rats and rats infected with *Escherichia coli*.

		Duration post-treatment with CTX			
Parameters	**Groups**	**1st Day**	**4th Day**	**7th Day**	**14th Day**
MCV (fl)	Group I	60.1 ± 1.90	60.1 ± 1.90	60.1 ± 1.90	73.0 ± 5.10
	Group II	63.1 ± 1.80	71.9 ± 5.90 [a]	71.9 ± 5.90 [a]	72.8 ± 2.10
	Group III	60.2 ± 1.90	81.7 ± 1.50[a]	83.7 ± 1.50 [a]	69.8 ± 6.00
	Group IV	77.0 ± 0.57	71.3 ± 0.83	73.3 ±2.33	69.0 ± 3.51
	Group V	73.0 ± 2.48	79.3 ± 0.60	74.6 ± 4.10	69.3 ± 4.17
MCH (g/L)	Group I	46.5 ± 2.08	33.5 ± 3.07	37.6 ±1.36	38.5 ± 0.86
	Group II	43.9 ± 1.45	33.0 ± 2.25	33.2 ± 0.03	33.2 ± 0.05
	Group III	39.0 ± 1.99	38.3 ± 0.40	33.2 ± 0.03	33.2 ± 0.03
	Group IV	25.6 ± 0.33[b]	23.3 ± 0.33 [b]	24.0 ± 0.57 [b]	23.0 ± 1.52 [b]
	Group V	23.6 ± 1.20 [b]	25.3 ± 0.66 [b]	23.6 ± 1.76 [b]	23.6 ± 1.76 [b]
MCHC (g/dL)	Group I	27.9 ± 0.36	24.7 ± 2.86	27.9 ± 036	24.7 ± 2.80
	Group II	27.7 ± 0.00	21.7 ± 2.21	23.9 ±1.96	24.0 ± 1.00
	Group III	21.3 ± 0.89	19.0 ± 0.84	27.1 ± 0.57	23.3 ± 1.85
	Group IV	33.3 ± 0.88	33.9 ±0.01	32.6 ± 0.33	33.6 ± 0.66
	Group V	33.0 ± 0.01	32.0 ± 1.00	32.0 ± 1.00	34.0 ± 1.00

MCV = Mean Corpuscular Volume, MCH = Mean Corpuscular Hemoglobin, MCHC = Mean Corpuscular Hemoglobin
Values are expressed as mean ± SEM (n= 3)
a =significance increase in comparison normal control group

b =significance decrease in comparison with the normal control group ($p<0.05$)

Table.3. Effects of ceftriaxone on the Differential Leucocyte counts in normal rats and rats infected with *Escherichia coli*.

		Duration of treatment			
Parameters	**Groups**	**1st Day**	**4th Day**	**7th Day**	**14th Day**
White Blood Cell $\times 10^3$/ul	Group I	7.26 ± 0.20	6.80 ± 0.30	6.9 ± 0.50	6.90 ± 0.30
	Group II	8.03 ± 0.11	5.36 ± 0.30	5.93 ± 0.10	3.60 ± 0.50 [b]
	Group III	8.56 ± 0.70	5.60 ± 0.10	5.53 ± 0.60	4.27 ± 0.40 [b]
	Group IV	6.90 ± 0.20	7.20 ± 0.45	6.90 ± 0.10	6.80 ± 0.65
	Group V	5.70 ± 1.40	6.40 ± 0.25	7.00 ± 0.60	8.00 ± 0.60
Neutrophil (%)	Group I	25.0 ± 2.30	25.0 ± 2.01	26.9 ± 0.50	28.0 ± 0.60
	Group II	20.3 ± 0.81 [b]	20.3 ± 0.80 [b]	5.93 ± 0.10 [b]	22.0 ± 0.10 [b]
	Group III	31.6 ± 4.20	31.6 ± 4.20	5.53 ± 0.60 [b]	27.6 ± 1.40 [b]
	Group IV	33.3 ± 6.07 [a]	40.0 ± 2.30 [a]	50.3 ± 12.3 [a]	29.0 ± 1.00
	Group V	56.0 ±3.70 [a]	58.0 ± 1.50 [a]	53.0 ± 1.55 [a]	26.3 ± 0.80
Eosinophil (%)	Group I	4.0 ± 0.51	4.0 ± 0.50	4.0 ± 0.50	4.0 ± 0.61
	Group II	3.3 ± 0.80	3.3 ± 0.80	3.3 ± 0.80	20.0 ± 0.81 [a]
	Group III	5.0 ± 0.57	5.0 ± 0.50	5.0 ± 0.54	26.0 ± 0.71 [a]
	Group IV	3.3 ± 0.80	3.3 ± 0.80	3.3 ± 0.80	3.0 ± 0.81
	Group V	5.0 ± 0.57	5.0 ± 0.50	5.0 ± 0.54	4.0 ± 0.71
Lymphocyte (%)	Group I	66.3 ± 1.70	66.3 ± 1.70	63.0 ± 1.50	65.3 ± 2.00
	Group II	71.3 ± 0.81	71.3 ± 0.81	72.0 ± 1.01	17.3 ± 6.31 [b]
	Group III	55.3± 5.30	55.3 ± 5.31	55.3 ± 5.31	16.0 ± 1.00 [b]
	Group IV	57.0 ± 15.5	62.3 ± 1.20	44.6 ±1.00	67.0 ± 2.17 [a]
	Group V	36.0 ±0.60 [b]	40.6 ± 1.30 [b]	44.0 ± 2.60 [b]	73.0 ± 1.50 [a]

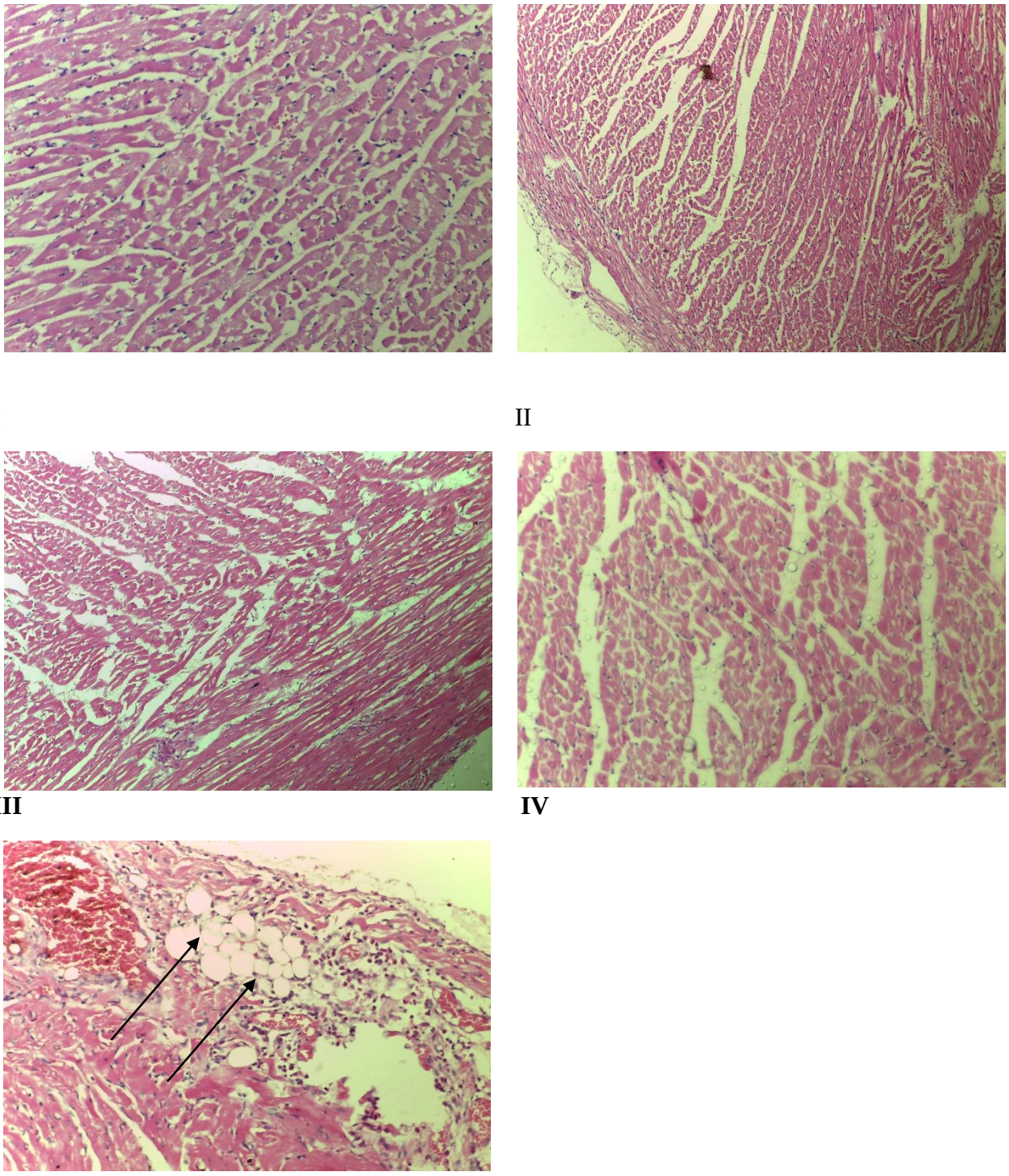
Monocyte (%)	Group I	6.6 ± 1.10	6.6 ± 1.10	6.6 ± 0.87	9.0 ± 0.60
	Group II	7.0 ± 0.60	7.0 ± 0.60	7.0 ± 0.60	18.6 ± 6.30 [a]
	Group III	5.3 ± 0.80	5.3 ± 0.80	5.3 ± 0.80	17.0 ± 2.82 [a]
	Group IV	5.0 ± 0.50	0.3 ± 0.35	1.7 ± 0.30	0.60 ± 0.10
	Group V	3.3 ± 0.65	1.3 ± 0.60	3.0 ± 1.56	0.60 ± 0.10
Platelets (×105/ul)	Group I	2.2 ± 0.40	2.1 ± 0.54	2.0 ± 0.30	2.3 ± 0.30
	Group II	2.0 ± 0.10	2.0 ± 0.40	2.3 ± 0.25	2.3 ± 0.40
	Group III	2.2 ± 0.30	2.2 ± 0.41	2.3 ± 0.13	2.3 ± 0.15
	Group IV	2.0 ± 0.10	2.0 ± 0.40	2.3 ± 0.20	2.3 ± 0.40
	Group V	2.2 ± 0.30	2.2 ± 0.40	2.3 ± 0.10	2.3 ± 0.10

Values are expressed as mean ± SEM (n= 3)
a =significance increase in comparison normal control group
b =significance decrease in comparison with normal control group
($p<0.05$)

Table.4. Effects of ceftriaxone on the Lipid Profile values in normal rats and rats infected with *Escherichia coli*.

		Duration of treatment			
Parameters	**Groups**	**1st Day**	**4th Day**	**7th Day**	**14th Day**
Cholesterol	Group I	2.0 ± 0.21	2.3 ± 0.12	2.0 ± 0.21	2.3 ± 0.14
(mmol/L)	Group II	2.2 ± 0.10	2.3 ± 0.30	1.8 ± 0.24[b]	1.6 ± 0.14 [b]
	Group III	2.1 ± 0.20 [a]	2.4 ± 0.19 [a]	2.1 ± 0.15[a]	2.5 ± 0.15 [a]
	Group IV	1.4 ± 0.22 [b]	2.0 ± 0.01[b]	1.0 ± 0.01[b]	1.6 ±0.07 [b]
	Group V	1.6 ± 0.02 [b]	1.5 ± 0.28 [b]	1.3 ± 0.22[b]	1.5 ± 0.01 [b]
Triglyceride	Group I	1.3 ± 0.23	1.3 ± 0.14	1.2 ± 0.22	1.0 ± 0.15
(mmol/L)	Group II	1.4 ±0.20 [a]	1.6 ± 0.14 [a]	1.5 ± 0.1 3 [a]	1.1 ± 0.10
	Group III	1.1 ± 0.20	1.3 ± 0.33	1.2 ± 0.10	1.9 ± 0.50 [a]
	Group IV	1.1 ± 0.20	1.5 ± 0.10 [a]	1.6 ± 0.10 [a]	0.4 ± 0.20[b]
	Group V	1.3 ± 0.07	0.9 ±0.18 [b]	1.7 ± 0.10 [a]	2.0 ± 0.18 [a]
HDLC	Group I	1.4 ± 0.20	1.5 ± 0.16	1.4 ± 0.18	1.5 ± 0.10
(mg/L)	Group II	1.5 ± 0.13	1.5 ± 0.23	1.3 ± 0.20	1.0 ± 0.15 [b]
	Group III	1.4 ± 0.14	1.2 ± 0.14	1.4 ± 0.11	0.8 ± 0.10 [b]
	Group IV	0.6 ± 0.18 [b]	1.0 ± 0.01[b]	0.4 ± 0.05 [b]	0.8 ± 0.01 [b]
	Group V	0.7 ± 0.04 [b]	0.7 ±0.15 [b]	0.5 ± 0.03 [b]	0.9 ± 0.02[b]
LDL	Group I	0.2 ± 0.11	0.3 ± 0.1 0	0.2 ± 0.10	0.3 ± 0.18
(mg/L)	Group II	0.2 ± 0.20	0.2 ± 0.10	0.1 ± 0.10	0.2 ± 0.18
	Group III	0.2 ± 0.10	0.2 ± 0.12	0.2 ± 0.10	0.1 ± 0.14
	Group IV	0.2 ± 0.03	0.1 ± 0.12	0.1 ± 0.02	0.2 ± 0.06
	Group V	0.2 ± 0.05	0.2 ± 0.10	0.2 ± 0.09	0.3 ± 0.02
VLDL	Group I	0.4 ± 0.04	0.5 ± 0.34	0.4 ± 0.02	0.5 ± 0.04
(mg/L)	Group II	0.4 ± 0.02	0.5 ± 0.60	0.3 ± 0.05	0.3 ± 0.02
	Group III	0.4 ± 0.04	0.4 ± 0.03	0.4 ± 0.03	0.3 ± 0.02
	Group IV	0.4 ± 0.02	0.5 ± 0.60	0.3 ± 0.05	0.3 ± 0.02
	Group V	0.4 ± 0.04	0.4 ± 0.03	0.4 ± 0.03	0.3 ± 0.02

Values are expressed as mean ± SEM (n= 3)
a =significance increase in comparison normal control group
b =significance decrease in comparison with normal control group
($p<0.05$)



I II III IV V

Figure 1. Photomicrograph of the heart (x 200) I- normal rat showing normal cardiac muscles, **II-** treated with 180mg/kg CTX with normal cardiac muscles, **III-** treated with 360mg/kg CTX with normal cardiac muscles, **IV**-- and rats infected with *E.coli* and treated with 360mg/kg CTX normal

cardiac muscle, **V-** rats infected with *E.coli* and treated with 180mg/kg showed inflammation of the pericardial sac

DISCUSSION

This study was designed to determine the effects of ceftriaxone injection on hematological and lipid profile values in normal rats and rats infected with *E.coli*. The results obtained from this study were time-dependent. The hematopoietic system is sensitive to drugs and toxic compounds, and it serves as an essential index for evaluating the physiological status in animals and humans (Adeneye *et al*., 2006). The adverse effects of a particular drug may be elicited by its mode of action and its metabolite on tissue, organs, or peripheral circulating cells (Aydin and Talini,2013).

The Packed cell volume (PCV) values were significantly increased in the rat group treated with 180mg/kg, 360mg/kg and rats infected with *E.coli* and treated with 360mg/kg CTX (II, III, and V) when compared to the control group. This result indicates that ceftriaxone at both doses, even during infection, may have the potential to stimulate erythropoietin release in the kidney. The PCV is the most accurate, simple, and inexpensive method for the detection of the degree of anemia because an increase in erythropoietin level is an essential factor considered during an increase in PCV and RBC (Fabbri, 2015). The Haemoglobin concentration (Hb) values were seen to be significantly decreased in the rat group treated with 180mg/kg, 360mg/kg, and rats infected with *E.coli* and treated with 360mg/kg CTX (II, III, and V). There were no significant changes in the Red blood cell counts (RBC) values of all treated groups (rats in groups II, III, V, and VI) compared to the control group.

Hematological indices results show that the Mean corpuscular volume (MCV) values were significantly increased in the rat group treated with 180mg/kg, 360mg/kg, rats infected with *E.coli* and treated with 180mg/kg, and rats infected with *E.coli* and treated with 360mg/kg CTX (II, III, IV, and V). In comparison, the mean corpuscular hemoglobin (MCH) was significantly decreased in rats infected with *E.coli* and treated with 180mg/kg and rats infected with *E.coli* and treated with 360mg/kg (IV and V). This result shows that ceftriaxone injection can interfere with the oxygen-carrying capacity of blood and the amount of oxygen delivered to the tissues since RBC and hemoglobin are essential factors for the transportation of respiratory gases because substances that significantly affect RBC and associated parameters can have effects on bone marrow, kidney and hemoglobin metabolism (Oyedeji and Bolarinwa, 2012; Elizalde-Velazquez *et al*.,2017; Mbegbu *et al*., 2019).

The White blood cell (WBC) counts reflect the status of the body's immune state of response. There was a significant decline in the WBC of rats treated with 180mg/kg and 360mg/kg (II and III), this may suggest that ceftriaxone may have the potentials to suppress the body defense mechanism, these findings do not concur with that of Adewusi and Afolayan (2009), Oyedeji and Bolarinwa (2013) whom both reported an increase in levels of Total white blood cell counts after treating albino rats with *Pelargonium reniforme* extract and metronidazole respectively.

There was a significant decrease in the neutrophil count of the 'rat's group infected with E.coli and treated with 180mg/kg and 360mg/kg CTX (V and VI). This result indicates that the ability of the body to attack and destroy invading bacteria, viruses, and other injurious agents (Phagocytosis)

has been compromised due to infections and concurrent treatment with ceftriaxone, our findings do not agree with that of (Abishek and Saumya, 2016) were, they documented an insignificant change in the neutrophil counts in albino rats after treatment with ceftazidime this dissimilarity may be due to the infections in the rats. The significant increase in eosinophil count in rat groups treated with 180mg/kg and 360mg/kg (II and III) may suggest that the anti-allergic and anti-parasitic infectious responses of the body have been stimulated by ceftriaxone injection. This finding agrees with that of (Elmajdoub *et al*.,2014) that documented, Eosinophilia post-amoxicillin treatment that occurs primarily due to dose-independent hypersensitivity that can be associated with aminopenicillin treatments. There was a significant decline in lymphocyte count in the rat group treated with 180mg/kg and 360mg/kg, infected with E.coli, and treated with 360-mg/kg (II, III, and V). This result suggests that the acquired immune response of the body has been compromised by ceftriaxone, while the significant increase noted in rats infected and treated with E.coli (IV) indicates that at lower doses, ceftriaxone can enhance the acquired immune system. The significant increase in monocyte count of the 'rat's group treated with 180mg/kg and 360mg/kg (II, III) probably indicates that ceftriaxone injection can trigger the phagocytic function body. The platelet count in all ceftriaxone treated groups were insignificantly changed, suggesting that it does not have the potential to stimulate thrombopoietin production, with the hemostatic capability of the blood maintaining the status quo since platelets mediate in the blood–clotting mechanism, these findings agree with that of (Oyedeji and Bolarinwa, 2013).

Several medications, particularly antibiotics, can affect lipid profile levels either directly or indirectly through their effects on weight gain and glucose metabolism, as dyslipidemia is one of the most important and modifiable risk factors for cardiovascular diseases (Moran *et al*., 2010: Herink and Ito, 2018). Ceftriaxone significantly decreased the cholesterol level of rats treated with 180mg/kg CTX (group II). In contrast, the triglyceride levels of all CTX treated rat groups (II, III, IV, and V) were significantly increased. The HDLC was significantly decreased in all ceftriaxone-treated rat groups. The increase in cholesterol and triglyceride levels indicates that ceftriaxone can induce lipid synthesis by enhancing glucose metabolism. The significant decrease in High-density lipoprotein levels may suggest that ceftriaxone can suppress the activity of lecithin-cholesterol acyltransferase (LCAT) that converts free cholesterol into ester, which is then sequestered into the core of the lipoprotein particles. This increase in cholesterol, triglyceride level with a corresponding decrease in HDL may predispose to cardiovascular disease as increased lipid profile values are the major risk factor associated with different forms of cardiovascular diseases (Garg *et al*., 2010). These obtained lipid profile changes support the histopathological section of the heart where pericarditis was noted in group V after infection with E.coli and treatment with 360mg/kg CTX.

IMPLICATION TO RESEARCH AND PRACTICE

The results from this study indicates that administration of ceftriaxone have significant effects on hematological and lipid profile values rats and may cause acute pericarditis during an infection.

CONCLUSION

In conclusion, this study confirms that intramuscular administration of ceftriaxone can cause Hypochromic anemia, thrombocytopenia, Neutropenia, Eosinophilia, Monocytosis, Lymphocytopenia, hypercholesterolemia, hypertriglyceridemia, and increased HDLC. This drug must be used with extreme care in established cases of anemia, immunosuppression, and cardiac-related problems as further deterioration of the condition may result. Our result provides useful data into the possible hematological and lipid profile changes that may occur post-infection and after treatment with ceftriaxone.

FUTURE RESEARCH

Further research need to be carried out to fully understand how it cause pericarditis.

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CONFLICTING INTEREST

There was no conflicting interest

AUTHORS CONTRIBUTION

Both authors conceptualize, designed, executed the research, analyzed the data and wrote the manuscript, and reviewed the manuscript

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