The Effect of Ciprofloxacin on Hematological and Biochemical Parameters in Albino Rats

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ABSTRACT

Ciprofloxacin is one of the most frequently used fluoroquinolone drugs used in treatment of infections caused by gram negative microbes. The aim of this studies was to evaluate the effect of this drug on serum enzymes and some hematological parameters to deduce possible physiological changes observed during it administration.The effect of ciprofloxacin was investigated in forty (40) albino rats which were divided into four groups with ten (10) rats in each group and administration of 0.9mg/kg/day, 2.0mg/kg/day and 5.0mg/kg/day of drugs to each respective group was carried out for ten days while the control group were fed with pelleted feeds and water only. The dosages administered decreased the hematological parameters – white blood cell count, red blood cell count, platelet count, packed cell volume, hemoglobin concentration at $p < 0.05$ but the activity of serum enzyme – Alanine aminotransferase, Aspartate aminotransferase, Alkaline phosphatase showed a significant increase. In this study, Ciprofloxacin altered the normal functioning of serum enzymes and some hematological parameters. Therefore its prescription should be strictly adhered to avoid likely harmful effects of its abuse.

Keywords: Ciprofloxacin, Rats, Enzymes, Blood.

INTRODUCTION

An ideal drug could be said to be one that shows efficacy in treatment of disease with tolerable disruption in cell functioning and side effect (Priyadharshini, 2013). Ciprofloxacin has been readily prescribed for treatment of gram negative bacteria in recent times with efficacy in respiratory, urinary tract, gastrointestinal and abdominal infections (Oliphant and Green, 2002, Kumar *et al*., 2011). It is an antibaterial agent belonging to second generation of the family of fluoroquinolones with broad spectrum characteristics against microbial pathogens (Al Nahari, 2014). Ciprofloxacin is administered orally or intravenously (Breecher, 2007) and it inhibits the actions of DNA gyrase which catalyzes the synthesis of bacterial DNA as well as inhibition of topoisomerase IV activities which include the separation of replicated chromosomal DNA into the respective daughter cells during cell division (Oliphant and Green, 2002). The most common side effects of taking ciprofloxacin include nausea, diarrhea, abnormal liver function test, vomiting and rash (Wolfson and Hooper, 1985, Afolabi and Oyewo, 2014). The aim of this research was to evaluate the effect of ciprofloxacin administration on hematological parameters such as red blood cells (RBC), white blood cells (WBC), packed cell volume (PCV), platelet count and hemoglobin concentration and biochemical enzymes such as Aspartate aminotransferase, Alanine aminotransferase and Alkaline phosphatase in wistar rats.

MATERIALS AND METHODS

CENOX (ciprofloxacin tablets USP 500mg) manufactured by Micro Labs Limited, India was purchased from Amela Pharmaceuticals, Uyo.

Experimental Animals

Forty albino wistar rats (male breed) weighing between 120 and 180 gram were obtained from animal house of the department of biochemistry, university of Uyo. These animals were kept in wooden cages under standard conditions (28^{o}C ambient temperature with 12 hours light-dark cycle).

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The animal room was well ventilated and the experimental animals were fed with standard diet and clean drinking water *ad libitum*. The animals were divided into four groups of ten (10) rats. The first group was administered with ciprofloxacin of 0.9 mg/kg/day, the second and the third groups were administered with 2.0mg/kg/day and 5.0 mg/kg/day respectively while the fourth group was the control fed with pelleted feeds and drinking water only . The administration lasted for ten days and sanitary condition was maintained appropriately. On the last day of administration, feeds were withdrawn from the rats twelve hours to the time of sacrifice.

Blood Samples

The rats were euthanized with chloroform, cardiac punctured and blood collected into sample tubes containing heparin for hematological analysis while blood sample meant for biochemical analysis was collected with centrifuge tubes without anticoagulant.

Determination of Hematological Parameters

Packed cell volume (PCV) count was determined by the micro-hematocrit method according to Dacie and Lewis (1991). The hemoglobin (Hb) concentration was determined according to Alexander and Griffiths (1993b). The red blood cell (RBC) count and white blood cell (WBC) count were determined according to Dacie and Lewis method (1991) and platelet count was determined by Neubauer hemocytometer method as approved by International Committee for Standardization in Haematology (1984).

Enzyme Assay

Alkaline phospatase was determined using carbonate acetate buffer by measuring the 4-nitrophenol liberated from 4-nitrophenyl phosphate at 400nm as reported by Wright *et al*. (1972 a&b). Serum Alanine aminotransferase was determined by monitoring the concentration of pyruvate hydrazone formed with 2,4 - dinitrophenylhydrazine (King, 1978). Determination of Aspartate aminotransferase activity was carried out as reported by Reitman and Frankel (1957) by monitoring the concentration of oxaloactate hydrazone formed with 2,4 – dinitrophenyl hydrazine.

Statistical Analysis

The mean and standard deviation (mean ± SD) were calculated for all values. Comparisons between the treated groups and the control were done using student's T – test at $p < 0.05$ significant level.

RESULTS

Result of the effect of Ciprofloxacin treatment on Hematological parameters and enzymes are shown in Tables 1 and 2 respectively.

Table 1: Effect of Ciprofloxacin treatment on Hematological Parameters of Albino Wistar Rats

Dose (mg/Kg/day)	RBC (10^6µl)	WBC (10^3 µl)	PCV (%)	Hb (g/dl)	Platelet (10^3 µl)
Control	5.5 ± 0.09	4.8 ± 0.27	32.3 ± 0.98	10.8± 0.57	288.0 ± 2.35
0.9	5.3 ± 0.08	4.7 ± 0.26	28.7 ± 0.23	9.5 ± 0.13	219.3 ± 4.02
2.0	5.0 ± 0.17	4.3 ± 0.40	30.0 ± 0.13	8.6 ± 0.06	193.3 ± 0.94
5.0	4.1 ± 0.16	3.7 ± 0.28	26.3 ± 0.40	9.0 ± 0.23	203.7 ± 1.00

P <0.05; information represented as (mean conc. ± SD)

Table 2: Effect of Ciprofloxacin treatment on Serum enzymes of Albino Wistar Rats

Dose (mg/Kg/day)	AST	ALT	ALP
Control	29.0 ± 0.66	7.7 ± 1.42	16.0 ± 0.71
0.9	30.3 ± 0.75	7.9 ± 1.61	17.3 ± 1.07
2.0	33.7 ± 0.40	8.3 ± 1.17	21.0 ± 1.64
5.0	37.1 ± 0.22	11.8± 0.90	20.8 ± 0.27

P <0.05; information represented as (mean conc. ± SD)

DISCUSSION

The presence of liver enzymes in the blood may be due to inflammation or injury in the liver and increase or decrease of enzyme in the blood could be a sign of liver impairment (Ebong *et al.,* 2014). The studies showed a significant increase ($p < 0.05$) in serum enzymes (Aspartate aminotransferase, Alanine aminotransferase and Alkaline phosphatase) when the result obtained from treatment groups are compared to the control group. The increased serum Aspartate aminotransferase and Alanine aminotransferase levels may be due to hepatocellular injury of the liver and damage of the nephrosystem (Al Nahari, 2014). However, these enzymes are diagnostic of liver function and their increased activity may be a consequence of increased permeability and subsequent leakage of cellular enzymes (Varshneya *et al.,* 1988, Giboney, 2007). Furthermore, raised level of serum alkaline phosphatase could also occur as a result of skeletal system disorder which involves osteoblast hyperactivity, osteomalacia and rickets (Burtis and Ashwood, 1999).

Ciprofloxacin when administered daily for ten days, showed a significant ($p < 0.05$) decrease in red blood cell count, hemoglobin concentration, platelet, packed cell volume and white blood cell counts. The reduction in hemoglobin concentration and red blood cell count may be due to suppression of bone marrow function which may result to anemia (www.emedicinehealth.com/script/main). Anemic condition which may be a consequence of iron deficiency (Palande, 2011) and unavailability (Gupta, 2014) may be as a result of coagulation of iron with ciprofloxacin thereby rendering the ion insufficient (Borcherding *et al.,* 1996). The depletion of iron reduces the synthesis of hemoglobin in the bone marrow which in turn decreases the red blood cell counts. The significant decrease in these two parameters (hemoglobin concentration and red blood cell counts) agreed with those obtained by Al Nahari (2014) who studied the physiological and hematological changes induced by the administration of ciprofloxacin in mice and found significant decrease in red blood cell count and hemoglobin concentration. Packed cell volume counts (hematocrit counts) is the measure of the percentage of red blood cells in whole blood (Cellmate Wellness System, 2002). The significant ($p < 0.05$) decrease in packed cell volume counts in all test groups compared to control group could be as a result of decrease in hemoglobin concentration which may be due to decrease storage of iron in the liver which stores iron as ferritin and haemosiderin, resulting from liver injury (Murray *et al.,* 1988). Another reason for this remarkable decrease in packed cell volume counts may be due to inability of bone marrow to synthesize hemoglobin owing to less availability of iron and this may result to anemia (Al Nahari, 2014, www.emedicinehealth.com/script/main). There was a slight decrease in white blood cell suggesting a disorder in the bone marrow which hampered the production of white blood cells (http://labtestonline.org/understanding/analytes/wbc). In this respect, the findings agreed with those obtained by Priyadharshini (2013) who reported the decrease in white blood cell count in rats during administration of ciprofloxacin. Reduced platelet count as seen in all the dosage administered may be caused by disorder in platelet production or conditions in which platelets are used up (consumed) or destroyed faster than normal (http://labtestonline.org/understanding/analytes/platelet) and this may result to thrombocytopenia which could lead to impairment of the normal physiological activities of the system (Stiene-Martin *et al.,* 1998).

In conclusion, this study has shown that ciprofloxacin exert alterations on the activities of some enzymes and hematological parameters in albino rats. Consequently, prescription by physicians should be strictly adhered by patients to prevent its abuse and attendant repercussions.

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