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Research Article

Effects of Coartem and Artesunate on Some Haematological and Biochemical Parameters in Albino Rats

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ABSTRACT: The effects of Coartem and Artesunate on the hematological and biochemical parameters of albino rats were investigated. Rats were given 0.57ml of 5.6mg/ml of coartem solution, (20mg artemeter and 120 mg lumefantrine) (group 1) and 0.6ml of 0.5mg/ml of artesunate solution (group 2). Group 3 was control. 5.0 mls of blood sample were collected from the rats through cardiac puncture into EDTA bottle for hematological analysis and 4 mls into plain bottles for biochemical analysis. The findings of this present study show that coartem and artesunate have effects on the hematological and biochemical parameters in albino rats. The hematological indices evaluated were RBC, WBC, differential WBC; Hb, and PCV. Biochemical parameters included Cl K, Na. HCO_3, creatinine and total protein. Artesunate and coartem had significant effects on the blood levels of white blood cells, neutrophils and lymphocytes without significant effects on other hematological parameters measured. WBC and lymphocyte were increased neutrophils was decreased These changes were within tolerable limits.

Keywords: *Coartem, artesunate, lymphocytes, neutrophils, biochemical parameter*

INTRODUCTION

Artemisinin derivatives are new generation anti-malarial drugs they are used in the treatment of acute attacks of severe malaria including cerebral malaria (Ecksain, 2003). Artemisinin is a sesquiterpene lactone endoperoxide derived from the weed qang hao (*Artenusia annua*) also called sweet wormwood or annual wormwood. The Chinese have ascribed medicinal value to this plant for more than to 2000 years (layman 1985). Three chemosynthetic derivatives with improved potency and bioavailability have since largely replaced the use of Artemisia. These include dihydroartemisinin, artemeter, and artesunate.

As a class, the Artemisinins are potent and fast-acting antimalarials with no clinical evidence of resistance they are particularly well suited for treatment of severe *p. falciparium* malaria and now play a key role in the combination therapy of drug resistant malarias (Wilson, 1993). Artesunate has proven exceedingly useful when combined with other anti-malarial for first line treatment of malaria (Adjink *et al*, 2004).The introduction of these new- generation anti-malarials was necessitated by the emergence of chloroquine-resistant strains of *p. falciparium* in different parts of the world especially India, South-East Asia, Africa and South America (Povoa *et al*, 1998). Artemether is rapidly metabolized into an active metabolite dihydroartemisinin (DHA).

Information on the safety of these new antimalarial drugs on body function is still scanty. The study was designed to investigate the effects of Coartem and Artesunate on Some Haematological and Biochemical Parameters in Albino Rats

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MATERIALS AND METHODS

This study was carried out between June and August 2010, in the Department of Physiology, Faculty of Basic Medical Sciences, Anambra State University, Uli, Nigeria.

Drugs: Coartem (Artesunate+Lumefantrine) and Artesunate were obtained from Chris Jen Pharmaceuticals, Awka. Anambra state, Nigeria. All other reagents were of analytical grade.

Animals: Thirty healthy, male albino rats of Wistar strain weighing between 180 and 220g were used in the study. The albino rats were obtained from Department of Hematology, University of Nigeria Teaching Hospital, Enugu and kept in the Animal house of the Department of Physiology Faculty of Basic Medical Sciences, Anambra State University Uli. The animals were housed under standard conditions of temperature (23±2°C), humidity (55±5%) and 12hr light/dark cycle. All animals were allowed two weeks of acclimatization before the commencement of experiments. They were kept in wire meshed cages and fed with commercial rat pellets and allowed water *ad libitum* until commencement of experiments.

Experimental Design: The animals were divided into three groups of 10 rats each. Group I was treated orally with coartem, group 2 with artesunate. Group 3 was the control group. The drugs were administered based on human dosages as found in the literature attached to the drugs.

Administration of Coartem. The rats in group 1 received 0.57ml of 5.6mg/ml of coartem solution, (20mg artemeter and 120 mg lumefantrine), given in the morning of the first day and 8 hrs later using oral cannula. Animals in the group continued with this dosage twice daily for two days.

Administration of Artesunate. The rats in group 2 received 0.6ml of 0.5mg/ml of artesunate solution , given twice for the first day, using oral cannula. Animals in this group continued with this dosage for the next four days but once daily after the first day.

Collection of blood samples. 5 ml of blood was collected from the rats through cardiac puncture - 1 ml was put into EDTA bottle for hematological analysis and 4mls was put into plain bottles for biochemical analysis using standard techniques.

Biochemical analysis: The biochemical parameters for this experiment were determined automatically to obtain accurate results. The biochemical parameters analyzed were sodium ion, potassium ion chloride ion creatinine, total protein and bicarbonate concentrations.

Hematological analysis. The hematological parameters for this experiment were determined using standard methods to obtain accurate results.

Statistical analysis. The data obtained were expressed as mean ± SEM. The Student's t- test was applied and *p*-values were determined. Differences were considered significant at $P< 0.05$.

RESULTS

Effects of coartem and artesunate on Hemoglobin concentration. Figure 1 shows the effects of coartem and artesunate on hemoglobin concentration in the first and second weeks post-administration. Artesunate caused significant decrease in the first week and insignificant decrease in second week, while coartem did not have any significant effect in both weeks compared to control.

They were kept in wire meshed cages a

Effects of coartem and artesunate on packed cell volume (PCV). Figure 2 shows that both coartem and artesunate increased PCV in the first week insignificantly. In the second week, coartem and artesunate caused an insignificant reduction compared to control.

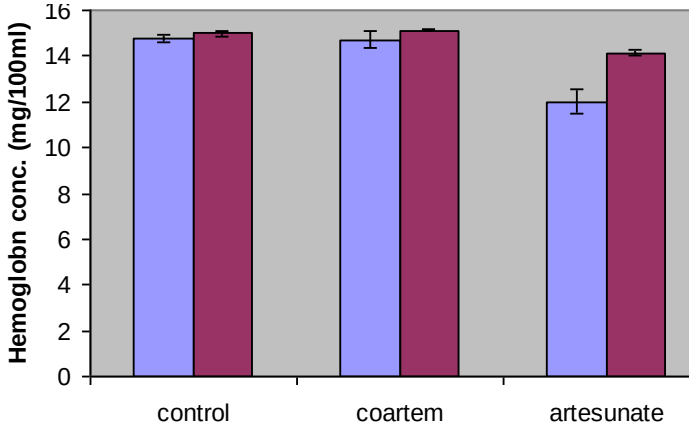

Fig. 1
Effects of Coartem and Artesunate on hemoglobin concentration in rats for weeks 1 and 2. Vertical bars represent Mean ± SEM of hemoglobin concentration after one week (light shaded bars) and two weeks (dark shaded bars)

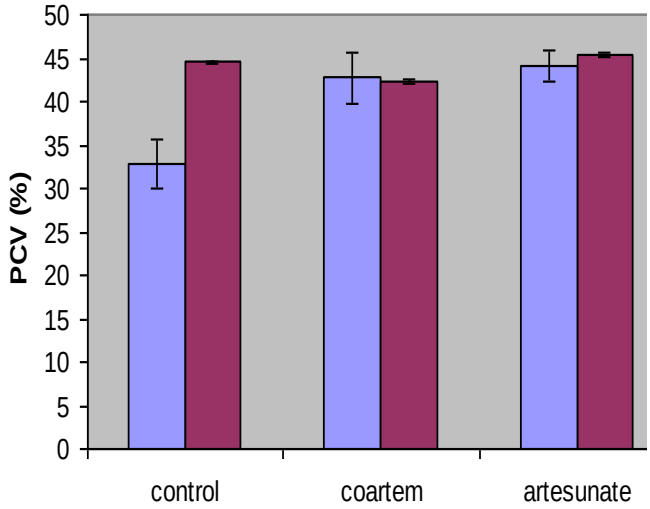

Fig. 2
Effects of Coartem and Artesunate on packed cell volume (PCV) in rats for weeks 1(light shaded bars) and 2(dark shaded bars)

Effects of coartem and artesunate on Blood cell counts. Coartem and artesunate increased WBC count in the first week, although only coartem increase was significant. In the second week, there were no significant changes in WBC levels among the three groups (Fig. 3a). Neither of the two drugs altered the erythrocyte (Fig. 3b) and neutrophils (Fig. 3c) counts to any significant level, although an increase in lymphocyte count was observed in the first week after exposure (Fig. 3d).

Effects of coartem and artesunate on biochemical parameters). There were no significant changes in all the biochemical parameters observed after the first week of Coartem and artesunate treatments (Table 1). The same pattern of no changes was observed in the second week, except for Cl^- (which was increased significantly by coartem and decreased by artesunate) similarly, $HC0_3^-$ concentrations were decreased by both drugs significantly in the second week.

DISCUSSION

The findings of this present study show that coartem and artesunate have effects on the hematological and biochemical parameters in albino rats. The hematological indices evaluated were: RBC, WBC and differential WBC count, Hb, PCV, while biochemical parameters included Cl-, K+, Na+, HC03-, urea and Protein. The effects were variable. In some they were positive, while in others they showed a negative trend.

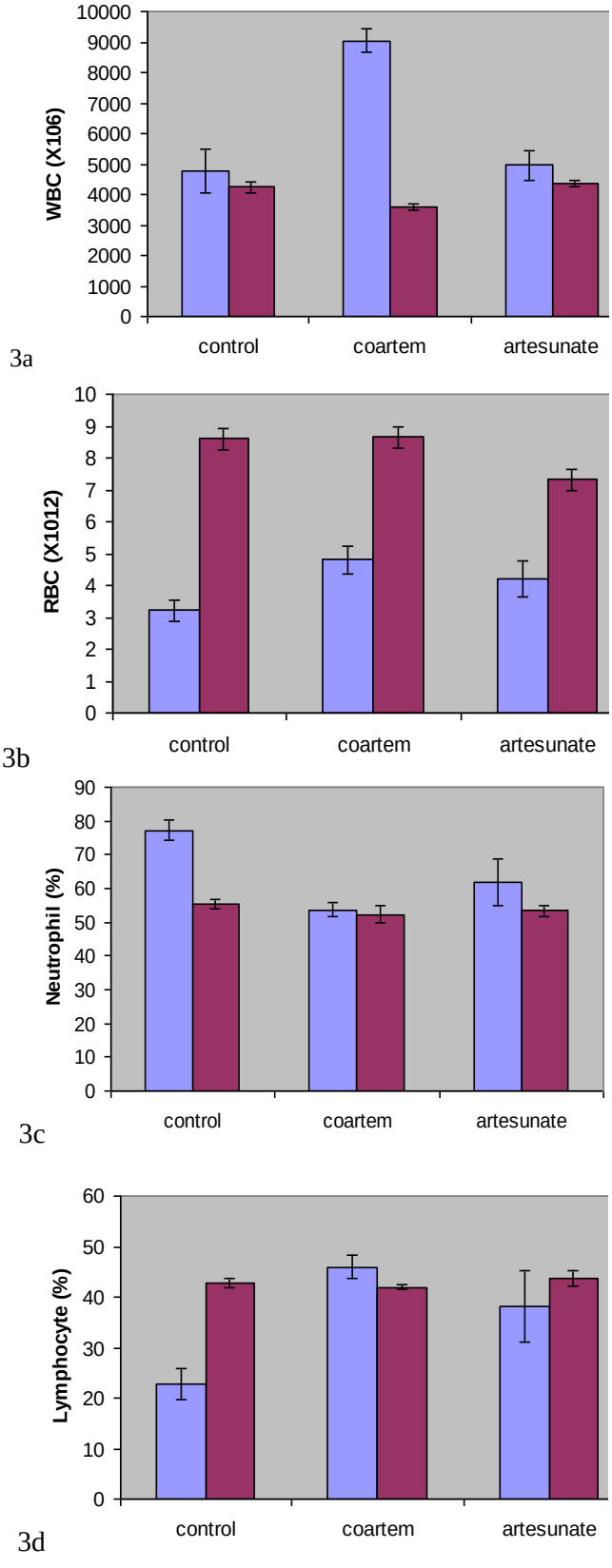

Fig. 3
Effects of Coartem and Artesunate on white blood cell (a), erythrocyte (b), neutrophil (c) and lymphocyte (d) counts in rats for weeks 1(light shaded bars) and 2(dark shaded bars)

Table 1:
Effects of coartem and artesunate on biochemical parameters in rats

Groups	Time	N_a^+	K^+	Cl^-	$HC0_3^-$	Urea	Creatinine	Total Protein
Control	Week 1	136±0.8	7.7±0.1	97.0±0.41	24±0.7	4.5±0.6	104.4±2.6	70.8±2.3
	Week 2	138.0±0.6	6.7±0.1	102.0±1.9	22.3±1.4	4.8±0.1	109.5±0.7	61±1.5
Coartem	Week 1	140.3±0.5	5.5±0.6	102.3±0.3	26.5±0.3	6.2±0.3	111.5±1.2	63.±0.3
	Week 2	136.6±0.3	7.5±0.2	144.0±3.06	18.3±0.3	6.4±0.4	112.5±1.2	62.7±1.5
Artesunate	Week 1	141.0±0.6	5.3±0.06	102.3±0.5	22.3±0.3	5.9±0.2	105.5±3.54	62.3±0.3
	Week 2	138.7±0.9	5.5±0.2	96.±0.9	15.7±0.3	4.7±0.1	112.5±1.2	61.7±0.3

Anti-malarial drugs are used in the prevention and curative treatment of malaria (While, 2004). Artemisia-based formulations e.g. coartem and artesunate are currently in used in Nigeria. There is a dearth of information on the toxicological effects of these drugs. However, these drugs appear to be hugely accepted. This suggests that they are well-tolerated. Coartem and artesunate are highly effective against multi-drug resistant strains of *plasmodium falcipanium*, hence its increasingly wide usage for treatment of malaria (Van et al, 1999)

The findings of this study showed that Coartem and artesunate had significant effects on the blood levels of WBC, neutrophils and lymphocytes without adverse effects on other hematological parameters. WBC and lymphocytes were increased while neutrophils were decreased. White blood cells in the body constitute a special system for combating infections and toxic agents. They are the mobile units of the body's protective systems. The increase in WBC and lymphocyte counts is suggestive of an immunological response induced by the drug (Guyton and Hall, 2006) Preclinical data suggested that repeated exposure to coartem may affect blood cell counts and predispose to anemia (Obianine *et al*, 2011).

In conclusion, coartem and artesunate had variable effects on biochemical parameters and reported adverse effects mainly mild to moderate and within tolerable limits.

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