

THE TOXIC EFFECTS OF MULTIPLE DOSES OF DIMINAZENE ACETURATE ON THE HAEMATOLOGICAL VALUES OF RATS.

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ABSTRACT

The haematological effects of increasing doses of diminazene aceturate on the blood of swiss albino rats was examined. Following the administration of the drug there was a significant increase in white blood cell (WBC) count ($P < 0.05$). The increase in WBC count occurred at all dose levels of 3.5, 7.0, 14.0 and 28.0mg/kg body weight. There was minor change in serum sodium and significant changes in serum potassium levels. All these changes were found not to be strictly dose dependent. This study shows that administration of diminazene aceturate produces increases in white blood cells.

KeyWords: Diaminazene, blood, white blood cells.

INTRODUCTION

Diminazene aceturate is a widely used drug for the treatment of trypanosomiasis in domestic animals in Nigeria (Aliu, 1981). The toxic effects of the drug on certain body organs have been reported by several authors. Brander and Pugh, (1982) reported its hypotensive effect. Williamson (1970) also reported its nephrotoxic and hepatotoxic effects and Homeida *et al.* (1981) reported its toxic effects on the brain in camels.

At present there is widespread abuse of the drug on the field by herdsmen. It is necessary therefore to carry out further work on its toxicological effects to see damages likely to arise as a result of the use of doses above the normal therapeutic dose level. The aim of this work therefore is to highlight the effects of acutely administered increasing doses of diminazene aceturate on hematological values particularly as blood is the main target of attack

by trypanosome parasites.

MATERIALS AND METHODS

Animals:

30 Swiss albino rats whose ages ranged between 5 -6 months and weighing between 150 - 170grams were obtained from the department of Veterinary Physiology and Pharmacology, University of Ibadan, Nigeria. Rats were randomly divided into 5 groups of 6 rats each. Allocation to a group was done without bias and no consideration was made with respect to sex. Groups 1 to 4 received varying doses of diminazene aceturate. Group 5 served as control. All rats were housed in cages, in a fly-proof house. They were provided with commercially prepared rat diet (21% protein, 3.5% fat, 6% fibre, 0.8% calcium and 0.8% phosphorus, (Ladokun and sons Livestock Feeds Nigeria Limited) and water *ad libitum*.

Drug administration and blood sampling:

A 23 gauge needle with 1ml syringe was used to administer drug intraperitoneally. Group one received 3.5mg/kg of diminazene aceturate, group two 7mg/kg, group three 14mg/kg and group four 28mg/kg. Group five served as control and were administered Physiological saline. Blood samples were collected after three hour of drug administration by cardiac puncture under ether anaesthesia according to the method of Schalm, (*1975). The blood samples were collected into plain vacutainer tubes where serum was harvested for analysis of sodium and potassium. Haematological and biochemical analyses, packed cell Volume (PCV) hemoglobin concentration (Hb), erythrocyte count, leucocyte count and erythrocyte indices were determined within 2 hours of collection according to the methods of Coles (1974) and Schalm (1975). Serum sodium and potassium

were determined using flame photometry (Gallenkamp, London).

Statistics:

Statistical evaluation of the result obtained was made through the use of student t test. The levels of significance chosen were $P < 0.05$ and $P < 0.01$.

RESULT

Changes in PCV, Hb, RBC, MCV, MCHC and WBC following administration of diminazene aceturate are presented in Table 1. There was a significant increase in white blood cell count at all dose levels of 3.5 7.0 14.0 and 28mg/kg body weight. There was no other significant change in other haematological values when compared to the control.

There was also a significant decrease in serum potassium at all dose levels of the drug used. However, only slight increase in sodium was recorded. (Table II)

DISCUSSION

A general increase in WBC was observed with dose range of 3.5mg/kg to 28.0mg/kg. The reason for the increase may be explained on the basis of immunological reaction to the drug following the release of histamine (Arowolo and Adepoju, 1981), coupled with dilatation of Blood vessels (Barret et al, 1986). Immature white cells could have been pushed into circulation from the bone marrow pool following the drug administration, contributing to the increase.

The changes observed in the serum electrolytes may be related to the nephrotoxic challenge by diminazene aceturate. De Bruin (1976) reported that nephrotoxic challenge is known to be a primary cause of changes in extracellular electrolyte content, and reports of Williamson (1970) and Homeida *et al* (1981) showed that large doses of diminazene aceturate produced serious hepatic and renal damage in animals. As observed by De Bruin (1976), uncertainty always follow the interpretation of such observed effects because mechanisms

through which electrolyte disturbances relate to the overall toxic manifestation are in many cases unsolved. There was no plausible explanation for the changes observed in electrolyte changes in this experiment. More information is required in order to throw more light on the subject.

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Table 1 HEMATOLOGICAL PARAMETERS OF SWISS ALBINO RATS RECEIVING THERAPEUTIC AND HIGHER DOSES OF DIMINAZENE ACETURATE (BERENIL®). (MEAN FROM A GROUP OF 6 RATS ± SEM)

Treatment groups Drug dosages (mg/kg)	Parameters						
	PCV (%)	RBC (x10 ⁶ /mm ³)	Mean Corpuscular values			WBC (x 10 ³ /mm ³)	
			Hb (g/dl)	MCV (fl)	MCHC (%)		MCH pg
1 (3.5)	45±0.5	6.0±0.8	11.8±0.3	63.0±2.0	34.1±1.7	19.4±0.7	5.5±0.1*
2 (7.0)	45±0.5	6.1±0.3	12.8±0.9	62.4±3.4	34.0±3.2	21.1±0.7	5.2±0.3*
3 (14.0)	46±0.8	6.9±0.2	15.2±0.2	63.1±1.4	31.4±0.5	19.8±0.3	5.5±0.3*
4 (28.0)	44±0.6	6.3±0.1	12.5±0.5	67.3±2.0	29.5±1.0	19.8±0.3	5.0±0.2*
5. Control	45±0.6	6.4±0.3	13.4±0.5	70.4±2.5	29.7±0.5	20.9±0.5	4.8±0.2

* = P < 0.05

SEM = Standard error of mean.

Table 2 CHANGES IN SERUM SODIUM AND POTASSIUM CONCENTRATION OF SWISS ALBINO RATS RECEIVING THERAPEUTIC AND HIGHER DOSES OF DIMINAZENE ACETURATE (EACH VALUE REPRESENTS THE MEAN OF 6 RATS ± SEM).

Treatment groups Drug dosage level (mg/kg)	SERUM ION VALUES			
	Sodium (mmol/l) Indices		Potassium (mmol/L) Indices	
	Mean ± SEM	± 2 x SD	Mean ± SEM	± 2ξΔ
1. (3.5)	135.6±3.7	128.7±144.8	3.2±0.09*	3.0±3.5
2. (7.0)	149.5±12.6	141.7±197.4	3.5±0.2*	3.2±4.0
3 (14.0)	140.8±4.0	131.6±149.3	3.1±0.1*	2.8±3.4
4. (28.0)	153.5±5.7	141.7±167.0	3.1±0.1	3.0±3.5
5. (Control)	140.2±2.3	134.1±146.8	4.7±0.5*	3.8±6.1

* = P < 0.05

SEM = Standard Error of mean