Effect of Berenil® and Cymelarsan® on the Alteration of Biochemical Parameters in Red-Fronted Gazelles (*Gazella rufifrons*) Experimentally Infected with *Trypanosoma brucei*

A.W. Mbaya[1*] M.M. Aliyu[2] C.O. Nwosu[1] U.I. Ibrahim[2]

Keywords

Gazella rufifrons – Gazelle – *Trypanosoma brucei* – Trypanosomosis – Biochemistry – Drug – Experimental infection – Nigeria.

Summary

A study was carried out to investigate the chemotherapeutic effects of diminazene aceturate (Berenil®) and melarsamine hydrochloride (Cymelarsan®) on the alteration of biochemical parameters in red-fronted gazelles experimentally infected with *Trypanosoma brucei*. A significant ($P < 0.05$) increase in serum cortisol, alanine aminotransferase, aspartate aminotransferase, total bilirubin, creatinine, urea, uric acid, total lipids, and a significant ($P < 0.05$) decrease in total serum proteins, albumin level and serum glucose were observed in the gazelles following parasitemia. Alkaline phosphatase activity fluctuated around normal values ($P > 0.05$). These biochemical alterations were effectively modulated to preinfection levels before the end of the experiment in gazelles treated with either 0.3 or 0.6 mg/kg body weight (BW) of Cymelarsan, or 7.0 mg/kg BW of Berenil. The results therefore suggested that an initial stress associated with an increased serum cortisol level and its immunosuppressive effect might have been responsible for the establishment and clinical manifestation of the infection in the gazelles. Furthermore, the severity of the biochemical effects experimentally induced indicated that trypanotolerance in wild gazelles could be compromised, especially when they are subjected to the stress of captivity. Results also showed that Cymelarsan at 0.3 or 0.6 mg/kg BW, and Berenil at 7.0 mg/kg BW were effective in managing the disease under experimental conditions.

■ INTRODUCTION

Changes in the essential serum enzymes and amino acid profiles in trypanosomosis infected animals have been reported (4, 15). One of the implications of amino acid deficiencies is immunosuppression, which features in trypanosomosis (18).

The toxic effects of trypanosome catabolites (P-hydroxylphenyl and phenylpyruvate) lead to the alteration of mitochondrial function and gluconeogenesis by inhibiting carboxylase and pyruvate transferase (35). The serum lipid concentration of trypanosome-infected rabbits is reported to have increased under natural and experimental conditions (12, 31). Decrease in liver glucose 6-phosphate and cytochrome oxidase activity has also been shown (37). Liver dysfunction in the trypanosome-infected host is suggested by decrease in serum albumin and cholinesterase and increase in the activity of liver enzymes (4, 5), while kidney dysfunction is suggested by increase in blood urea and creatinine levels (4).

Most of the literature available on biochemical changes due to trypanosomosis is on domestic or laboratory animals. Despite several articles in clinical trypanosomosis in captive wild animals (23, 29), information on clinical biochemical changes due to trypanosomosis in wild animals in general and the red-fronted gazelles (*Gazella rufifrons*) in particular is scarce. Such baseline data are important because of the increasing interest in the *ex situ* conservation of these animals in captive breeding centers and zoological gardens. An added consideration is the fact that the red-fronted gazelle is almost domesticated in the semiarid zone of Northeastern Nigeria where it occurs naturally in abundance in the Saharo-Sahelian ecosystem and in farms where it is reared alongside sheep and goats (24).

1. Department of Veterinary Microbiology & Parasitology, University of Maiduguri, PMB 1069, Maiduguri, Nigeria.
2. Department of Veterinary Medicine, University of Maiduguri, Nigeria.
* Corresponding author
Tel.: 80 36 01 17 74; E-mail: awmbaya@yahoo.com

This study was designed to investigate the biochemical changes of an experimental *Trypanosoma brucei* infection in wild red-fronted gazelles subjected to captivity and treated with either diminazene aceturate or melarsamine hydrochloride.

■ MATERIALS AND METHODS

Experimental animals

Thirty apparently healthy red-fronted gazelles of both sexes aged between two to three years and weighing between 20 and 25 kg were obtained directly from the wild under authorization of the Ministry of Environment, Borno State, Nigeria. They were screened for blood, intestinal and external arthropod parasites according to standard criteria (38).

Ten of the gazelles harbored trypanosomes and were treated with DL-α-difluoromethyl ornithine (Merrill and Dow, USA) at 400 mg/kg orally for four consecutive days, while nine harbored helminths and were treated with Morantel (Pfizer, USA) at 400 mg/kg orally for four consecutive days. On the other hand, six harbored rickettsial organisms and were treated with oxytetracycline hydrochloride at 1 mL/10 kg of body weight (BW). They were allowed 40-day acclimatization to allow the drugs to be properly metabolized before beginning the experiment. They were housed in concrete-floored and fly-proof pens throughout the experiment and fed on wheat bran supplemented with bean husks, guinea corn and chopped cucumber while water was provided *ad libitum* throughout the period of the experiment. All handling procedures were in accordance with the International Ethics on Animal Welfare (8).

Source of trypanosomes

Trypanosoma brucei brucei (Mkar/84/Nitr/6) used for the study were obtained from the Nigeria Institute for Trypanosomosis Research (NITR) in Kaduna, Nigeria. The organism was first isolated in 1984 from a fatal outbreak of porcine trypanosomosis in Mkar in Benue State, Nigeria (3).

It was identified based on morphology and the negative blood inhibition and infectivity test (BIIT), stabilized by four passages in rats and stored in liquid nitrogen. The stabilates were passaged twice in rats and then transferred into Red Sokoto goats. Blood from the infected goats was diluted with phosphate buffered glucose saline (PBSG, PH 7.2). Each gazelle was inoculated via the jugular vein with blood from the goat containing 1.5 x 10^6 trypanosomes. Detection of parasitemia was by wet mount and hematocrit buffy-coat microscopy (BMC) (38), while the degree of parasitemia was estimated by the rapid matching technique as described by Herbert and Lumsden (14).

Experimental design

The infected gazelles were randomly separated into six groups (A through F) of five gazelles each. Groups A and B were treated subcutaneously with melarsamine hydrochloride (Cymelarsan®) at a single standard dose rate of 0.3 and 0.6 mg/kg BW, respectively, while groups C and D were treated intramuscularly with diminazene aceturate (Berenil®) at a single standard dose rate of 3.5 and 7.0 mg/kg BW, respectively. Groups E and F served as infected and untreated, and uninfected controls, respectively. All treatments began at the onset of parasitemia, by day 8 postinfection.

Biochemical analysis

The gazelles were bled every other day for a period of 52 days via the jugular vein. Blood samples (3 mL) for biochemical analysis were collected into vacutainer tubes without anticoagulant, allowed to separate at 4ºC and stored until used.

Total lipids in heart and liver tissue homogenates were estimated by the sulfo-phosphatevanillin reaction of Chabrol and Charonnat, cited in Chaudry (9). The aspartate and alanine aminotransferase activity was estimated by use of commercial kits (Randox Laboratories, UK) as described by Reitman and Frankel (33). Cortisol levels were however estimated by the method described by the World Health Organization (40). Total protein and albumin were determined by the Burette reaction and the bromocresol green methods, respectively (2). Serum creatinine was measured by the Jaffe reaction method of Seaton and Ali (34), while urea estimation was carried out by the diacetyl monoxime method (2). The uric acid level was determined by the enzymatic method (13) using commercial kits (Randox Laboratories, UK). The bilirubin concentration was determined by the Van den Berg reaction method (25), while the glucose level was determined by the oxidase procedure of Folin-Wu (10) and values were read with a spectrometer (Boehringer, 4010; Germany) at various wavelengths. Levels were calculated using standard formulae (10).

Statistical analysis

Data collected were analyzed using a two-way analysis of variance at 95% confidence limit (22).

■ RESULTS

Trypanosomes were first detected in circulation with a mean parasite count of 5.5 x 10^3/µL for all infected groups following infection with a prepatent period of eight days. Only a single peak without relapse or death was encountered in groups treated with Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW, while the group treated with Berenil at 3.5 mg/kg BW had a count of 250.0 x 10^3/µL during the first wave and of 500.0 x 10^3/µL during relapsed parasitemia. Successive peaks with similar values were also encountered in the infected and untreated control (Figure 1).

The effects of various drugs on serum cortisol changes in the red-fronted gazelles experimentally infected with *T. brucei* are presented in Figure 2. Berenil or Cymelarsan at the various dosages did not significantly ($P > 0.05$) modulate the continuous rise in mean serum cortisol levels. Mean preinfection serum cortisol levels were 10.8 ± 1.54 mmol/L. They were 12.2 ± 1.75 mmol/L by day 4 postinfection before the appearance of parasitemia, which occurred by day 7-8 postinfection, and reached peak values above 60 mmol/L by day 52 postinfection in all the infected groups. Similarly, the uninfected control reached a peak above 30 mmol/L.

On the contrary, following the appearance of parasitemia, the glucose levels significantly decreased ($p < 0.05$) in all groups. The decrease was continuous to the end of the study when the lowest values were attained in the infected and untreated group, and in the group treated with Berenil at 3.5 mg/kg BW, with the death of all the gazelles in the two groups occurring between days 46 to 52 postinfection (Figure 3).

Progressive but significant decrease ($p < 0.05$) in mean total serum protein and albumin levels also occurred following parasitemia and continued to day 20 postinfection. Thereafter, the levels were restored to normal preinfection levels which were maintained until the end of the study in groups treated with Cymelarsan at 0.3 or 0.6 mg/kg BW, and with Berenil at 7.0 mg/kg BW. The decrease continued until the end of the study in the group treated with Berenil at 3.5 mg/kg BW, and the infected and untreated control in relation to the uninfected control which had stable values (Figures 4 and 5).

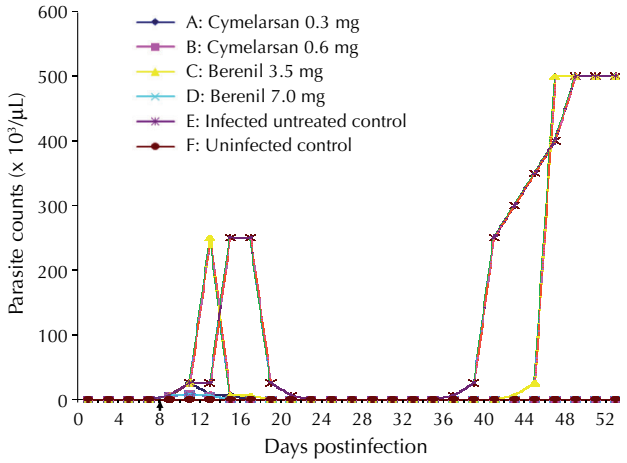

Figure 1: *Parasite counts in the blood of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

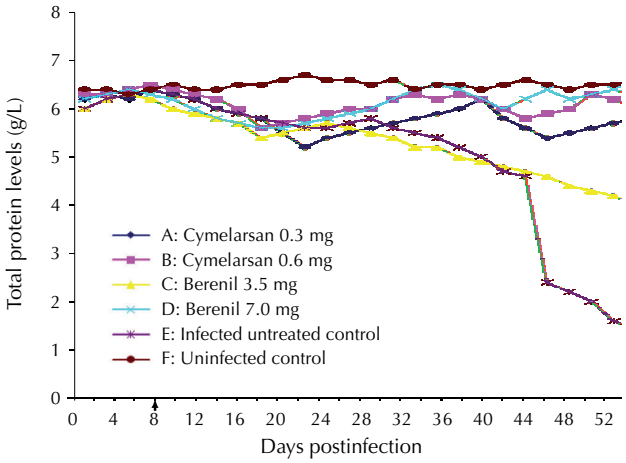

Figure 4: *Mean total protein of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

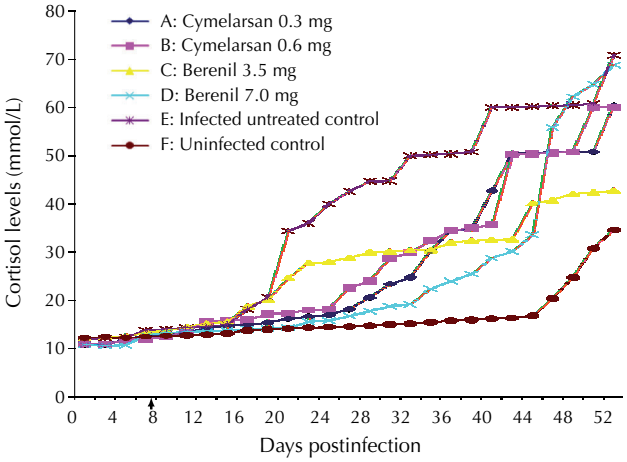

Figure 2: *Mean serum cortisol of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

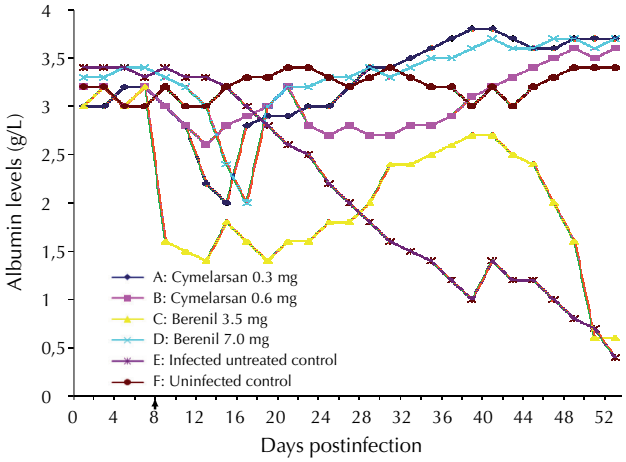

Figure 5: *Mean serum albumin of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

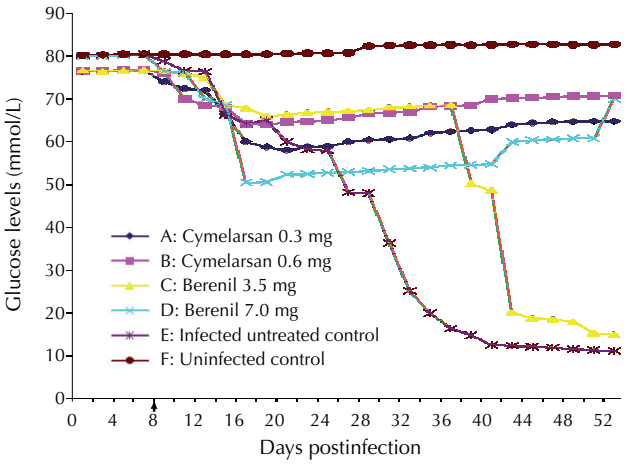

Figure 3: *Mean serum glucose of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

With regard to liver enzymes, serum alanine amino and aspartate aminotransferase or total bilirubin remained within normal preinfection levels throughout the observation period in the healthy control group and those treated with either Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW. Meanwhile, the levels of these enzymes showed a continuous rise in the group treated with Berenil at 3.5 mg/kg BW, and in the infected and untreated control (Figures 6, 7 and 8).

On one hand, administration of Cymelarsan at 0.3 or 0.6 mg/kg BW, and Berenil at 3.5 or 7.0 mg/kg BW following parasitemia affected significantly ($p < 0.05$) serum alkaline phosphatase concentrations. On the other hand, they fluctuated significantly ($p < 0.05$) at relatively higher levels in the infected and untreated control (Figure 9).

The effect of Cymelarsan or Berenil on mean serum urea, creatinine and uric acid concentrations in the red-fronted gazelles are presented in Figures 10, 11 and 12. The levels remained within the preinfection range in the uninfected control group throughout the

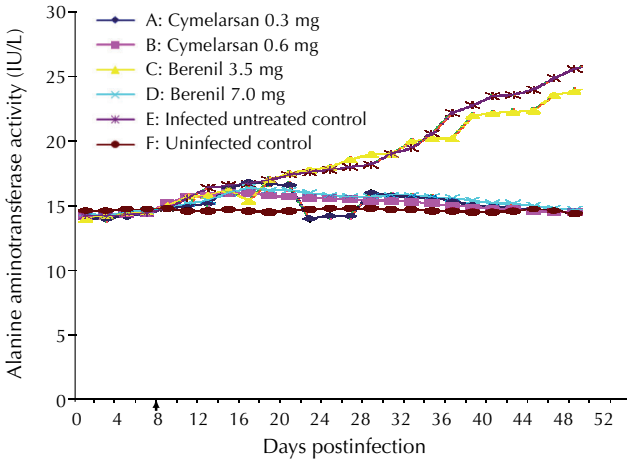

Figure 6: *Mean alanine aminotransferase activity of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

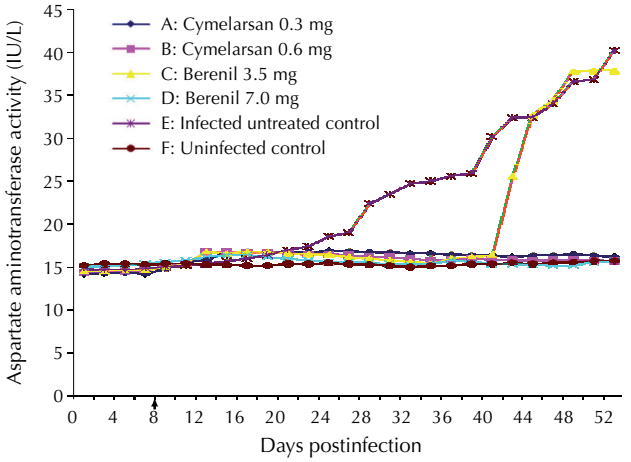

Figure 7: *Mean aspartate aminotransferase activity of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

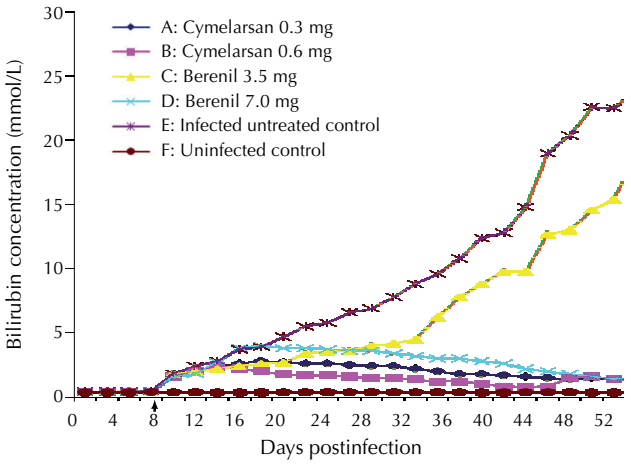

Figure 8: *Mean total serum bilirubin concentration of red-fronted gazelle experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

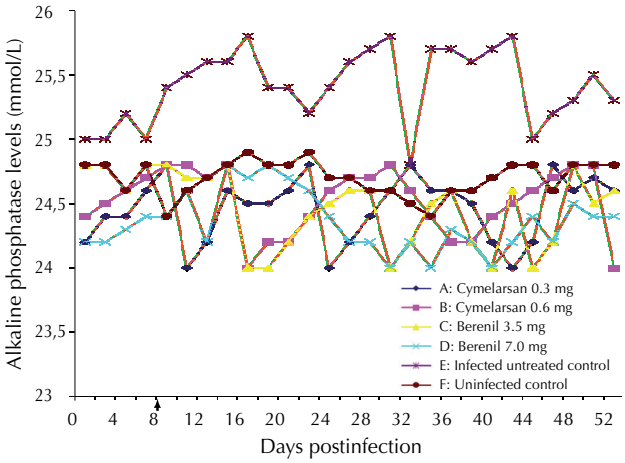

Figure 9: *Mean alkaline phosphatase activity of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

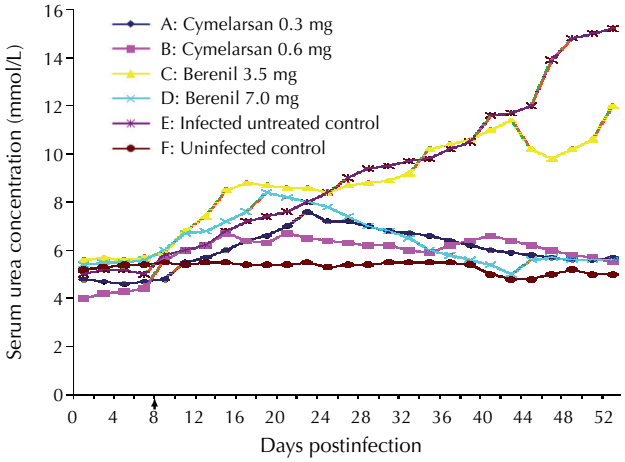

Figure 10: *Mean serum urea concentration of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

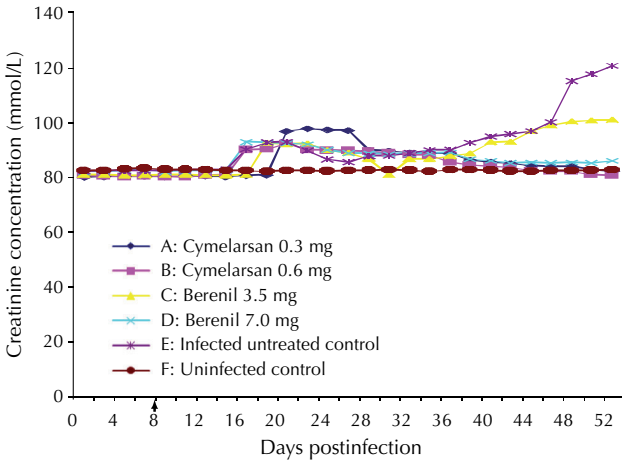

Figure 11: *Mean serum creatinine concentration of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

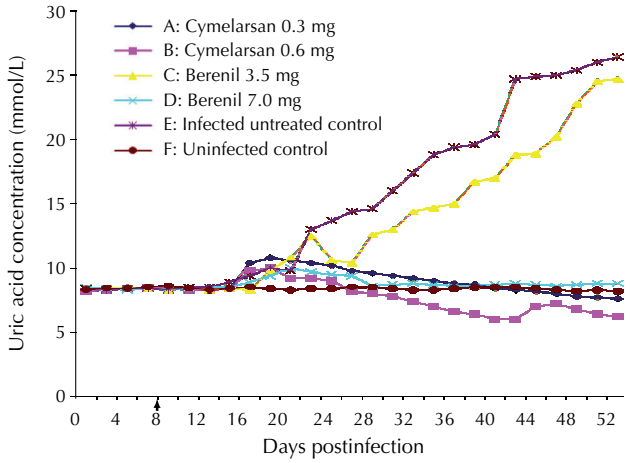

Figure 12: *Mean serum uric acid concentration of red-fronted gazelles experimentally infected with* Trypanosoma brucei *and treated with either Cymelarsan or Berenil, and their controls. Arrow: day of treatment.*

study period. However, the levels were significantly high ($p < 0.05$) in all infected groups following the first appearance of parasitemia. The increase in enzyme concentrations were noted between days 14 and 32 in the groups treated with either Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW. Thereafter, the concentrations of serum urea, creatinine and uric acid in these groups were restored almost to preinfection levels and remained as such throughout the observation period.

■ DISCUSSION

The results of the present study showed that biochemical alterations in red-fronted gazelles occurred after experimentally inducing an infection with *T. brucei*. These biochemical alterations were however reversed with the administration of Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW. There was a graded dose-response in the use of the two drugs, as the higher dosages of Cymelarsan at 0.6 mg BW or Berenil at 7.0 mg/kg BW produced greater response than the lower dosages. This was clearly shown with Berenil at 3.5 mg/kg BW, which was rarely effective in modulating biochemical alterations leading to the death of all the gazelles in the group, probably as a result of the relapsed parasitemia encountered only in this group.

The reversal of biochemical changes due to trypanosomosis in domestic animals has been extensively studied (1, 7, 17, 21, 28). All the gazelles in both infected but treated groups and their controls manifested unabated increased serum cortisol levels from day 4 postinfection, before the appearance of the parasites in circulation. Although the initial rise in the cortisol level was low, it has been however reported that small rises of cortisol, if sustained, can cause imunosupression in goats (26). This showed that the wild gazelles experienced some degree of somatic stress due to handling or physiological stress via visual and auditory stimuli due to their new environment in spite of the long period of acclimatization. This initial corticosteroid output before the onset of parasitemia in the infected gazelles might have contributed to the establishment of the infection and continued to persist to unprecedented levels following the appearance of parasitemia. It was however noted that the level of serum cortisol was highest in the infected and untreated control, which showed that the infection exacerbated the level of stress in the infected gazelles. Similar observations were reported in *T. congolense* infection of goats (26) and were found to be insignificant in cattle (27). Also, the strong alteration of cortisol by day 44 postinfection, particularly in the uninfected control, was an indication that stress due to handling was responsible for the cortisolemia since no infection was encountered in this group.

The pathophysiology of captivity-induced stress in domestic animals has been associated with an increased adrenal cortical activity 30 minutes from the onset of captivity, resulting in the secretion of 11-hydroxy corticosteroids (11-oxy) (30). In this study, however, the gazelles manifested cortisol secretion four days after the onset of captivity. The increase in circulating cortisol in trypanosomosis is expected to produce metabolic features similar to the Cushing's syndrome, which is known to resemble diabetes mellitus in some respect (41). Consequently, high circulating cortisol levels are reported to impair glucose tolerance and may produce hyperglycemic and glycosuric effects since cortisol has an opposite action to insulin. In this study however, hypoglycemia was noted in spite of the persistent hypercortisolemia. This might probably be associated with the fact that the high-energy demand in the host during the high parasitemia impaired glucose release from the gluconeogenic pathway in the infected animals, as well as the fact that trypanosomes during high parasitemia consume a large amount of host glucose (16).

Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW effectively modulated the hypoglycemic effects of the infection to preinfection levels, by eliminating the parasites from circulation. Trypanosomes have been reported to destroy blood glucose due to aerobic glycolysis (16). The organism metabolizes glucose to produce 4-hydroxy-4-methyl α-ketogluterate, which is inhibitory to the tricarboxylic acid cycle (TCA) in the mitochondria leading to energy deficit in the host (6, 16). This suggests that TCA and oxidative phosphorylation may be inhibited, thus leading to failure to generate energy from energy-rich compounds. Conn and Stompf showed that 90% of the energy available in glucose is released when pyruvate is oxidized to Co_2 and H_2O through the TCA and electron transport chain (11). This might therefore explain the profound weakness experienced by the gazelles in the course of the infection, which was more severe in both those treated with Berenil at 3.5 mg/kg BW and those infected and untreated.

The increase in lipid deposits in the heart muscles of the gazelles treated with Berenil at 3.5 mg/kg BW, or in the infected and untreated control contrasted with the situation observed in gazelles treated with either Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW and agreed with earlier reports in rabbits infected with *T. brucei* (12, 32) (Table I). The increase in lipid deposits in the heart suggested alterations in lipid and carbohydrate metabolism which might have contributed to the protein catabolism and muscle wasting seen in the gazelles treated with either Berenil at 3.5 mg/kg BW, or in the infected and untreated control.

The infection also produced changes in the level of alkaline phosphatase in gazelles treated with Berenil at 3.5 mg/kg, or the infected and untreated control, while the values of gazelles treated with either Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW returned to the preinfection status. The increased level of enzymes in trypanosomosis has been associated with liver and bone damage (39).

The infection was associated with a decrease, which remained unabated, in total serum proteins and the albumin level in gazelles treated with Berenil at 3.5 mg/kg BW, or in the infected and untreated control. On the other hand, an increase was effectively modulated to preinfection levels posttreatment in groups treated with Cymelarsan at 0.3 or 0.6 mg/kg BW, or with Berenil at 7.0 mg/kg BW. Decrease in total serum protein and albumin levels in *T. brucei* infections may be linked with hepatic damage due to tissue invasion by the organism (39). The tissue invasion might have explained the aparasitemic phase

Table I

Effect of Berenil or Cymelarsan on the total lipid concentration in the heart of red-fronted gazelles that died or were sacrificed at the end of the study

Group	Treatment	Lipid concentration (g/kg)	Num. affected*
A (n = 5)	Treated with Cym at 0.3 mg/kg BW	23 ± 0.2[a]	0
B (n = 5)	Treated with Cym at 0.6 mg/kg BW	23 ± 0.2[a]	0
C (n = 5)	Treated with Ber at 3.5 mg/kg BW	40 ± 3.16[b]	1.74
D (n = 5)	Treated with Ber at 7.0 mg/kg BW	23.9 ± 0.4[a]	0
E (n = 5)	Infected/untreated	42.8 ± 3.27[b]	1.83
F (n = 5)	Uninfected control	23.0 ± 0.2[a]	0

* Number of gazelles affected by an increase in lipid concentration in relation to control

n: number of gazelles in each group; BW: body weight

Cym: Cymelarsan; Ber: Berenil

[a,b] Values with different superscripts differ significantly ($p < 0.05$)

encountered between the first and second waves of parasitemia in the infected untreated control. This is in agreement with earlier reports in several domestic animals infected with *T. brucei* (19, 20, 28).

Elevated serum levels of creatinine, urea and uric acids also accompanied the experimental infection. The presence of these enzymes in sera during a trypanosomosis has been associated with kidney dysfunction (5, 32). The retention of urea and uric acid in the body showed that the kidneys were disabled to the extent whereby they could not excrete by-products. The high level of creatinine in the gazelles treated with Berenil at 3.5 mg/kg BW, or in the infected and untreated control might be due to severe muscle wasting that occurred in the course of the infection or to renal failure preventing the kidneys to excrete by-products.

In the course of the experiment, increased levels of aspartate and alanine aminotransferase, and of total serum bilirubin were effectively modulated to preinfection values in gazelles treated with either Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW. This suggested that the liver damage in these groups was not severe due to the efficacy of the therapies in contrast with groups treated with Berenil at 3.5 mg/kg BW, or the infected and untreated control. Increased levels of hepatic enzymes are indicative of hepatic damage (36).

■ CONCLUSION

Trypanotolerance in wild animals and especially in red-fronted gazelles can be compromised when subjected to the stress of captivity with an evolution of biochemical alterations following the onset of parasitemia due to tissue damage caused by the organism. It is therefore necessary that such animals should be kept under stressless conditions or in near-reality conditions and that they be treated with either Cymelarsan at 0.3 or 0.6 mg/kg BW, or Berenil at 7.0 mg/kg BW when affected by trypanosomosis.

Acknowledgments

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REFERENCES

1. ADAH M.I., OTISELE E.B., JOSHUA R.A., 1992. Changes in levels of transaminase in goats experimentally infected with *Trypanosoma congolence. Revue Elev. Méd. vét. Pays trop.*, **45**: 284-286.

2. AFONJA O.A., 1997. Basic clinical biochemistry practice. Ibadan, Nigeria, Macmillan, p. 85-88.

3. AGU W.E., BAJEH S.T., 1986. An outbreak of *Trypanosoma brucei* infection of pigs in Benue State of Nigeria. *Trop. Vet.*, **4**: 25-28.

4. ANOSA V.O., 1988. Haematological and biochemical changes in human and animal trypanosomiasis. Part II. *Revue Elev. Méd. vét. Pays trop.*, **41**: 151-164.

5. AROWOLO R.O.A., ELHASSAN E.O., AMURE B.O., 1988. Assessing hepatic dysfunction in rabbits experimentally infected with *Trypanosoma brucei. Revue Elev. Méd. vét. Pays trop.*, **41**: 277-281.

6. ASHMAN P.U., SEED J.R., 1973. Biochemical studies in the vole, *Microtus montanus*. II. The effects of a *Trypanosoma brucei gambiense* infection in the diurnal variation of hepatic glucose-6-phosphate and liver glycogen. *Comp. Biochem. Physiol.*, **451**: 379-392.

7. AYO J.O., OLADELE S.D., 1996. Road transport stress in food animals in Nigeria: A review. *Nigerian vet. J.* (Special Edn): 49-57.

8. BROOM D.M., JOHNSON K.G., 1993. Stress and animal welfare. London, UK, Chapman and Hall, p. 120-140.

9. CHAUDRY K., 1989. Total lipids and urea. In: Biochemical techniques, 1st Edn. London, UK, Joy. Pec., p. 76-98.

10. COLES F.H., 1980. Veterinary clinical pathology, 3rd Edn. London, UK, WB Saunders, p. 112-145.

11. CONN E.E., STOMPF P.K., 1976. In: Outline of biochemistry, 4th Edn. New York, NY, USA, John Wiley, p. 279-343.

12. DIEHL E.J., RISBY E.L., 1974. Serum changes in rabbits experimentally infected with *Trypanosoma gambiense*. *Am. J. trop. Med. Hyg.,* **23**: 10-19.

13. FOSSATI P., PRENCIPTI L., BERTI G., 1980. Methods for determination of serum uric acid. *Clin. Chem.*, **26**: 227-231.

14. HERBERT W.J., LUMSDEN W.H.R., 1976. *Trypanosoma brucei:* A rapid matching method for estimating the host's parasitaemia. *Exp. Parasitol.*, **40**: 427-432.

15. IGBOKWE I.O., 1990. Biochemical approaches to the pathogenesis of trypanosomosis. In: Proc. OBABS, University of Maiduguri, Nigeria, 12-16 Feb. 1990, p. 103.

16. IGBOKWE I.O., 1994. Nutrition in the pathogenesis of African trypanosomosis. *Prot. Abst.*, **19**: 799-809.

17. IGBOKWE I.O., MOHAMMED A., 1992. Some plasma biochemical changes in experimental *Trypanosoma brucei* infection in Sokoto Red goats. *Revue Elev. Méd. vét. Pays trop.*, **45**: 287-290.

18. JOSE D.G., GOOD R.A., 1973. Protein metabolism in African trypanosomosis. *J. exp. Med.*, **137**: 1.

19. KALU A.U., IKWEGBU O.A., OGBONNAH G.A., 1989. Serum protein and electrolyte levels during trypanosome infection and following treatment in West African dwarf goat. *Bull. Anim. Health Prod. Afr.*, **37**: 41-45.

20. KATUNGUKA-RWAKIHAYA E., MURRAY M., HOLMES P.H., 1992. The pathophysiology of ovine trypanosomosis: Haematology and biochemical changes. *Vet. Parasitol.*, **45**: 17-32.

21. KAUSHIK R.S., GUPTA S.L., BHARDWAJ R.M., 1989. Some biochemical changes in the blood of pups experimentally infected with *Trypanosoma evansi. J. vet. Parasitol.*, **2**: 117-119.

22. MAED R., CURNOW R.N., 1983. Statistical methods in agriculture and experimental biology. London, UK, Chapman and Hall, p. 132.

23. MARIE C.J., 1998. African animal trypanosomosis (Nagana tsetse disease). In: Foreign animal disease. Richmond, VA, USA, United States Animal Health Association, p. 29-40.

24. MBAYA A.W., 2007. Studies on trypanosomosis in captive red-fronted gazelles (*Gazella rufifrons*) in Nigeria. PhD Thesis, University of Maiduguri, Nigeria, 63 p.

25. MICHAELSON M., 1991. Records of trypanosomosis in free-living wild animals. *Trop. Med. Parasitol.*, **178**: 490-520.

26. MUTOYOBA B.M., GOMBE S., 1989. Effect of African trypanosomosis on plasma cortisol and thyroxin concentration in goats. *Res. vet. Sci.*, **3**: 315-318.

27. OGWU D., NJOKU C.O., OGBOGU V.C., 1992. Adrenal and thyroid dysfunction in experimental *Trypanosoma congolence* infection in cattle. *Vet. Parasitol.*, **41**: 15-26.

28. OTESILE E.B., FAGBEMI B.O., ADEYEMO O., 1991. The effects of *Trypanosoma brucei* infection on serum biochemical changes in boars on differential planes of dietary energy. *Vet. Parasitol.*, **40**: 207-216.

29. PARIJA S.C., BHATTACHARYA S., 2001. Guest editorial, the tragedy of the tigers: Lessons to learn from Nandankan episode. *Ind. J. Med. Microbiol.*, **19**: 116-118.

30. PLASHENKA S.I., SIDORV V.T., 1987. Stress in farm animals. *Agro Perimizdat Moscow*, **192**: 56-57.

31. RABO J.S., 1998. Toxicity studies and trypanosuppressive effects of stem bark of *Butyrospermum paradoxum* in laboratory animals. PhD Thesis, University of Maiduguri, Nigeria, 97 p.

32. RABO J.S., ONYEYILI P.A., SALAKO M.A., KHALIL M.I., 2002. Acute toxicity studies on aqueous extract of stem bark of *Butyrospermum paradoxum* in rats. *Bull. Anim. Health Prod. Afr.*, **48**: 39-43.

33. REITMAN S., FRANKEL S., 1957. Reitman and Frankel's method of estimating SGOT and SGPT. *Am. J. clin. Pathol.*, **28**: 56-63.

34. SEATON B., ALI A., 1984. Serum creatinine estimation. *Med. Lab. Sci.*, **41**: 327-336.

35. SEED J.R., HALL J.F., 1985. Pathophysiology of African trypanosomiasis. In: Tizard I. Ed., Immunology and pathogenesis of trypanosomiasis. Boca Raton, FL, USA, CRC Press, p. 1-11.

36. SHALM O.W., JAIN N.C., CARROLL E.J., 1995. Veterinary haematology, 3rd Edn. Philadelphia, PA, USA, Lea and Fabinger, p. 498-512.

37. SHERTZER H.G., HALL J.E., SEED J.R., 1982. Hepatic microsomal alterations during trypanosomosis in the field vole *Microtus montanus*. *Mol. Biochem. Physiol.*, **71**: 25-32.

38. SOULSBY E.J.L., 1982. Helminths, arthropods and protozoa parasites of domesticated animals. London, UK, Bailliere Tindall, p. 100-140.

39. TEITZ N.W., 1994. Fundamentals of clinical chemistry with clinical correlation, 1st Edn. London, UK, Bailliere Tindall, p. 234.

40. WHO, 1987. Methods recommended for essential clinical, chemical and haematological tests for intermediate hospital laboratories. Geneva, Switzerland, WHO, p. 1-92.

41. ZILVA J.F., PANNALL P.R., 1984. Clinical chemistry in diagnosis and treatment, 4th Edn. London, UK, Lloyd-Luke Medical Books, p. 1-24.

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Résumé

Mbaya A.W., Aliyu M.M., Nwosu C.O., Ibrahim U.I. Effets de l'acéturate de diminazène et de l'hydrochlorure de mélarsamine sur les modifications des paramètres biochimiques chez des gazelles au front rouge (*Gazella rufifrons*) expérimentalement infectées avec *Trypanosoma brucei*

Une étude a été menée pour déterminer les effets chémothérapeutiques de l'hydrochlorure de mélarsamine (Cymelarsan®) et de l'acéturate de diminazène (Bérénil®) sur les paramètres biochimiques sanguins chez des gazelles au front rouge expérimentalement infectées par *Trypanosoma brucei*. Suite à la parasitémie des gazelles, les observations suivantes ont été faites : une augmentation significative ($p < 0,05$) de cortisol sérique, de l'alanine aminotransférase, de l'aspartate aminotransférase, de la bilirubine totale, de la créatinine, de l'urée, de l'acide urique et des lipides totaux, ainsi qu'une baisse significative des protéines sériques totales, du niveau de l'albumine et du glucose. En revanche, l'activité de la phosphatase d'alcaline a fluctué autour des valeurs normales ($p > 0,05$). Ces modifications biochimiques sont revenues à des valeurs proches de celles de la période de préinfection avant la fin de l'expérience chez les gazelles traitées avec 0,3 ou 0,6 mg/kg de poids vif (PV) de Cymelarsan ou 7,0 mg/kg de Bérénil. Les résultats semblent indiquer qu'un stress initial, associé à une augmentation du niveau du cortisol sérique et à son effet immunodépresseur pouvaient être responsable de l'installation et de l'expression clinique de l'infection chez les gazelles au front rouge. Par ailleurs, la sévérité des effets biochimiques produits expérimentalement a montré que la trypanotolérance chez les gazelles sauvages pouvait être compromise, surtout lorsque ces dernières étaient exposées au stress de la captivité. Les résultats ont aussi montré que le Cymelarsan à 0,3 ou 0,6 mg/kg PV et le Bérénil à 7,0 mg/kg PV étaient efficaces pour contrôler la maladie dans les conditions de l'expérience.

Mots-clés : *Gazella rufifrons* – Gazelle – *Trypanosoma brucei* – Trypanosomose – Biochimie – Médicament – Infection expérimentale – Nigeria.

Resumen

Mbaya A.W., Aliyu M.M., Nwosu C.O., Ibrahim U.I. Efecto de Berenil® y Cymelarsan® sobre las alteraciones de parámetros bioquímicos en gacelas de frente rojo (*Gazella rufifrons*) infectadas experimentalmente con *Trypanosoma brucei*

Se llevó a cabo un estudio para investigar los efectos quimioterapéuticos del aceturato de diminazeno (Berenil®) y de la melarsamine (Cymelarsan®) sobre la alteración de los parámetros bioquímicos en gacelas de frente rojo infectadas en forma experimental con *Trypanosoma brucei*. Seguido a la parasitemia, se observó en las gacelas, un aumento significativo ($P < 0,05$) en el cortisol sérico, la alanina aminotransferasa, aspartato aminotransferasa, bilirrubina total, creatinina, urea, ácido úrico, lípidos totales y una disminución significativa ($P < 0,05$) de las proteínas séricas totales, de los niveles de albumina y de glucosa sérica. La actividad de la fosfatasa alcalina fluctuó alrededor de valores normales ($P > 0,05$). Estas alteraciones bioquímicas fueron moduladas efectivamente hacia niveles pre infección antes del fin del experimento en las gacelas tratadas con 0,3 o 0,6 mg/kg de peso corporal (PC) de Cymelarsan o 7,0 mg/kg PC de Berenil. Los resultados de los diversos experimentos sugieren que el estrés debido a un aumento asociado de cortisol sérico y su efecto inmunosupresor podrían haber sido responsables del establecimiento y de la manifestación clínica de la infección en las gacelas de frente rojo. Aún más, la severidad de los efectos bioquímicos inducidos en forma experimental en las gacelas indican que la tripano-tolerancia en gacelas salvajes podría verse comprometida, especialmente cuando están sujetas al estrés del cautiverio. Los resultados muestran también que 0,3 o 0,6 mg/kg PC de Cymelarsan y 7,0mg/kg PC de Berenil fueron efectivos en el manejo de la enfermedad bajo condiciones experimentales.

Palabras clave: *Gazella rufifrons* – Gazelle – *Trypanosoma brucei* – Tripanosomosis – Bioquímica – Medicamento – Infección experimenta – Nigeria.