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Effect of Chemotherapy on Thyroxine and Progestrone Levels in Nubian Goats Experimentally Infected with from *T. evansi*

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Abstract: The action of Cymelarsan[R] and/or Oxytetracycline (OTC) in goats experimentally infected with *T. evansi* investigated. Cymelarsan and Cymelarsan OTC combination cleared the parasite from peripheral blood; OTC delayed the death as compared to the untreated group. Thyroxine (T4), progesterone levels decreased post-infection significantly. Their levels returned significantly to normal values after treatment with Cymelarsan[R] and Cymelarsan [R]OTC. OTC did not correct the decrease in infected animals.

Key words: Nubian goats, *T. evansi,* chemotherapy, thyroxine and progestrone

INTRODUCTION

Infection with *T.congolense* in cattle caused hypothyrodism (Abebe and Eley, 1992). Similarly Dam *et al.* (1996) reported similar results in infected *T. vivax* goats. *T. congolense* infection induced a non-fertile oestrus (Obasi *et al.*, 1997) in Bunaji heifers. Osaer *et al.* (1998) mentioned that progesterone levels were significantly lower in infected *T. congolense* ewes during synchronized cycle. Trypanosomosis may some times be associated with other infections such as parasitic and bacterial infection for this reason the main objective of this study is to investigate the stimultaneous effect of the Cymelarsan[R] and (OTC) in animals experimentally infected with *T. evansi.* The study is planned to study the therapeutic effect of Cymelarsan[R] and/or (OTC) by recording changes in the hormonal levelsin animals infected with *T. evansi.* Control groups include non -infected treated and infected non-treated groups.

MATERIALS AND METHODS

Experimental animals: Animals used in the study were twenty-five healthy Nubian goats of both sexes, 8-12 months old.

Adaptation period: All animals were stabled in insect prove pens at the Department of Preventive Medicine and Public Health at the Faculty of Veterinary Medicine. They were fed on lucerne and millets and water was given *ad libitum* for two weeks.

Experimental period: The data for all groups was categorized into 3 periods:

Pre-infection = two weeks prior to infection
Infection = from day of inoculation to patency and treatment
Post-treatment = from treatment day to the end of experiment

The parasite: *T. evansi* was isolated from an infected camel at Elmewelh market. It was brought originally from Elgadarif- Eastern Sudan, which is confirmed as non-tsetse zone. The *T. evansi* isolate so obtained was designated as Gad tryp (1).

Drugs: Two drugs were used in this study:
1- Cymelarsan[R](Rhône-mèrieux-France).
2-Oxytetracycline (EMBAcycline*5) (Rhône-mèrieux-France).
Group (C) Uninfected- untreated.
Group (R) Infected- treated with Cymelarsan[R].
Group (O) Infected- treated with OTC.
Group (Z) Infected-treated with Cymelarsan[R] and OTC combination.
Group (A) Infected- untreated group.
Group (C2) Uninfected- treated with the combination of the two used drugs.

Experimental inoculation: Each goat was inoculated intravenously with 0.75 ml blood of rat infected it contained (5×10^5 organisms).

Blood values determination: Blood samples for parsitological methods were withdrawn from the jugular veins of all goats before and after infection and after treatment using a vacutainer system (Becton-Dickinson France) with an anticoagulant (Ethylene Diamine Tetra acetic Acid (EDTA).

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Parasitological methods: The examination of wet blood film, thin film, thick film and buffy coats technique (BCT) was done to determine the presence of trypanosomes in goats.

Blood collection: Blood samples for serum were withdrawn from the jugular veins of all goats pre and post-infection and after treatment using a vacutainer system (Becton-Dickinson.France).

Serum total tetraiodthyronine (Thyroxin): Thyroxin was measured by radio immunoassay (RIA) technique. (Larsen, 1978) with kits(Amersham International, Amersham, Bucks, UK) in a gamma counter (Nuclear Enterprises, NE, 1612 Turbo) at the Sudan Atomic Energy Commission (SAEC),Khartoum. Serum total thyroxin was measured by radio immunoassay (RIA) When the tracer antigen (Ag)-antibodies (Ab) complexes reaction reached an equilibrium, the free fraction of both antigen and antibody are removed using appropriate separating agent, then the Ab-Ag (tracer) complex is counted for radioactivity using appropriate gamma counter. Standard Ag concentration is always used as calibrate to calculate antigen concentration.

Progesterone Radio Immunoassay (RIA)

Antibody coated tube method: The procedure was done according to FAO/IAEA Assay Protocol version 3.1 (1996). The kits (Agriculture Ag. Laboratory Seibersdrof. Austria. Kits.) were developed for the purpose of measuring progesterone in plasma, serum or skimmed milk of livestock. The kits used were assembled by the Animal Production Unit, International Atomic Energy Agency (IAEA).

The method depends on the competition between progesterone in serum samples and I-lapelled for a limited number of binding sites on a progesterone specific antibody immobilized (coated) on the internal walls of the test tubes (solid phase). The proportion of the I-lapelled progesterone bond to the antibody is inversely related to the concentration of the progesterone present in the serum. After completion of the reaction and separation of bound from free hormone, it possible to calculate blood progesterone concentration from a standard curve, using serum standard.

Statistical analysis: All data were computerized using MSTAT-C program (Michigan State University), for the analysis of variance and for means separation.

RESULTS

Parasitological findings

Pre-patent period: Incubation period ranged between 4-9 days, seven out of twenty animals showed parasitaemina in 4 days.

Table 1: The Mean ±SE of serum progesterone and thyroxin in Nubian goats infected with *T. evansi*

Parameter/ Groups	Progesterone	Thyroxin (T4)
Group(C1)	4.380±0.001 [a]	3.864±0.071 [a]
Group(R)	3.588±0.010 [a]	2.54±0.005 [a]
Group(O)	2.740±0.012 [b]	1.897±0.010 [a]
Group(Z)	4.458±0.001 [a]	3.936±0.001 [a]
Group(A)	2.620±0.010 [b]	2.111±0.003 [a]
Group(C2)	5.852±0.012 [a]	5.169±0.001 [b]

The different letter in one column showed the significant changes p=0.05

Parasitaemia: Parasitaemia was variable between one per field to uncountable parasite (Table 1).

Course of infection: Death was frequently preceded by appearance of trypanosomes in the peripheral blood. In group (A) death began by the 2nd week, all animal died by day 20. The treated groups (group (R) and (Z) were found negative within 26 hours of drug inoculation and all animals, group (O) death began on day 47 and all animals died by day 54.

Hormonal changes: Significant changes were observe in thyroxine hormone level post-infection and post-treatment. It decreased post-infection and increased post-treatment. This was summrized in Table 1.

Also in progesterone in the infected groups showed decrease post-infection and it increased post-treatment. This was summrized in Table 1b.

DISCUSSION

Decrease in the level of progesterone in infected goats in present work might be due to the primary hypothalmic-pituitary dysfunction during the trypanosome infection.

The inconsistency in the pattern of progesterone release and the variation in the duration of cycles within the animals was reported by FAO (1982) and Abdel Rahim (1989).The difference in the progesterone level the treated groups may be attributed to the seasonal variation in their ovarian activity, where the goats showed only follicular development during the breeding season and ovulate only in response to coitus accordingly the short rise followed by the decrease in progesterone levels, to almost zero.

The possibility of primary hypothalamic-pituitary dysfunction during trypanosomosis has been indicated by hormonal imbalances related to reproductive and adrenal steroid hormonal pathway. If hypothysectomy occurs after puberty, then growth would not be affected since, the animal would have reached adult proportion but deficiencies in thyroid functions would appear (Abebe and Eley,1992).

Histopathological examination of the thyroid glands of the infected animals, showed no apparent structural damage apart from slight congestion

Table 1b: The Parasitaemia in the different groups

Groups	Animal No	Base - line	Days											
			4	7	10	13	16	19	26	33	40	47	54	61
C	1 2 3 4 5	-ve												-ve
R	6 7 8 9 10		+	+	++ + ++ ++	++++ ++ +++ ++ +++	-ve							
O	11 12 13 14 15		+	++ ++ + ++	++ + ++ ++	+++ + ++ ++ +	+++ + ++ + ++	+++ ++ ++ ++ ++	+++ ++ ++ ++ ++	+++ ++ ++ ++ ++	++++ ++ ++ +++ ++	Died +++ ++ ++ ++	Died Did ++ ++++ +++	Died
Z	16 17 18 19 20		+	++ + ++ + ++	+++ + ++ + ++	++++ + ++ ++ ++	++++ + ++ +++ ++	-ve						
A	21 22 23 24 25		++ ++ ++ ++ +	+++ + ++ + ++	Died									

Parasitaemia grade: 1-3 =+, 3-5=++,5-10=+++ and above 10=++++

(Fairouz, 2000). It was suggested that the change in thyroxin levels precede the pathological changes of the thyroid gland often seen in chronic trypanosomosis. The significant decrease on the level of thyroid hormones after the effect of pituitary insufficiency, as stated by Abebe and Eley (1992) might affect the animals. The possibility of primary hypothalamic-pituitary dysfunction during trypanosomosis has been indicated by hormonal imbalance related to thyroid hormonal pathway (Mutayoba *et al*., 1988). These findings imply that the use of Cymelarsan^{R} can protect against an except thyroid damage latter.

Endotoxins have been isolate from plasma of *T. congolese* infected animals. The endotoxine have a simultaneous effect on two different target hormones, it ought to have a common site of action. This site could be the pituitary gland, most probably at the hypothalmic level. Stress, is known to be mediated by the hypothalamus and trypanosomosis causes severe stress in infected animals (Mutayoba and Gombe, 1989).

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