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**MISUSE OF ANTITRYPANOSOMAL DRUGS
AND THEIR IMPACT ON CAMEL REPRODUCTION
IN SUDAN
(With 1 Table)**

By

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دراسة عن سوء استخدام الأدوية المضادة للترباتسوما
وتأثير هذه الأدوية على الكفاءة التناسلية للجمال في السودان

هشام إسماعيل سري ، إدريس ، البشير ، البرشام ، الصديق

تم تقييم استخدام أدوية أنتريسيد ، سورامين ، سيميلارسان على الكفاءة التناسلية للجمال في السودان . وقد لوحظ أن الإصابة المزمنة بالتريبانوسوما تسبب الإجهاض والولادات غير المكتملة النمو إضافة إلى عدم قدرة الأمهات على رضاعة وليدها. أن الضبط الدقيق للجرعة الدواء المستخدم ذو أهمية كبيرة في مقاومة المرض ويمكن أن تتحقق المقاومة الناجحة للسيطرة على المرض باستخدام دوائيين أو أكثر أو استخدام دواء جديد لم تحدث منه مناعة.

SUMMARY

In this paper, the impact of misuse and the resistance of trypanocidal drugs on the reproductive performance of camels was reviewed. The effect of Antrycide, Suramin and Cymelarsan on trypanosomosis infection was reported. Chronic cases of camel trypanosomosis caused abortions, premature births and inability to feed the young. The problem of drug resistance exhibited by various species of trypanosomes increases if the choice of drug is made without regard to the species in the locality. Strict control of dosage should be enforced as resistant strains can build up very quickly. Successful treatment can often be

achieved by combining two or more different drugs or by using a drug unrelated to one to which resistance has developed. In general great care should be exercised in using antitrypanosome drugs prophylactically unless the regime can be strictly controlled. Short term-prophylaxis can be useful for camels migrating through an area of known high risk.

INTRODUCTION

Animal trypanosomosis is, by far, one of the major constraints to socio-economic development in Africa. The disease is spread over an area of approximately 10 million Km² across the continent extended between latitude 29°S and 14°N. Sudanese camels are seriously threatened by 3 major debilitating diseases, namely mange "Jereb" (Nayel/Abu-Samra, 1986), haemonchosis "Holaa" (Eisa, 1966) and trypanosomosis "Gufar". Trypanosomosis is the most important protozoan disease of camels and probably the most health problem of all. The causal organism is normally *Trypanosoma evansi* or *T. brucei*. The acute form of the disease commonly affects adults and is characterized by very rapid emaciation. The chronic form, more common than the acute, is characterized by progressive weight loss, intermittent high fever, marked generalized muscular atrophy, pale mucous membrane and hyper lacrimation. Overall decrease in food consumption and irregular grazing activity (Wilson, 1984). Mild cases develop relapsing parasitaemia with or without pyrexia (Mahmoud/Osman, 1979). Edema is fairly constant symptom with complications involving the respiratory, gastrointestinal/ nervous systems (Wilson, 1984). Animals may also exhibit a characteristic sweet odor due to an increased urinary ketone levels (Rottcher/Hunter, 1986). Common laboratory findings are decreased PCV between 18-20% (normal 24-42% with an average of 30%), a responsive anemia and perhaps the demonstration of the parasite in stained blood smears. The problems associated with antigenic variation of trypanosomes had made the development of an effective vaccine difficult (Nantulya, 1986). Real immunity is never acquired although pre-immunity is fairly common. Young, do not acquire immunity through their dams (Wilson, 1984).

Chemotherapy remains the most common method to control infections. The introduction of Suramin in 1920 marked the start of trypanosome treatment using modern drug therapy. Commercially available drugs for animal trypanosomosis are limited to several

compounds: homidium (Etidium[®], Novidium[®]) diminazine aceturate (Berenil[®]), isometamedium chloride (Samorin[®], Trypamidium[®]), Suramin (Naganol[®], Antrypol[®]), and quinapyramine sulphate (Antrycide[®], Trypacide[®]) (table 1). No new drugs have been introduced on market in the last 25 years. DL- α -difluoromethylornithine (DFMO) was used to treat sleeping sickness in man, and Cymelarsan (RM 110) to treat camel trypanosomosis. Drugs used against the common trypanosomes of other domestic animals (*T. vivax*, *T. congolense*) are not always very efficient against the camel trypanosomes. For example isometamedium (Samorin), in addition to being poorly tolerated by the camel, has a very low success rate against *T. evansi* and treatment has to be relatively prolonged (Balis/Richard, 1977)

However, the effectiveness of Suramin, the most commonly used drug against surra has diminished after more than 60 years of use (Ross/Barns, 1995), and the quinapyramine drug Antrycide has been reintroduced despite the swift appearance of resistance to this drug when it was first used (Schillinger/Rottcher, 1986). A new drug melarsomine hydrochloride (Cymelarsan) has been developed with activity against trypanosome of the *T. brucei* sub-group and has been licensed for use in camels (Raynaud *et al.*, 1989).

The problem:

Chemotherapy and chemoprophylaxis have played and will continue to play an important role in control of trypanosomosis. The use of a limited number of drugs has led to the development of drug resistant trypanosome strains. The development of resistance in the field can be due to several factors, such as under-dosing due to incorrect estimation of body weight. This is very difficult to avoid when large numbers of animals are involved, as in mass treatment campaigns. In addition, continued administration of trypanocides to animals kept in high fly challenge areas, irregular dosing with prophylactic drugs or stopping of treatment when the animals are still under trypanosomosis risk could contribute to the development of resistance. Studies on five different stocks of *Trypanosome brucei evansi* isolated from naturally infected camels in Sudan were tested for drug sensitivity in mice by Intisar (1990). All five stocks expressed resistance to Antrycide (Quinapyramine sulphate) when given at therapeutic dose of 3 mg/kg body weight, but were cured in mice with Antrycide at 2 times the recommended dose (6 mg/kg body weight). All isolated stocks showed

resistance in mice to Naganol (Suramin) at the recommended dose of 10-mg/kg b.w. and to Trypamidium (Isometamedium chloride) at the recommended dose of 0.05 mg/kg but it had a low trypanocidal effect at a dose level of 0.1 or 0.15 mg/kg (Intisar, 1990). Eight out of ten different stocks isolated from naturally infected camels expressed resistance to Trypacide (Quinapyramine sulphate) at a dose of 10-mg/kg body weight (Intisar, 1997). Only two stocks were sensitive to a therapeutic dose of 3 mg/kg body weight. Seven isolated stocks showed resistance in mice to Suramin at the recommended dose of 10-mg/kg body weight. It is suggested that resistant strains of *T. evansi* to Cymelarsan were induced in immunocompetant mice (Zhang *et al.*, 1993). *T. brucei* resistant strains were also induced (Scot *et al.*, 1996). Infections with *T. vivax*, *T. brucei* and *T. congolense* relapsed after treatment with the recommended doses of Ethidium, Berenil and Isometamedium (Mohammed-Ahmed *et al.*, 1992). Serum progesterone concentration showed irregular cycles in infected animals, but after the injection of Cymelarsan the level of serum progesterone was regulated into the normal cycle (A/Salam, 1999).

Table 1: Chemotherapeutic agents commonly used as curative or prophylactic trypanocides.

Group	Drug	Trade name(s)	Action	Infection	Host	Dosage
Diamidine	Diaminazine	Berenil Veriben Ganseng	C	<i>T. vivax</i> <i>T. congolense</i> <i>T. brucei</i>	Cattle, sheep, goats, equidae	3.5 mg/kg.
Phenanthridine	Homidium	Ethidium Novidium	C	<i>T. vivax</i> <i>T. congolense</i>	Cattle, sheep, goats.	1 mg/Kg
	Isometamedium	Samorin Trypamidium	C, P	<i>T. vivax</i> <i>T. congolense</i> <i>T. brucei</i>	Cattle, sheep, goats, equidae, canidae.	0.25-1 mg/kg
Quinoline	Quinapyramine	Antrycide Trypacide Quintrycide	C, P	<i>T. vivax</i> <i>T. congolense</i> <i>T. brucei</i>	Cattle, sheep, goats, equidae, canidae, camilidae	3-5 mg/kg
Naphthalidine	Suramin	Antrypol Naganol	C, P	<i>T. brucei</i> sub species <i>T. evansi</i>	equidae, canidae, camilidae, humans	5 mg/kg
Arsenical Melaminyl	Cymelarsan	RM 110 Mel Cy	C	<i>T. brucei</i>	Camilidae, bovidae	0.25 mg/kg

C = Curative, P = Prophylactic, Intisar (1997)

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