SUST
Journal of Agricultural and Veterinary Sciences
Journal homepage:
http:// journals.sustech.edu

The Efficacy of Sulphadimidine, Gentamicin, Oxytetracycline and their Combinations in Nubian Goats Exprimentally Infected with *Trypanosoma evansi*

D. L. Nyieny,*[1] O. S. A. Mohamed,[2] F. M. Youssif [3]

1. Department of Medicine, Pharmacology & Toxicology- Faculty of Veterinary Medicine- Upper Nile University- South Sudan.
2. Department of Medicine, Pharmacology & Toxicology- Faculty of Veterinary Medicine- Sudan University for Science & Technology-P. O Box.204. Khartoum North, Sudan
3. Central Veterinary Research Laboratory-Animal Resources Research Corporation- Ministry of Science and Technology- P. O. Box.8067. Khartoum, Sudan.
Corresponding Author:(Email. dengnyieny@gmail.com)
Article history: Received: January 2016
Accepted: February 2016

Abstract
The objective of the present study was to evaluate the efficacy of sulphadimidine, gentamicin, oxytetracycline and their combinations in Nubian goats experimentally infected with *T.evansi.* Eight groups were used in this study. All experimental groups were infected with *T.evansi* except group (1) uninfected and untreated. While group (2) was infected and untreated, groups (3, 4, and 5) were treated with single i/m dose of sulphadimidine (200mg/kg), gentamicin (4mg/kg) and oxytetracycline (20mg/kg) respectively. Groups (6, 7 and 8) were each treated with single i/m dose of combination of sulphadimidine (200mg/kg) + gentamicin (4mg/kg), sulphadimidine (200mg/kg) + oxytetracycline (20mg/kg) and gentamicin (4mg/kg) + oxytetracycline (20mg/kg) respectively. No clinical signs were shown on goats of groups (3-8) post treatment. No significant changes were observed for the temperature, respiratory rate, pulse rate and heart rate in groups (2-8) and for the RBCs count, PCV, haemoglobin concentration and the red blood cells indices and WBCs count, eosinophils, basophils and serum total proteins concentrations compared to the control group 1. Significant decreases were recorded in glucose and albumin serum concentration, while significant increases in the neutrophils, monocytes, lymphocytes, globulins, urea serum concentration and in the activity of GOT in most treated groups. Doses of sulphadimidine, oxytetracycline and their combinations cleared the peripheral blood from the parasite since week 4 post treatment to the end of the experiment, while single i/m of gentamicin and its combinations with sulphadimidine and oxytetracycline cleared the parasitaemia of the peripheral blood at week 8 and 9 post treatment respectively.
The present results concluded that, the drugs tested and their combinations had trypanocidal efficacy. The study recommended the possibility of treatment of trypanosomiasis with sulphadimidine, gentamicin, oxytetracycline and their combinations.

Keywords: *Trypanosoma evansi*, Efficacy, Sulphadimidine, Gentamicin, Oxytetracycline.

Introduction

In Republic of South Sudan, goats are reared for milk, meat and socially in marriage and play a very important role in the rural economy. It is well known that trypanosomosis is a vector-born disease of humans and livestock. It is caused by a unicellular, flagellated protozoa of the genus trypanosoma, and it is a major health problem for domestic and wild life animals particularly in Africa, Asia and South America.

Trypanosomosis in goats produces acute, subacute, chronic or subclinical forms. The most causative trypanosomes for goats are *T.evansi, T.vivax,* and *T. conglense.* Generally four groups of anti-trypanosome are used: Diamidines compounds, Aminophenanthridium compounds, Quinapyramine compounds and other compounds such as Melarsorpol, Cymelarsan (Arsenical compounds), Suramine, Samorine and Nitrovinylferan (Bywater, *et al.,* 1991). It is important to realize that drugs alone will not treat the disease because trypanosomosis overwhelms the immune system. Treatment will be more effective in well fed and rested animals as chemotherapy stopping the multiplication of trypanosomes and this helps the immune system to overcome the infection (Osman, *et al.,* 1992). The control of trypanosomosis depends on two ways: the use of chemotherapy/chemoprophylaxis programs and vector control. However, the treatment/prophylactic programs is the current method going on because it is easier to eradicate the trypanosomes than the vectors. The appearance of trypanosomes drug-resistant makes also the use of the available drugs a problem facing the veterinarians in the field for treatment of trypanosomosis. In addition, almost no new drugs have been developed for more than 30 years and some have been withdrawn from the market either the manufacturer stopped as in case of Quinapyramine or withdrawn due to its ineffectivity due to resistant. Thus, those remaining in use require careful management in order to minimize resistance problem (Brown, *et al.,* 1990).

In Sudan, field veterinarians use antibiotics such as Sulphadimidine, Gentamicin and Oxytetracycline in combination with the available trypanocide for the treatment of trypanosomiasis. These antibiotics are used in order to control the secondary bacterial invasion due to the suppressed immune status. But its observed that in many instances when the trypanocidal drugs are not available specially in nomads herds, how treated the animals with the above mentioned antibiotics in order to overcome the secondary infection and the animal relies on its immune system. There was a believe that, these antibiotics had a trypanocidal effect, because the animals were improved and their blood was free of the parasites when were examined. For these reasons the present experiment was conducted to investigate the efficacy of Sulphadimidine, Gentamicin, Oxytetracycline and their combinations in Nubian goats experimentally infected with *T.evansi.*

Materials and Methods

Experimental Design

Twenty four (24) Nubian goats of both sexes aged 1-3 years and weighing 13-20 kg were purchased from local markets. All animals were housed in a Fly-proof barn at the College of Veterinary Medicine, Sudan University of Science and Technology. They were supplied with limited concentrates and minerals twice a day and grass fodder *Sorghum vulagarae*, with free access water. Animals were allowed to acclimatize for one month before the commencement of the experiment during which animals were carefully examined for blood parasites, internal and external parasites. Animals were divided randomly into 8 groups each consisted of three goats. Control negative (group 1) was uninfected and untreated. The

remaining experimental groups (2-8) were all inoculated intravenously with 1ml blood containing 5 x 10^5 parasites *T.evansi* stock Gad tryp (1) as count using modified scoring method (Ismail, 1988). The parasites were activated by adding phosphate buffered saline with glucose (PSG) before inoculation. Control positive (group 2) was infected and untreated. Animals in groups 3, 4, and 5 were each given single i/m dose of sulphadimidine (200mg/kg), gentamicin (4mg/kg) and oxytetracycline (20mg/kg) respectively.While animals in Groups 6, 7 and 8 were each given single i/m dose of combination of sulphadimidine (200mg/kg) + gentamicin (4mg/kg), sulphadimidine (200mg/kg) + oxytetracycline (20mg/kg) and gentamicin (4mg/kg) + oxytetracycline (20mg/kg) respectively. The treatment started immediately after the appearance of parasite in peripheral blood. The duration of the experiment was 9 weeks.

Techniques used for blood collection

Blood was collected daily for parasitaemia investigation, while the blood was collected every three days for haematological and biochemical investigations throughout the duration of the experimental period. Blood was collected through jugular vein puncture using 5ml disposable syringe. 2ml of collected blood was harvested into vacuota-iners containing ethylene diamine tetraacetic acid (EDTA) for parasitological and haematological investigations. Parasitol-ogical investigations were determined using the methods of wet blood film, buffy cout technique (Murray *et al.*, 1977) and haemocytometer technique (Ismail, 1988).

The haematological investigations determi-ned by measurement of Hb concentr-ation using commercial kits (Muslcosj-Saudi Arabia for Laboratory Limited)**,** RBCs count, PCV, MCV, MCH, MCHC, WBCs count and differential white blood cells count (Schalm *et al.*, 2000). The remaining 3ml of blood was used for serum analysis. Samples were collected into plain vacuotainers left for 3-4 hours at room temperature then separated by using a centrifuge with 3000 rounds/minute and the clear serum was harvested and kept at -20C^0 until analysed for the measurement of glucose, total proteins and albumin using commercial kits (Fortress Diagnostics Limited, United Kingdom), while globulins were measured by subtracting the albumin from total proteins concentration. GOT serum activity and urea concentration were measured using commercial kits (Medical Device Safety Services, Germany).

Clinical parameters

All experimental animals were inspected several times a day for physical changes and clinical signs. Rectal temperature, respiratory rate, pulse rate and heart rate were recorded every three days for duration of 9 weeks.

Statistical analysis

All data were computerized using MSTAT- C program (Michgan State University), for the analysis of variance and for mean separation (version 10).

Results

Clinical signs

All goats of group 2 (control positive) showed lack of appetite, weight loss, emaciation, recumbency and death on week 3 post-infection. No clinical signs and mortality were recorded for groups 3, 4, 5, 6, 7 and 8 post-treatment till the end of the experiment (week 9). The clinical parameters in Nubian goats experimentally infected with *T.evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations are shown in table (1). No significant changes were observed for the rectal temperature, respiratory rate, pulse rate and heart rate in the infected and the infected-treated goats compared to the control group1.

Haematological parameters

The haematological parameters in Nubian goats experimentally infected with *T.evansi* and treated with sulphadimidine, gentamicin and oxytetracycline and their combinations are shown in table (2). There were no significant changes recorded for the RBCs count, PCV, haemoglobin concen-tration and the red blood cells indices. But, decreases in the RBCs count, PCV, haemoglobin concentration and the MCH were noticed in most treated groups. The white blood cells and the differential white blood cells count in Nubian goats experimentally infected with *T.evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations are shown in table (3). There were no significant changes observed in the tested groups for the WBC counts, basophils and eosinophils, while significant increases were observed for the neutrophils in groups (3-7), lymphocytes (4- 8) and the monocytes (groups 2-8) compared to the control group 1.

Serobiochemical parameters

The biochemical parameters in Nubian goats experimentally infected with *T.evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations are shown in table (4). Significant decreases were recorded in glucose and albumin serum concentration in groups (2-8) while significant increases in the globulins in groups (2-8) and urea serum concentration in groups (2- 6 and 8) and in the serum activity of GOT in groups (2, 4, 6 and 8).

The efficacy of sulphadimidine, gentamicin, oxytetracycline and their combinations.

The efficacy of sulphadimidine, gentam-icin, oxytetracycline and their combinations in Nubian goats experimentally infected with *T.evansi* is shown in table (5) and figures (1-6). Results showed that single i/m dose of sulphadimidine, oxytetracycline and their combinations cleared the parasite from the peripheral blood at week 4 to the end of the experiments, while single i/m dose of gentamicin and its combinations with sulphadimidine and oxytetracycline cleared the parasitaemia of the peripheral blood at week 8 and 9 respectively, during this period no clinical signs.

Discussion

The objectives of the present study were to investigate the efficacies of Sulphadimidine, Gentamicin, Oxytetracycline and their combinations in Nubian goats experiment-ally infected with *T.evansi.*

Sheep and goats are extensively used as model laboratory animals for various pathological and pharmacological studies of *T.evansi* (Dargantes *et al.,* 2005, Youssif, 2005). In this study the parasitaemia in all infected groups started to appear in week 1 and reached the maximum on week 2, and on weeks 3 post infection. Youssif *et al.* (2008) studied the efficacy and toxicity of Cymerlarsan in Nubian goats experimentally infected with *T. evansi* and found that the parasite was detected in the peripheral blood of goats was mild on days 4-5 and moderate on day 6 and severe on days 7-10 until the animal died on days 9-11 post infection. Dargie *et al.* (1979); Murray and Dexter, (1988), mentioned that peaks of the parasitaemic waves are usually high within this acute period. Death may occur at any phase of the disease or the animal may recover naturally (Uzoigwe, 1986).

Drug resistance emerged as a real problem facing the treatment of animal trypano-somiasis (Elrayah *et al.,* 1999) and this forcing towards the need for newer drugs to be used as trypanocidal agents. Katzung (2007) mentioned the use of antibiotics in treatments of protozoans, for example tetracycline and doxycycline are active against malaria and toxoplasmosis.

Sulphonamides are used for the treatment of protozoal diseases for example Riviere and Papich,(2009) mentioned that treatment of coccidiosis in birds and animals. This may be the first trail to use a folate inhibitor in treatment of trypanosomiasis.

In the present study when sulphadimidine was given at single i/m dose animals survived and the peripheral blood was cleared from the parasite since week 4 to the end of the experiment. Stephen *et al*. (2007) mentioned that folic acid is an important co-factor in all living cells, and bacteria and protozoa are unable to take up exogenous folate and must synthesize it themselves. This is carried out in a series of reactions involving first the synthesis of dihydr-opteroic acid from one molecule each of pteridine, P-aminobenzoic acid (PABA) and sulphonamides are structural analogues of PABA competitively inhibit the incorpo-ration of PABA into dihydropteroic acid and inhibit subsequent metabolism.

The efficacy of gentamicin at single i/m dose cleared the peripheral blood of the parasite since week 8 till the end of the experiment. This might be the first time to use gentamicin for treatment of trypano-somes.

Katzung (2007) mentioned that the mecha-nism of aminoglycosides are irreversible inhibitors of protein synthesis, and inside the cell, aminoglycosides bind to specific 30S-subunit ribosomal proteins and the protein synthesis is inhibited.

The efficacy of oxytetracycline at single i/m dose succeeded to eliminate the parasite from the peripheral blood at week 4 and all the animals were survived until the end of the experiment. Rang *et al.*(2009) mentioned that tetracyclines are bacteri-ostatic inhibitors of protein synthesis and accumulated intracellularly and binds bacterial ribosomal subunit (30S).

Masocha *et al.* (2006) mentioned that minocycline impedes African trypanosome invasion of the brain in a murine model that daily administration of minocycline impedes the penetration of leucocytes and trypanosomes into the brain parenchyma of *T. brucei-brucei* infected mice, and the loss of weight occurring during infection was not observed after treatment and those mice also survived longer than non-treated mice with minocycline. Minocycline and other tetracyclines antibiotics have been used in combination therapy against other parasitic diseases.

Although the mode of action of antibiotics in treatment of protozoan till now is not clearly understood, but we believe that it acts to a certain level as its mode of action on bacteria and other microorganisms.

The efficacy of the combination of single i/m dose of sulphadimidine and gentamicin combination eliminated the parasite on week 9 and the animals were survived till the end of the experiment, while the efficacy of the combination of single i/m dose of gentamycin and oxytetracycline eliminated the parasite from the peripheral blood on week 8 but the single i/m dose of sulphadimidine and oxytetracycline eliminate the parasite on week 4 and the animals were survived till the end of the experiment.

Riviere and Papich, (2009)described many drug combinations used in treatment of protozoal diseases, such as treatment of *Sarcocystis neurona* in horses (pyrem-ethamine + sulphadizine), *Neuspora caninum* in dogs (pyremmethamine + sulphadizine), *Toxoplasma gondii* in dogs and cats (pyremmethamine + sulphadizine), *Eimeria sp* and *Isospora sp* in dogs and cats (ormetoprim + sulphadizine) also (trimethoprim + sulphadiazine) and coccidiosis in cats also treated by combination of (Amprolium + sulphadimethoxine).

Bywater *et al.* (1991) mentioned in multi-drug therapy it sometimes happens that the

response seen is less than the sum of the component responses, in which case there has been antagonism between the drugs used. Antagonism can sometimes be explained on the basis of one drug interfering with or even reversing the action of the other. The use of a mixture which contains a bacteriostatic sulphonamide and bactericidal antibiotic exemplifies this possibility is that penicillin achieves its greatest antibacterial effect when the organism is multiplying rapidly. A sulphonamide arrest cell division and so reduces the usefulness of the antibiotic. Antibiotics are generally used alone, but may on occasion be prescribed in combinations. Combining two antibiotics may result in synergism, indifference or antagonism. In case of synergism, neutral inhibition is achieved at concentrations below that for each agent alone and may prove advantageous in treating relatively insusceptible infections (penicillin + gentamicin), another advantage is that it may enable the use of toxic agents where dose reduction is possible (amphotericin B + 5-flucylosine), another advantage is to prevent resistance emerging during treatment (fusidic + flucloxacillin), but the most common reason for using combined therapy is in treatment of confirmed or suspected mixed infection where a single agent alone will fail to cover all pathogenic organisms (metronidazole + aminogl-ycosides or a broad spectrum cephalo-sporins). Finally in cases who are seriously ill and about when uncertainty exists concerning the microbiological nature of the infection (Denyer *et al.,* 2004).

No clinical signs were shown by the groups infected with *T. evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations.

Clinical parameters in this study showed no significant changes recorded for the temperature, respiratory rate, pulse rate and heart rate in any of the experimental animals, although, there was slight increase in the temperature in some groups infected and treated. Body temperature varies according to the phases of the disease. Fiennes, (1970), Valera *et al.*(2005) and Akinwale *et al.* (2006) noticed that febrile changes in trypanosomosis could be demonstrated by plotting three-day average peak, with regular intervals each lasting for 2-3 days. A period following a temperature peak when *trypanosomes* were being destroyed in very large numbers is termed cold crisis (Fiennes, 1970). Youssif (2000) revealed that hyperthermia and hypothermia in goats infected with *T.vivax* is controversial. Youssif (2005) recorded the decrease in pulse rate and respiratory rate and increase in heart rate in *T.vivax* infected goats. While Anosa and Isoun, (1980) reported increase in respiratory rate in cattle infected with *T.vivax*.

There were no significant changes recorded in this study for the RBCs count, PCV, haemoglobin concentration and the red blood cells indices. But, decreases in the RBCs count and Hb concentration, PCV, MCH and the MCV were noticed specially in infected and treated groups compared to the control group. This coincides with findings of Saror, (1980); Sekoni *et al.* (1990) and Silva *et al.* (1999) in *T.vivax* and *T.congolense* infections in cattle and Sharma *et al.*(2000) in *T.evansi* infection in Barbari goats. The decrease in PCV might be correlated with the decrease in total red blood cells count or due to haemodilution while the decrease in Hb concentration may be due to the decrease in PCV and RBCs count. The decrease in the above mentioned parameters indicates the state of anaemia in the infected groups (Sharma *et al.,* 2000). This anaemia might be due to the haemolysis by proteases, phospholipases and nueramidases induced by trypanosomes (Soulsby, 1982). Trypanosomes may cause

direct mechanical injury to erythrocytes and other cells by the lashing action of their powerful flagella and microtubule-reinforced bodies (Vickerman and Tetley, 1978).

In the present study there were no changes in the total white blood cells count, eosinophils and basophils, while an increases in the neutrophils, monocytes and lymphocytes were seen in some of the treated groups.Taylor and Authei, (2003) reported increase in phagocytosis of leukocytes, platelets in animals infected with *T.congolense* and *T.vivax.* Goosssens *et al*. (1998) also revealed increase in WBCs count in chronic phase in sheep infected with *T.congolense.* Total leukocyte counts may drop by 30 to 50% in trypanosomes infected animals; the initial decrease is due mainly to an absolute decrease in T-cell, eosinophils, lymphocytes and neutrophils (Wellde, 1983 and Anosa, 1988). In contrast, monocytes may have a transient increase. Macrophages, neutrophils and eosinophils are able to destroy opsonized trypanosomes and to remove circulating immune complexes (Taylor and Authei, 2003).

The serobiochemical parameters in this study showed significant decreases in serum glucose concentration in the tested groups compared to that of the control negative, this agree with Kadima *et al.*(2000) that reported hypoglycaemia may occurred at the periods of high parasitaemia or at the terminal stage in cattle with acute *T.vivax* infection but did not occur in chronically infected cattle. Decrease of serum glucose was noticed in sheep infected with *T.congolense* or *T.brucei* (Taiwo *et al*., 2007).

Significant increases were observed in serum urea concentration and GOT activity in the tested groups compared to that of the control negative, this agree with Steven *and Micheal*. (2002) mentioned that GOT is a common marker of hepatocytes damage, but muscle damage, haemolysis and other processes also increase serum GOT activity. Youssif (2005) reported the increase of GOT activity in Nubian goats infected with *T.evansi*. The increase of serum urea agree with (Cheesbrough, 1998). A decreasing GFR (Glomerular Filtration rate) is the best indicator of renal insufficiency, and since UN (urea nitrogen) and CT (creatinine) are both freely filtered by the glomerulus they are the analysts most commonly used to estimate GFR. As the GFR decreases plasma UN and CT increase, however GFR must be reduced by 75% before UN and CT increase in blood plasma. Because azotemia is not evident until 75% of nephron are no longer functioning adequately, and because the ability to concentrate urine is best after 66% of nephons are compromised.

Thrall *et al.*(2012) mentioned that decreased serum UN implies decreased production of urea, either due to hepatic failure or post systemic shunt. The same author mentioned that dehydration, hypovolumia and shock are non renal factors that increase serum UN and CT, while gastrointestinal haemorrhage increase the UN only.

No significant changes were recorded for serum total proteins for all experimental groups. Tabel *et al*. (1980) recorded an increase of total proteins and albumin in sheep infected with *T.congolense*. Adeiza *et al*. (2008) recorded decrease of total proteins in sheep and goats infected with *T.congolense, T.vivax* and *T.brucei*. A decrease of albumin and elevation of globulins in sheep, goats and cattle infected with *T.congolense* and *T.vivax* was reported by Anosa and Isoun, (1976).

Thrall *et al.*(2012) mentioned that an increased concentration of serum albumin is seen only with dehydration. Decreased serum albumin is seen with glomerular diseases and is also seen with diseases in

gastrointestinal, liver and cardiovascular system.

This study concluded that treatment of trypanosomiasis with sulphadimidine, gentamicin, oxytetracycline and their combinations were successful in elimination the parasite from the peripheral blood of the infected animals without any serious adverse effects on the vital organs, and the animals were survived for 9 weeks post infection. Also it is recommended to use of the above mentioned drugs and their combinations as new treatment strategies of trypanosomiasis. Further studies are needed to highlights on the mode of actions of these antibiotics on the trypanosome.

Table 1: Clinical parameters in Nubian goats infected with *T.evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations (Mean±SE)

Groups/Parameters	Temperature °C	Respiratory rate (inspiration/min)	Pulse rate (thrills/min)	Heart rate (beats/min)
Group 1 uninfected and untreated (control negative)	38.3 ± 0.26^{a}	32.4 ± 0.27^{a}	80.2 ± 0.44^{a}	92.7 ± 0.51^{a}
Group 2 infected and untreated (control positive)	39.1 ± 0.29^{a}	34.4 ± 0.26^{a}	78.6 ± 0.37^{a}	87.5 ± 0.47^{a}
Group 3 infected and treated with sulphadimidine 200mg/kg b.w	38.9 ± 0.27^{a}	30.0 ± 0.26^{a}	83.1 ± 0.47^{a}	99.0 ± 0.50^{a}
Group 4 infected and treated with gentamicin 4mg/kg b.w	38.8 ± 0.26^{a}	35.7 ± 0.22^{a}	86.1 ± 0.41^{a}	102 ± 0.53^{a}
Group 5 infected and treated with oxytetracycline 20mg/kg b.w	38.8 ± 0.28^{a}	29.8 ± 0.25^{a}	83.5 ± 0.49^{a}	104 ± 0.52^{a}
Group 6 infected and treated with sulphadimidine +gentamicin (200mg/kg +4mg/kg) b. w	39.0 ± 0.20^{a}	26.3 ± 0.19^{a}	87.4 ± 0.27^{a}	106 ± 0.72^{a}
Group 7 infected and treated with sulphadimidine + oxytetracycline (200mg/kg +20mg/kg) b. w	38.8 ± 0.28^{a}	29.8 ± 0.25^{a}	83.5 ± 0.49^{a}	104 ± 0.52^{a}
Group 8 infected and treated with gentamicin +oxytetracycline (4mg/kg +20mg/kg) b. w	39.0 ± 0.21^{a}	33.9 ± 0.24^{a}	85.9 ± 0.50^{a}	102 ± 0.53^{a}

Table 2: Haematological parameters in Nubian goats infected with *T.evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations (Mean±SE)

Groups/Parameters	RBCs ($x10^{6}/mm^{3}$)	PCV (%)	Hemaglobin (g/dl)	MCV (Fl)	MCH (Pg)	MCHC (g/dl)
Group 1 uninfected and untreated (control negative)	7.39 ± 0.03^{a}	26.1 ± 0.18^{a}	9.42 ± 0.04^{a}	61.6 ± 0.20^{a}	55.4 ± 0.03^{a}	34.3 ± 0.26^{a}
Group 2 infected and untreated (control positive)	5.43 ± 0.04^{a}	21.1 ± 0.16^{a}	9.40 ± 0.05^{a}	59.0 ± 0.18^{a}	41.6 ± 0.02^{a}	44.7 ± 0.23^{a}
Group 3 infected and treated with sulphadimidine 200mg/kg b.w	4.96 ± 0.02^{a}	20.8 ± 0.20^{a}	6.82 ± 0.03^{a}	55.7 ± 0.13^{a}	29.8 ± 0.01^{a}	36.8 ± 0.27^{a}
Group 4 infected and treated with gentamicin 4mg/kg b.w	4.15 ± 0.03^{a}	19.9 ± 0.14^{a}	6.74 ± 0.03^{a}	58.9 ± 0.17^{a}	31.7 ± 0.01^{a}	40.4 ± 0.23^{a}
Group 5 infected and treated with oxytetracycline 20mg/kg b.w	4.84 ± 0.02^{a}	19.5 ± 0.18^{a}	7.35 ± 0.03^{a}	49.0 ± 0.12^{a}	19.2 ± 0.01^{a}	40.2 ± 0.22^{a}
Group 6 infected and treated with sulphadimidine + gentamicin (200mg/kg +4mg/kg) b. w	4.43 ± 0.02^{a}	20.9 ± 0.15^{a}	7.73 ± 0.05^{a}	65.6 ± 0.28^{a}	36.7 ± 0.02^{a}	41.1 ± 0.27^{a}
Group 7 infected and treated with sulphadimidine + oxytetracycline (200mg/kg +20mg/kg) b. w	4.84 ± 0.02^{a}	19.5 ± 0.18^{a}	7.35 ± 0.03^{a}	49.0 ± 0.22^{a}	19.2 ± 0.01^{a}	40.2 ± 0.22^{a}
Group 8 infected and treated with gentamicin +oxytetracycline (4mg/kg +20mg/kg) b. w	4.00 ± 0.02^{a}	19.4 ± 0.18^{a}	7.19 ± 0.02^{a}	62.0 ± 0.22^{a}	24.2 ± 0.01^{a}	40.0 ± 0.21^{a}

Table 3: White blood cells count in Nubian goats infected with *T.evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations (Mean±SE)

Groups/Parameters	WBCs ($x10^{3}/mm^{3}$)	Neutrophils (mm^{3})	Lymphocytes (mm^{3})	Monocytes (mm^{3})	Basophils (mm^{3})	Eosinophils (mm^{3})
Group 1 uninfected and untreated (control negative)	6.40 ± 0.05^{a}	0.77 ± 0.03^{a}	5.45 ± 0.02^{a}	0.84 ± 0.04^{a}	0.05 ± 0.00^{a}	0.23 ± 0.01^{a}
Group 2 infected and untreated (control positive)	6.73 ± 0.03^{a}	0.52 ± 0.02^{a}	5.55 ± 0.03^{a}	1.84 ± 0.02^{b}	0.09 ± 0.00^{a}	0.07 ± 0.00^{a}
Group 3 infected and treated with sulphadimidine 200mg/kg b.w	7.44 ± 0.04^{a}	1.55 ± 0.04^{b}	7.89 ± 0.06^{a}	2.42 ± 0.01^{b}	0.05 ± 0.00^{a}	0.31 ± 0.01^{a}
Group 4 infected and treated with gentamicin 4mg/kg b.w	6.65 ± 0.03^{a}	1.16 ± 0.03^{b}	13.0 ± 0.09^{b}	1.55 ± 0.02^{b}	0 ± 0.0^{a}	0.29 ± 0.01^{a}
Group 5 infected and treated with oxytetracycline 20mg/kg b.w	7.95 ± 0.04^{a}	1.26 ± 0.02^{b}	9.44 ± 0.04^{ab}	2.80 ± 0.02^{b}	0.02 ± 0.00^{a}	0.59 ± 0.02^{a}
Group 6 infected and treated with sulphadimidine +gentamicin (200mg/kg +4mg/kg) b. w	7.14 ± 0.04^{a}	0.82 ± 0.03^{b}	10.9 ± 0.09^{b}	3.33 ± 0.05^{b}	0.04 ± 0.00^{a}	0.27 ± 0.01^{a}
Group 7 infected and treated with sulphadimidine + oxytetracycline (200mg/kg +20mg/kg) b. w	7.95 ± 0.04^{a}	1.26 ± 0.01^{b}	9.44 ± 0.04^{ab}	2.80 ± 0.02^{b}	0.02 ± 0.00^{a}	0.59 ± 0.02^{a}
Group 8 infected and treated with gentamicin +oxytetracycline (4mg/kg +20mg/kg) b. w	6.39 ± 0.04^{a}	0.99 ± 0.01^{a}	10.5 ± 0.07^{ab}	1.33 ± 0.01^{b}	0.07 ± 0.00^{a}	0.19 ± 0.01^{a}

(a,b,):Different letters in one column showed the significant at $p\leq0.05$ difference

Table (4) Serobiochemical parameters in Nubian goats infected with *T.evansi* and treated with sulphadimidine, gentamicin, oxytetracycline and their combinations (Mean±SE)

Groups/Parameters	Glucose (g/dl)	Total proteins (g/dl)	Albumin (g/dl)	Globulin (g/dl)	Urea (mg/dl)	GOT (U/l)
Group 1 uninfected and untreated (control negative)	74.1 ± 0.27^{a}	8.50 ± 0.05^{a}	5.49 ± 0.04^{a}	3.01 ± 0.01^{b}	55.9 ± 0.24^{a}	217 ± 1.23^{a}
Group 2 infected and untreated (control positive)	58.8 ± 0.27^{b}	7.14 ± 0.02^{a}	3.62 ± 0.02^{b}	3.52 ± 0.02^{b}	88.4 ± 0.22^{b}	251 ± 1.29^{b}
Group 3 infected and treated with sulphadimidine 200mg/kg b.w	56.3 ± 0.26^{b}	8.06 ± 0.06^{a}	3.71 ± 0.02^{b}	4.98 ± 0.02^{b}	71.8 ± 0.26^{b}	213 ± 1.21^{a}
Group 4 infected and treated with gentamicin 4mg/kg b.w	55.4 ± 0.22^{b}	7.58 ± 0.04^{a}	3.30 ± 0.01^{b}	4.15 ± 0.02^{b}	80.3 ± 0.25^{b}	251 ± 1.23^{b}
Group 5 infected and treated with oxytetracycline 20mg/kg b.w	50.6 ± 0.20^{b}	7.68 ± 0.05^{a}	3.56 ± 0.02^{b}	4.12 ± 0.01^{b}	68.0 ± 0.19^{b}	219 ± 1.23^{a}
Group 6 infected and treated with sulphadimidine +gentamicin (200mg/kg +4mg/kg) b. w	51.8 ± 0.25^{b}	7.00 ± 0.03^{a}	3.23 ± 0.02^{b}	3.77 ± 0.01^{b}	73.1 ± 0.22^{b}	239 ± 1.27^{b}
Group 7 infected and treated with sulphadimidine + oxytetracycline (200mg/kg +20mg/kg) b. w	50.6 ± 0.20^{b}	7.68 ± 0.05^{a}	3.56 ± 0.02^{b}	4.12 ± 0.01^{b}	68.0 ± 0.19^{a}	219 ± 1.23^{a}
Group 8 infected and treated with gentamicin +oxytetracycline (4mg/kg +20mg/kg) b. w	49.7 ± 0.16^{b}	7.29 ± 0.04^{a}	3.06 ± 0.01^{b}	4.23 ± 0.02^{b}	70.4 ± 0.20^{b}	242 ± 1.29^{b}

(a,b,): Different letters in one column showed the significant at $p\leq0.05$ difference

Table (5) Efficacy of sulphadimidine, gentamicin, oxytetracycline and theircombinations in Nubian goats experimentally infected with*T.evansi* (Mean±SE)

Groups/Weeks	1	2	3	4	5	6	7	8	9
Group 1 uninfected and untreated (control negative)	0±0.0^a	0±0.0^a	0±0.0^a	0±0. 0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a
Group 2 infected and untreated (control positive)	0.5±0.02^b	0.93±0.03^b	0.28±0.04^a	Animals were died					
Group 3 infected and treated with sulphadimidine 200mg/kg b.w	0.56±0.02^b	1.96±0.04^b	0.43±0.03^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a
Group 4 infected and treated with gentamicin 4mg/kg b.w	0.1±0.01^a	0.96±0.03^b	0.57±0.04^a	0.86±0.02^b	0.28±0.04^b	0.28±0.04^b	0.28±0.04^b	0±0.0^a	0±0.0^a
Group 5 infected and treated with oxytetracycline 20mg/kg b.w	0.54±0.02^b	0.94±0.03^b	0.43±0.03^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a
Group 6 infected and treated with sulphadimidine +gentamicin (200mg/kg +4mg/kg) b. w	0±0.0^a	0.97±0.04^b	1.76±0.05^c	0.61±0.08^{bc}	0.18±0.02^c	0.57±0.08^b	0.28±0.04^a	0.28±0.04^a	0±0.0^a
Group 7 infected and treated with sulphadimidine + oxytetracycline (200mg/kg +20mg/kg) b. w	0.54±0.03^b	0.94±0.03^b	0.43±0.02^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a	0±0.0^a
Group 8 infected and treated with gentamicin +oxytetracycline (4mg/kg +20mg/kg) b. w	0.1±0.01^a	1.5±0.02^b	1.16±0.04^b	0.94±0.03^b	0.24±0.03^b	0.43±0.04^b	0.14±0.02^b	0±0.0^a	0±0.0^a

(a,b,): Different letters in one column showed the significant at p≤0.05difference

References

Adeiza, A. A.; Miakai, V. A. and Lawal, A. I. (2008). Comparative haematological changes in experimentally infected Savannah brown goats with *T.brucei* and *T.vivax*. Afri. J. Biotech. 7:2295-2298.

Akinwale, O. P.; Nock, I. H.; Esievo, K. A. N.; Edeghere, H. U. and Olukosi, Y. A., (2006). Study on the susceptibility of Sahel goats to experimenta *T.vivax* infection.*Vet. Parasit*. 137:210-213.

Anosa, A. I. and Isoun, T. T., (1976). Serum protein, blood and plasma volumes in experimental *T.vivax* infection of sheep and goats *Trop. Anim. Hlth. Prod*. 8:14-19.

Anosa, A. I. and Isoun, T. T., (1980). Haematological studies of *Trypanosoma vivax* infection of goats and splenectomised sheep. J. *Comp. Pathol.*90:155-168.

Anosa, V.O. (1988). Haematological and biochemical changes in human and animal Trypanosomosis. Part 11. *Revue. Elev. Med. Vet. Pays. Trop*., 41(2):151-164.

Brown C. G. D, Hunter A. G and Luckins A. G. (1990). Diseases caused by Protozoa. In: Handbook on Animal Diseases in the Tropics (eds: Swell and Brocklesby), 4th ed., Bailliere Tindall, London.

Bywater, R.J.,G.C. Brander, D.M. Pugh and W.L., Jenkis, (1991). Veterinary Applied Pharmacology and Therapeutics, pp 468-469.

Cheesbrouh, M. (1998). District Laboratory Practice in Tropical Countries Part 1. *Tropical Health Technology. Cambridge University press UK*. Pp:333-370.

Dargantes A. P., Reid S. A. and Copeman D. B. (2005). Experimental *Trypanosoma evansi* infection in the goat. Clinical signs and clinical pathology. Journal of Comparative Pathology 133 (4), 261-266.

Dargie JD *et al*, (1979). Bovine trypanosomiasis: the red cell kinetics of Ndama and Zebu cattle infected with *Trypanosoma congolenses*. Parasitology, 78:271-286.

Denyer S. P., Hodges N. A. and Gorman S. P. (2004). Pharmaceutical Microbiology (Hugo and Russel's), Seventh edition, Blackwell Science, Pp.82-83.

Elrayah EI, Kaminsky R, Schmid C, El Malik KH. (1999). Drug resistance in Sudanese *Trypanosoma evansi,* Veterinary Parasitology. Jan 28:80 (4):281-7.

Fiennes RNTW, (1970). Pathogenesis and pathology of animal trypanosomiasis. In: Mulligan HW, ed., The African Trypanosomiasis. London, UK: George Allen & Unwin, 729-773.

Goossens, B.; Osaer, S.; and Kora, S. (1998). Haematological changes and antibody response in trypanotolerant sheep and goats following experimental *T.congolense* infection. *Vet. Parasit*.79:283-297.

Ismail A. A. (1988). The Susceptibility of Orma and Galana Boran Cattle to Trypanosome Infection. Ph.D Thesis, University of Nairobi.

Kadima, K. B.; Gyang, E. O.; Saror, D. I. and Esievc, K. A. M (2000). Serum biochemical values of *T.vivax* infected cattle and the effects of lactose in saline infusion. *Vet.arhif*. 70:67-74.

Katzung, B. G. (2007). Basic and Clinical Pharmacology, 10th edn, Middle East edn., Mc Graw Hill, Pp. 755.

Masocha W. Rottenberg M. E and Kristensson K. (2006). Minocycline impedes African trypanosome invasion of the brain in a murine model. Antimicrobial Agents and Chemotherapy, 50(5):1798-1804.

Murray M, Dexter TM, (1988). Anaemia in bovine African trypanosomiasis. A review. Acta Tropica, 45(4):389-432.

Murray M, Murray PK, Mclntyrye WIM, (1977). An improved parasitological technique for the diagnosis of African trypanosomiasis. Transactions of the Royal Society of Tropical Medicine and Hygiene, 71:325-326.

Osman, A. S., Jennings, F. W., and Holmes, P. H. (1992). The Effect of treatment with oxytetracycline during the acute stages of experimentally induced equine ehrlichial colitis in ponies. (AJVR) American Journal of Veterinary Research 53(12):2300-2304.

Rang H. P., Dale M. M., Riller J. M., Flower R. J. (2009). Rang and Dale's Pharmacology, six edn, international edn., Churchil Livingstone, Elsevier. Pp 652.

Riviere J. E. and Papich M. G. (2009). Veterinary Pharmacology & Therapeutics. Ninth edition, Wiley-Blackwell Publication, USA.

Saror, D.I. (1980). Observations on the course and pathology of *Trypanosama vivax* in Red Sokota goats. Res. Vet. Sci. 28,36-38.

Schalm, O. W; Jain, N,C; Joseph, G. Z. and Bernard, F. F. (2000). Veterinary Heamatology, 5th ed. Lea and Febiger, Phelladelphia, Pp.110-111.

Sekoni, V.O.; Saror, D. I.; Njoku, C. O.; Kumi-Diaka, J. and PLUWA, G. I. (1990b). Comparative haematological change following *Trypanosoma vivax* and *Trypanosoma congolense* infections in Zebu bulls. *Vet. Parasitol*. 35: 11-19.

Sharma DK, Chauhan PPS, Agrawal RD, (2000). Interaction between *Trypanosoma evansi* and Haemonchus contortus infection in goats. Veterinary Parasitology, 92(4):261-267.

Silva, R.A. M. S.; Ramirez, L., Souza, S. S., Ortiz, A. G., Pereira, S. R., and Duvila, A. M. R. (1999). Haematology of natural goats trypanosomosis in the Brazillian Pantanal and Bolivian wetlands.

Soulsby, E. J. T. (1982). Helminthes, Arthropod and Protozoa of Domestic Animals. Seventh Edition. Baillier Tindall and Cassel (London), pp; 525-537.

Stephen P. D., Norman A. H., Sean P. G. (2007). Hugo Russell's Pharmaceutical Microbiology, 7th edn, Blackwell publishing, Pp 216.

Steven, L. S. and Micheal A. S. (2002). Fundamental of Veterinary Clinic Pathology. Lawa state press, 4th edit. A Blackwell Co. Ltd.

Tabel, H.; Losos, G. J. and Maxie, M. G. (1980). Experimental bovine Trypanosomiasis. *(T.vivax & T.congolense)* serum levels of total protein, albumin, haemolytic complement and complement component C3. *Tropenmed. Parasite*. 32: 149-153.

Taiwo, V.O.; Olaniyl, M. O. and Ogwnsami A. O. (2007). Comparative plasma biochemical changes and susceptibility of erythrocytes in vitro per oxidation experimental *T.congolese & T. brucei* infection in sheep. *J. Vet. Med. Ass*. 58:435-443.

Taylor, K., and Authei, E. M. L. (2003). The trypanosomiasis. Maudlin, I.; Holmes, R. and Miles, M. A. (Eds) Pathogenesis to African Trypanosomiasis. Pp: 331-363. CABI international publisher.

Thrall, Mary Anna, Glade Weiser, Robin W. Allison, Terry W. Campbell (2012). Veterinary Haematology and Clinical Chemistry. Second edition, Wiley-Blackwell, A Johhn Wiley & Sons, Inc., Publication.

Uzoigwe N. R, (1986). Self-cure in zebu calves experimentally infected with *Trypanosoma vivax.* Veterinary Parasitology, 22(1/2):141-146.

Valera, Z.; Parra, O.; Alvarad, M.; Barboza, G.; Escalona, F. and Ramirez, R., (2005). Effect of experimental *T.vivax*infection of hematological parameters of sheep. *Revistax Crentitca, Faca. Deceincias. Vet. Unir Zulia,* 15: 412-420.

Vickerman K and Tetley L, (1978). Biology and Ultrastructure of Trypanosomes in Relation to Pathogenesis. In: Losos G, Chouinard A, eds. Pathogenicity of Trypanosomes. Proceedings of a Workshop, Nairobi, Kenya, 20-23 November, 23-31.

Wellede, B.T.; Chamo, D.; Adoyo, A. M.; Kovatch, R. M. Mwongela, G. N. and Opiyo, E. A., (1983). Haemorrhagical syndrome in cattle associated with *T.vivax* infection. *Trop Anim. Hlth. Prod*. 15:95-102.

Youssif, F. M. Mohammed O. S. A. and Hassan T. (2008). Efficacy and toxicity of Cymelarsan® in Nubian goats infected with *Trypanosoma evansi*. Journal of Cell and Animal Biology 2 (7):140-149.

Youssif, F. M. (2005). Pharmacotoxity of some trypanocidal drugs in food animals (*Camelus dromedaries* and Nubian goats). A thesis submitted for Ph.D. Vet. Fac. Med. U.K Sudan.

Youssif, F. M. (2000). Pharmacoclinical studies on *T. evansi* infected goats. A thesis submitted for MVSc. Degree. K.U. Fac. Vet. Med.

فاعلية عقار السلفا دايمدين والجلنتامايسين والاوكسيتتراسايكلين ومخاليطه في الماعز النوبي المصاب تجريبياً *Trypanosoma evansi*

دينق لونج نيانج[1] ، عثمان سعد علي محمد[2] وفيروز محمد يوسف[3]

1. الدراسات الإكلنيكية كلية الطب البيطري – جامعة اعالي النيل –جنوب السودان
2. الدراسات الإكلنيكية كلية الطب البيطري جامعة السودان
3. المعمل المركزي للبحوث البيطرية – وزارة العلوم والتقانة

المستخلص

هدفت هذه الدراسة لتقييم فعاليةدواء سلفادايميدين، جنتاميسين، أوكسيتيتراسيكلين ومخالطيهم في الماعز النوبي المصابة تجريبيا بطفيل*T.evansi*.استخدمت ثماني مجموعات في هذه الدراسة. المجموعة (1) غير مصاب وغير المعالجة (المراقبة السلبية). المجموعة (2) المصابة وغير المعالجة (مراقبة إيجابية)، المجموعة(5,4,3) حقنت بالعضل مرة واحدة بجرعة مقدارها 200مج بعقارسلفادايميدين، الجنتاميسين4مجو أوكسيتيتراسيكلين 20 مج على التوالي. المجموعة (8,7,6) حقنت بجرعة مرة واحدة بالعضل بمخلوط بعقارسلفادايميدين200مج / كجم) والجنتاميسين 4مج / كجم) ومخلوط سلفادايميدين(200مج / كجم) وأكسي تتراسكلين (20مج / كجم من وزن الجسم) ومخلوط الجنتاميسين (4مج/كجم) و أوكسيتيتراسيكلين (20 مج/كجم وزن الجسم) على التوالي. لم يظهر أي علامات سريريه من قبل المجموعات المعالجة، لم يلاحظ تغييرات معنويةفي درجة الحرارة ومعدل التنفس، ومعدل النبض و ضربات القلب في الماعز المصابة والمعالجة مقارنة مع مجموعة التحكم 1. كما لم تكن هنالك أي تغييرات معنوية في عدد كرات الدم الحمراء،PCV (حجم الخلايا المرصوصة)، وتركيز الهيموغلوبين ومعاملات كرات الدم الحمراء. المجموعات المصابة والمعالجة تم تسجيل انخفاض معنوية في مستوى السكر في الدم والزلال، في حين زيادات معنوية في الجلوبيولين واليوريا وفي النشاط مصلGOT (ناقلإنزيمي قلوتاميك اوكزالواسيتيت)في معظم المجموعات المعالجة. لم يلاحظ أي تغييرات معنوية في كل من مجموعات المعالجة في كرات الدم البيضاء، والخلايا الحمضية والخلايا القاعدية بينما لوحظت زيادات معنوية في الخلايا وحيدة النواة، والخلايا الليمفاويةوالخلايا العدلة في معظم المجموعات المعالجة.وأظهرت النتائج أن الجرعة من عقار السلفادايميدين، أوكسيتيتراسيكلين والجمع بينهما حررت الدم من الطفيليات من الأسبوع الرابع إلى نهاية التجارب، في حين جنتاميسين عند الجرعة الواحدة والجمع بينها والسلفادايميدين وأوكسيتيتراسيكلين حررت الطفيليات من الدم من الأسبوع الثامن والتاسع على التوالي. استنتجت النتائج اعلاه انه يمكن استعمال اللادوية اعلاه ومخالطيها في علاج المرض. نوصي باستخدام الادوية المذكوره أعلاه في علاج مرض طفيل تريبانسوما.