Journal of Coastal Life Medicine

journal homepage: www.jclmm.com

Original article doi: 10.12980/jclm.4.2016j5-170

Changes in blood sugar levels of rats experimentally infected with *Trypanosoma brucei* and treated with imidocarb dipropionate and diminazene aceturate

Nwoha Rosemary Ijeoma Ogechi[1*], Omamegbe Joseph Omalathebu[2]

[1]*Department of Veterinary Medicine, Michael Okpara University of Agriculture Umudike, Umudike, Abia State, Nigeria*

[2]*Department of Surgery and Theriogenology, Michael Okpara University of Agriculture Umudike, Umudike, Abia State, Nigeria*

ARTICLE INFO

Article history:
Received 7 Sep 2015
Received in revised form 21 Sep 2015
Accepted 10 Oct 2015
Available online 21 Dec 2015

Keywords:
Blood sugar
Trypanosoma brucei
Albino rats
Imidocarb dipropionate
Diminazene aceturate

ABSTRACT

Objective: To determine the effect of *Trypanosoma brucei* (*T. brucei*) on blood sugar level of infected rats.
Methods: The experiment was done with 42 albino rats grouped into 3 groups of 14 members each. Group A was uninfected (control group), Group B was infected with *T. brucei* and treated with diminazene aceturate, and Group C was infected with *T. brucei* and treated with imidocarb dipropionate. Blood samples were collected from the media canthus of the experimental rats on Days 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 for the assessment of change in blood sugar levels. The blood sugar levels were determined with a glucometer (Accu-chek active serial No. GN: 10023338).
Results: By 4 to 5 days post infection, there was a significant increase ($P < 0.05$) in the blood sugar of Group B and Group C. By Day 6 post infection (Day 2 post treatment), no significant difference ($P > 0.05$) was observed in the groups when compared with the control group till Day 12 of the experiment.
Conclusions: *T. brucei* caused a significant increase in blood sugar of infected rats.

1. Introduction

Trypanosomes are microscopic unicellular protozoan which belong to the genus *Trypanosoma* in the family Trypanosomatidae. Trypanosomes are blood parasites of vertebrates including common domestic animals and man[1]. Trypanosomosis is associated with the release of inflammatory response which causes degenerative changes in infected animals[2]. Such degenerative changes could be found on the islets of Langerhans in the pancreas and thus attribute to alterations in blood sugar levels and diabetes mellitus[3]. The condition is associated with depressed immunity and suppressed phagocytosis, and thus enhances the level of susceptibility to opportunistic infections[3-8]. In addition to severe anaemia, mortality in trypanosomosis could be related to alteration in blood sugar. Hence, the relevance of this study is to determine the effect of *Trypanosoma brucei* (*T. brucei*) on blood sugar of infected rats and treated with imidocarb dipropionate and diminazene aceturate rats.

2. Materials and methods

A total of 42 pathogen-free albino rats aged nine weeks old of both sexes weighing between 150–300 g were used in the study. The rats were breed in the laboratory animal house of Department of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike. The rats were fed and watered *ad libitum* prior to commencement of the study. Each rat was identified with picric acid stain.

The *T. brucei* parasite used in this study was a Federe strain obtained from the National Institute of Trypanosomosis and Onchocerciasis Research Vom, Plateaue State, Nigeria. The

*Corresponding author: Nwoha Rosemary Ijeoma Ogechi, Department of Veterinary Medicine, Micheal Okpara University of Agriculture Umudike, Umudike, Abia State, P.O. box 824, Nigeria.
Tel: 08030987115
E-mail: rosemarynwoha@yahoo.com

parasites were cryopreserved in liquid nitrogen from where the donor rats were initially infected. The parasites were maintained by serial passage in rats at the Department of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike.

An estimated 2.5×10^6 trypanosome suspended in 1 mL of normal saline was used to infect each experimental rat through the intraperitoneal route using 1 mL tuberculin syringes. The quantity of parasite was estimated using the rapid matching method of Herbert and Lumsden[9].

Imidocarb dipropionate (12%) (Imizole®. Intervet/Merck Animal Health NADA 141-071, Approved by FDA Germany) was administered to the Group C at the dose of 24 mg/kg subcutaneously for 2 consecutive days.

Diminazene aceturate (Veribin® CEVA Sante Animale-La Ballasteiére 33501 Libourne Cedex, France), a generic brand of trypanocide, was also administered to Group B at the dose of 3.5 mg/kg intramuscularly stat.

2.1. Ethical approval

All authors hereby declare that "Principles of Laboratory Animal Care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

2.2. Experimental design

A total of 42 albino rats were randomly grouped into 3 groups of 14 members each. Group A was uninfected (control group); Group B was infected with *T. brucei* and treated with diminazene aceturate at the dose of 3.5 mg/kg once and Group C was infected with *T. brucei* and treated with imidocarb dipropionate at the dose of 24 mg/kg for 3 consecutive days. All treatment commenced on Day 5 post infection.

The blood sugar test was initially determined at Day 0 prior to the commencement of experiment. Subsequently, it was determined 2 days post infection till Day 12 of the experiment.

2.3. Determination of blood sugar

Blood samples were collected from the media canthus of the experimental rats on Days 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 for the assessment of blood sugar levels. The blood sugar levels were determined with a glucometer (Accu-chek active serial No. GN: 10023338). The instrument was first charged with a chip before use according to the manufacturer's instructions and the results of blood samples were read only when the reading on the glucometer remained steady for 3 s but not more than that.

2.4. Statistical analysis of data

Data obtained from this study were presented as mean ± SEM. Statistical significance was analyzed using One-way ANOVA and Duncan's multiple range test with SPSS version 16 software package. The acceptance of significance level was at $P < 0.05$[10].

3. Results

From the experimental groups (Table 1), Group B and Group C were infected with *T. brucei* on Day 2 of the experiment and established parasitaemia by Day 4 post infection. By Days 5 and 6, there were significant increases ($P < 0.05$) in the blood sugar levels of both Group B and Group C. Treatment from Day 5 with diminazene aceturate at 3.5 mg/kg once in Group B and with imidocarb dipropionate at 2.4 mg/kg for 3 consecutive days in Group C respectively improved the blood sugar levels in the groups. And by Day 7, there was no significant difference ($P > 0.05$) between the infected groups (Group B and Group C) until by Day 10 of the experiment. There was no mortality recorded throughout the experimental period.

Table 1

Blood sugar levels of rats with experimental *T. brucei* infection and treated with diminazene aceturate and imidocarb dipropionate.

Experimental period (days)	Groups		
	Group A (control)	Group B	Group C
0	113. 30 ± 2.01[a]	110.60 ± 2.13[a]	114.62 ± 2.41[a]
1[#]	98.90 ± 2.00[a]	96.70 ± 0.01[a]	97.80 ± 9.00[a]
2	101.02 ± 0.01[a]	100.20 ± 0.10[a]	113.34 ± 0.01[a]
3	98.20 ± 1.01[a]	97.80 ± 0.01[a]	96.80 ± 1.01[a]
4	92.30 ± 2.01[a]	113.35 ± 2.01[b]	101.10 ± 2.01[b]
5[+*]	81.00 ± 1.10[a]	112.01 ± 1.66[b]	100.34 ± 1.67[b]
6[*]	113.10 ± 2.01[a]	100.00 ± 1.01[a]	121.23 ± 1.00[a]
7[*]	98.00 ± 1.10[a]	84.14 ± 1.10[a]	71.43 ± 2.00[a]
8	121.23 ± 1.11[a]	100.03 ± 1.01[a]	123.24 ± 2.01[a]
9	111.10 ± 0.12[a]	100.24 ± 2.01[a]	121.12 ± 0.01[a]
10	96.86 ± 8.06[a]	110.10 ± 1.45[a]	112.23 ± 5.78[a]

All values were expressed as mean ± SE. [a,b]: The homogeneity between the experimental groups at probability $P < 0.05$; [#]: Day of *T. brucei* infection; [+]: Day of treatment with diminazene aceturate; [*]: Day of treatment with imidocarb dipropionate.

4. Discussion

Several factors could be responsible for hyperglycaemia recorded in Group B and Group C by the 4th and 5th days post infection. Previously, trypanosomes have been associated with alteration in blood sugar levels of infected animals and a significant decrease ($P < 0.05$) in blood sugar level was attributed to rapid consumption of sugar by trypanosomes[11]. Hypoglycaemia was also recorded in both *T. brucei* and *Trypanosoma congolense* infected sheep and *Trypanosoma congolense* infection in rabbits[12,13]. Conversely, a significant increase ($P < 0.05$) in blood sugar levels was associated

with some degrees of degenerative changes in the pancreas which may precipitate type 2 diabetes mellitus[14]. However, type 2 diabetes mellitus is a condition characterized by persistent hyperglycemia which was not observed in this study[15]. Hence, the increases in blood sugar levels observed in Group B and Group C may be not due to degenerative changes in the pancreas or from classical diabetes mellitus. Though administration of certain drugs elevates blood glucose level in the body[16], it however was not drug induced due to null effect of diminazene aceturate on blood glucose level in rats[17]. In addition, imidazole derivates such as copper II imidazole complexes are likely to induce hypoglycaemia rather than hyperglycaemia in diabetic rats[18]. Nonetheless, transient elevations in blood glucose in this study may have resulted from conditions of some degrees of liver damage and acute stress reaction[19]. Severe liver damage may result from the sequestration of *T. brucei* parasites in the liver tissues during disease process[20]. Such liver damage may compromise the sugar regulatory function of the liver which normalized on treatment. Similarly, acute stress may induce transient increase in blood sugar level which could be induced by mere presence of trypanosomes in the blood[21]. It then seems that transient increase in *T. brucei* infected groups in this study was due to acute stress reaction or slight liver damage in the infected rats. The study therefore showed that *T. brucei* infection induced a transient elevation in blood sugar in the infected rats.

Conflict of interest statement

We declare that we have no conflict of interest.

References

[1] Robinson TP, Harris RS, Hopkins JS, Williams BG. An example of decision support for trypanosomiasis control using a geographical information system in Eastern Zambia. *Int J Geogr Inf Sci* 2002; **16**(4): 345-60.

[2] Akanji MA, Adeyemi OS, Oguntoye SO, Sulyman F. *Psidium guajava* extract reduces trypanosomosis associated lipid peroxidation and raises glutathione concentrations in infected animals. *EXCLI J* 2009; **8**: 148-54.

[3] Musa BOP, Onyemelukwe GC, Hambolu JO, Bakari AG, Anumah FE. Cell-mediated immunity in type 2 diabetes mellitus patients in diabetic ketoacidosis, patients with controlled type 2 diabetes mellitus and healthy control subjects. *J Med Med Sci* 2010; **1**(7): 290-5.

[4] Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). *FEMS Immunol Med Microbiol* 1999; **26**(3-4): 259-65.

[5] Graves DT, Kayal RA. Diabetic complications and dysregulated innate immunity. *Front Biosci* 2008; **13**; 1227-39.

[6] Tanaka Y. [Immunosuppressive mechanisms in diabetes mellitus]. *Nihon Rinsho* 2008; **66**(12): 2233-7. Japanese.

[7] Ponce-De-Leon A, Garcia-Garcia Md Mde L, Garcia-Sancho MC, Gomez-Perez FJ, Valdespino-Gomez JL, Olaiz-Fernandez G, et al. Tuberculosis and diabetes in Southern Mexico. *Diabetes Care* 2004; **27**: 1584-90.

[8] Martens GW, Arikan MC, Lee J, Ren F, Greiner D, Kornfeld H. Tuberculosis susceptibility of diabetic mice. *Am J Respir Cell Mol Biol* 2007; **37**(5): 518-24.

[9] Herbert WJ, Lumsden WH. *Trypanosoma brucei*: a rapid "matching" method for estimating the host's parasitemia. *Exp Parasitol* 1976; **40**: 427-31.

[10] Snedecor GW, Cochran WG. *Statistical methods*. 6th ed. Amess: Iowa State University Press; 1967.

[11] Chaudhuri M, Ott RD, Hill GC. Trypanosome alternative oxidase: from molecule to function. *Trends Parasitol* 2006; **22**: 484-91.

[12] Taiwo VO, Olaniyi MO, Ogunsanmi AO. Comparative plasma biochemical changes and susceptibility of erythrocytes to *in vitro* peroxidation during experimental *Trypanosoma congolense* and *T. brucei* infections in sheep. *Isreal J Vet Med* 2003; **58**: 112-7.

[13] Takeet MI, Fagbemi BO. Haematological, pathological and plasma biochemical changes in rabbits experimentally infected with *Trypanosoma congolense*. *Sci World J* 2009; **4**: 29-36.

[14] Locatelli F. Metabolism of glucose in trypanosomiasis. *Compte rendu des seances de la Societe de biologie* 1930; **105**(31): 449-51.

[15] Pais I, Hallschmid M, Jauch-Chara K, Schmid SM, Oltmanns KM, Peters A, et al. Mood and cognitive functions during acute euglycaemia and mild hyperglycaemia in type 2 diabetic patients. *Exp Clin Endocrinol Diabetes* 2007; **115**(1): 42-6.

[16] Walker R, Rodgers J. *Type 2 diabetes-your questions answered*. London: Dorling Kindersley; 2006.

[17] World Health Organization. Diminazene. Geneva: World Health Organization; 2001. [Online] Available from: http://www.inchem.org/documents/jecfa/jecmono/v25je09.htm [Accessed on 10th August, 2015]

[18] Abdul-Ghani AS, Abu-Hijleh AL, Nahas N, Amin R. Hypoglycemic effect of copper(II) acetate imidazole complexes. *Biol Trace Elem Res* 1996; **54**(2): 143-51.

[19] Wikipedia. Blood sugar. San Francisco: Wikipedia; 2012. [Online] Available from: https://en.wikipedia.org/wiki/Blood_sugar [Accessed on 10th August, 2015]

[20] Akpa PO, Ezeokonkwo RC, Eze CA, Anene BM. Comparative efficacy assessment of pentamidine isethionate and diminazene aceturate in the chemotherapy of *Trypanosoma brucei brucei* infection in dogs. *Vet Parasitol* 2008; **151**: 139-49.

[21] Biryomumaisho S, Katunguka-Rwakishaya E. The pathogenesis of anaemia in goats experimentally infected with *Trypanosoma congolense* or *Trypanosoma brucei*: use of the myeloid: erythroid ratio. *Vet Parasitol* 2007; **143**: 354-7.