EFFECT OF DEXAMETHOSONE ON BABESIOSIS IN *TATERA INDICA* (HARDWICKE)

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ABSTRACT

Two subcutaneous injections of 0.15 mg of dexamethasone/kg of body weight caused a substantial crease in *Babesia microti.* Parasitized RBC of *Tatera indica*, indicating that this was a useful method for revealing the presence of latent infections. A relative neutrophilia, lymphocytopenia, and eosinopenia were also seen in the long term. *B. microni* infected carrier *T. indica* after 0.15 mg or 0.01 mg of dexamethasone/kg Noninfected *T. indica* treated with dexamethasone had a neutrophilic leucocytosis and a transient lymphocytopeni. Spleen to body weight ratios of noninfected *T. indica* decreased significantly ($p< 0.02$) after three injections with either dosage level. These ratios did not significantly ($P>0.05$) decrease in dexamethasone treated infected indica.

Introduction

Babesiosis, an acute, tick-transmitted disease of mammals manifested by anemia and hemoglobinuria, is caused by numerous intraerythrocvtic protozoan species of the genus *abesia*. Babesiosis refers to subclinical or latent babesial infections (Carson 1981) in animals that have recovered from the clinical disease to identify mammals with babesiosis, stained blood smears are examined for the presence of parasitized RBC, although splenectomy of these animals frequently may he required to exacerbate latent infections and reveal the parasite in peripheral blood (Kuttler, 1967; Frerichs, 1970). The use of corticosteroids or their synthetic analogs has been suggested as an alternative to splenectomy for enhancing babesial parasitemia (Young, 1971). Corticosteroids reactivate various hemoparasitic infections in cattle and horses (Hoffman, 1971; Ibanez, 1976). Administration of hetamethasone during the period of recovery in rats and mice infected with *B. microti* resulted in increased numbers of parasitized RBC (Young, 1971).

The purpose of the present study was to determine the influence of dexamethasone on hamsters with long-term *B. microti* infections. The Indian gerbil (*T. indica*) was used because mortality is not typically associated with *Babesia* infection and potency is followed by a carrier state in which parasitized RBC are rare or absent in blood smears

(Lykins, 1971). Dexamethasone was evaluated as an alternative to splenectomy to exacerbate latent babesial infection in the *T. indica* and thus assist in the detection of the carrier state.

Materials and Methods

Indian gerbil (*T. indica*) Fifty, 2 1/2 month-old, male gerbil were inoculated intraperitoneally with 0.1 ml of heparinized fresh hamster blood containing approximately $1x10^7$ *B. microti* infected REC. The *B. microti* isolated originated from a mouse that had been captured on Huh Valley in 1988. The isolate was subsequently maintained through 5 gerbil passages, with periodic storage in liquid nitrogen. Inoculated gerbil developed anemia and parasitized RBC were observed on post oculation days (PID) 15 to 25. All inoculated hamsters recovered from the acute infection and were given normal rations for 6 months. Twentynine 2 1/2 month old, male gerbil were used as non infected controls.

Dexamethasone treatment-six months alter inoculation of infected blood, hamsters were assigned to 2 treatment groups, group-1 contained 21 infected and 22 noninfected gerbil given 0.15 mg of dexamethasone/kg of body weight (subcutaneously) two times at 24-hours intervals. Group-2 contained 19 infected and 20 noninfected gerbil treated similarly, except the dosage level was 0.01 mg/kg. Group-3 contained 10 infected and 6 noninfected gerbil not given dexamethasone. All gerbil were weighed, and blood was collected at 1 day before, twice during, and 3 days after the steroid treatment. Blood smears were giemsa stained, at least 1,004) RBC were observed for the presence of babesiae, and differential WBC counts were completed. Gerbils were killed on posttreatment day (PTD)7. Their spleens removed and weighed. Spleen to body weight ratios were calculated (±SD). Statistical analysis of variance, general linear models procedure, was used to determine differences in WBC populations and percentage of parasitcmias between and within 3 treatment groups. Student's test was used to detect significant differences in spleen to body weight ratios.

Results

When 0.15 mg of dexamethasone/kg was given, there was a significant increase of *B. microri* parasitized RBC in the infected gerbils after two injections ($P = 0.0290$). The parasitemia continued to increase for at least 2 days after the 3 injections ($P = 0.0002$). A significant increase in parasitized RBC was not observed in infected gerbils treated 2 times with 0.01 mg of dexamethasone/kg. Infected gerbils that were not treated (group-3) had mean parasitemias of 0.25 1 0.02%, although at least 15% were negative for infection based on blood smears examination at any given blood collection. Both dosage regimens caused a relative neutrophilic leucocytosis ($P<0.01$) in non-infected and *B. microti* carrier gerbils. However, on PTD 9, only infected gerbils given 0.15 mg of dexamethasone/kg had a significant nut niphilic leucocytosis ($P < 0.0$ 1).

Dexamethasone/kg caused a lymphocytopcnia (P<001) in noninfected gerbils, and only after the last injection. In eosinopenia (3% initial to 0.2% final; P<0.01), which appeared after the last injection of either dosage level and continued. Total WBC counts were precluded by the small volume of blood that was obtained in samples from the tail veins. Dexamethasone treatment decreased spleen weights of noninfected gerbils, but did not significantly change those of infected gerbils (Table-1). Three doses of dexamethasone (0.01 mg/kg) resulted in mean spleen per body weight ratio of 65.2 ± 28.0 mg/100 g (P<0.05) in noninfected gerbils, where as 0.15 mg of dexamethasone resulted in a mean ratio of 48.1, ± 10.3 mgil00 g (P < 0.02). The effect of dexamethasone treatment on spleen weights within the infected gerbil model was not significant (P<0.05) spleen weights of non-infected gerbils (x = 103.6 ± 20.2 mg/100 g) where significantly (P<0.02) less than those of long term *B. microti* carriers (x = 210.0 + 110.0 mg/100 g).

There were no significant changes in initial and final body weights of noninfected or infected gerbils after the treatment period. However, the mean initial weight (110.0 ± 2.3 g) of the infected gerbils was less than that of the noninfected gerbils (120 ± 10.0 g; P < 0.05).

TABLE-1

Effect of Dexamethasone on Spleen Weights of noninfected and Babesia infected Gerbils

Gerbils (N)	Spleen (mg/100 SD)
Group 3-dexamethasone (none)	
Noninfected (6)	103.6± 20.2
Infected (10)	210.0 ±110.0*
Group-2 dexamethasone (0.01 mg/kg)	
Noninfected (20)	6.2 ± 28.0+
Infected (19)	180.6 ± 99.8+
Group 1-dexamethasone (0.15 mg/kg)	
Non-infected (22)	48.6 ± 10.3+
Infected (21)	225.0 ± 80.3*

* = P 0.02 as compared with noninfected gerbils
\+ = P 0.05 as compared with non treated, noninfected gerbils.
Dexamethasone treatment within infected groups were not significant in spleen weight reduction.

Discussion

Use of dexamefiasone to suppress the immune system resulted in an increase of B. micron parasitized RBC in infected gerbils, but deaths were not seen. Therefore, dexamethasone treatment appears to he a practical and useful means of detecting babesiosis in gerbil. Dexamethasone may also be useful with wild rodents in detecting natural *B. microti* infections because anesthesia and subsequent surgical procedures often produce high mortalities in small animals.

Because glucocorticoid treatment is known to produce lymphocytopcnia (Muscoplat, 1975; Fauci, 1976) it is not surprising that gerbil treated with dexamcthasonc also had this response. However, in healthy gerbils, lymphocytopenia was seen only after the first injection of the drug; whereas in infected gerbils, it persisted during the treatment period. Therefore, babesiosis, may hamper the body's capacity to normalize its circulating cellular components. Glucocorticoid treatment may also produce neutrophilia and eosinopenia (Muscoplat, 1975). Although neutrophilia was seen in infected and noninfected gerbils, cosinopcnia was only observed in the infected gerbils. There are currently 2 contrasting hypotheses of ensinophil function, one in which it is seen as a phagocytic cell and the other in which it is viewed as an anti-inflammatory, immunomodulatory cell (Bass, 1979). Eosinophils may also function with other cells, such as most cells or macrophages in host defense against parasites. Eosinophils from human beings parasitized by metazoans have altered maturation, lowered state of activation, and reduced accessibility or altered configuration of their surface receptors, e.g. immunoglobulin G and complement 3 b (Desimone, 1982) Dexamethasone mediated interference with normal cosinophilic function and removal from circulation could deprive that host of an important immune mediator for regulating latent babesial infections. Recrudescence may also be caused by the effect of steroid, treatment on other cellular or Immoral factors. General body wasting and persistent splenomegaly were seen in the long-term *B. microti* carrier gerbils. Splenomegaly was not affected by the dexamethasone treatment at their dosage level. Because there are excessive numbers of plasma cells in the spleen of animals with prolonged infections (Ristic, 1981), it is unclear why dexamethasone (Bach, 1975) failed to reduce spleen weight in the *B. microti* carrier animals.

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