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Kuttler, K.L.

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## Efficacy of Oxytetracycline and a Dithiosemicarbazone in the Treatment of Bovine Anaplasmosis

K. L. Kuttler, D.V.M., Ph.D.

### SUMMARY

The combination of a dithiosemicarbazone (356C61) and oxytetracycline proved more efficacious in the treatment of anaplasmosis than did either drug administered alone. The *Anaplasma marginale* carrier state in splenectomized calves was suppressed for as long as 120 days and was possibly eliminated by 3 injections of 356C61 (5 mg./kg.) and oxytetracycline (11 mg./kg.) given simultaneously at 48-hour intervals.

The need for an inexpensive, efficient, and simple treatment to eliminate the carrier state of *A. marginale* in cattle is increasing as more serious considerations are given to the possibility of eradication and control of anaplasmosis. A program of "test and treatment" has been proposed,<sup>3,11</sup> and pilot studies utilizing this principle are currently in progress.<sup>6</sup>

The value of tetracyclines in the treatment of anaplasmosis has been established.<sup>4,5,10</sup> Elimination of carrier infections requires multiple injections of large volumes of drug or a relatively long period of oral therapy. Both methods can become costly in both money and time. Several workers<sup>2,8,9</sup> have reported on the use of a dithiosemicarbazone (356C61)\* to treat anaplasmosis. In preliminary

experiments, treatment with 356C61 sufficient to eliminate infection proved to produce toxic effects.<sup>1,7</sup> The administration of smaller amounts resulted in the elimination of parasitemia and the increase in packed cell volumes (PCV), but was followed in 30 to 50 days by a relapsing *A. marginale* infection. Treatment with 356C61 at the dosage level of 5 mg./kg. each day for 5 consecutive days did not eliminate the carrier infection.<sup>7</sup>

The purpose in the present study was to administer oxytetracycline and 356C61, separately and together in different dose concentrations, at different intervals, and for different periods in order to eliminate the carrier infection.

### Materials and Methods

Treatment was administered to 14 splenectomized, *A. marginale*-infected Holstein-Friesian calves ranging in age from 6 to 18 months.

Group I consisted of 5 calves treated with 356C61. The drug was diluted in 200 ml.

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From the Institute of Tropical Veterinary Medicine, Texas A&M University, College Station, Texas 77843.

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\* Gloxazone ( $\alpha$ -Ethoxyethylglyoxal dithiosemicarbazone), Burroughs Wellcome and Company, Inc., Tuckahoe, N.Y.

TABLE 1—Results of Treatment of *Anaplasma*-Infected Splenectomized Calves with Oxytetracycline and a Dithiosemicarbazone (356C61)

Calves		Parasitemia at the time of treatment (%)	Duration of parasitemia before treatment (days)	Treatment						Results of treatment	Relapse or observation time (days)
				Oxytetracycline		356C61		No. of injections	Interval between injections		
No.	Age (mo.)			Dose (mg./kg.)	Route	Dose (mg./kg.)	Route				
<b>GROUP I</b>											
119	18	1.0	74	...	.....	5	I.V.	3	48 hr.	Relapse	48
140	10	0.2	81	.....	.....	10	I.V.	3	48 hr.	Relapse	48
174	6	7.0	49	.....	.....	5	I.M.	4	4 days	Relapse	45
176	6	2.0	49	.....	.....	5	I.M.	4	4 days	Relapse	49
180	6	1.0	49	.....	.....	5	I.M.	4	4 days	Relapse	45
Average	9	2.24	60								47
<b>GROUP II</b>											
244	6	2.0	40	11	I.V.	....	.....	3	24 hr.	Relapse	14
206	11	0.3	26	11	I.V.	....	.....	3	24 hr.	Relapse	14
242	6	10.0	18	11	I.V.	....	.....	3	24 hr.	Relapse	17
Average	8	4.1	28								15
<b>GROUP III</b>											
141	7	0.6	37	11	I.V.	5	I.V.	3	48 hr.	No relapse	120
197	10	3.0	102	11	I.V.	5	I.V.	3	48 hr.	No relapse	120
183	11	0.1	77	11	I.V.	5	I.V.	3	48 hr.	No relapse	120
426	9	0.6	67	22	I.V.	5	I.V.	3	48 hr.	No relapse	120
421	9	2.0	46	22	I.V.	5	I.V.	3	48 hr.	No relapse	120
500	9	64.0	6	22	I.V.	10	I.V.	3	24 hr.	No relapse	120
Average	9	12.0	56								120

I.V. = intravenous route; I.M. = intramuscular route.

TABLE 2—Influence of Treatment with Oxytetracycline and a Dithiosemicarbazone on Packed Cell Volumes (PCV) and Complement-Fixation (CF) Test Responses of *Anaplasma*-Infected, Splenectomized Calves

Item	Group I	Group II	Group III	Significance
Average PCV at time of treatment (%)	18	15	20	N.S.
Average PCV at 40 days after treatment (%)	31	20	30	P < 0.01; D.R.S., 3.4
Average CF titer at time of treatment	1:160	1:127	1:90	N.S.
Average time required for CF titer to decrease below 1:5 (days)	Titer retained	Titer retained	61 ± 28 (S.D.)	..
Average CF titer at 61 days after treatment	1:40	1:57	< 1:5	..

Group I = 5 calves treated with 356C61 only; group II = 3 calves treated with oxytetracycline only; group III = 6 calves treated simultaneously with 356C61 and oxytetracycline; N.S. = not significant; D.R.S. = difference required for significance.

of physiologic saline solution (pss) (0.85% NaCl) and injected intravenously (i.v.) or was nondiluted and injected intramuscularly (i.m.). Calf 119 was given 5 mg./kg., administered i.v., 3 times at 48-hour intervals; calf 140 was given 10 mg./kg., administered i.v., 3 times at 48-hour intervals; calves 174, 176, and 180 were given 5 mg./kg., administered i.m., 4 times at 4-day intervals.

Group II consisted of 3 calves treated with oxytetracycline. The drug was diluted in 200 ml. of pss. Calves 244, 206, and 242 were given 11 mg./kg., administered i.v. 3 times at 24-hour intervals.

Group III consisted of 6 calves treated with oxytetracycline and 356C61 simultaneously. The dose of each drug was added to and mixed in 200 ml. of pss and injected i.v. Calves 141, 197, and 188 were given oxytetracycline at the dose of 11 mg./kg. and 356C61 at the dose of 5 mg./kg., administered i.v., 3 times at 48-hour intervals; calves 426 and 421 were given oxytetracycline at the dose of 22 mg./kg. and 356C61 at the dose of 5 mg./kg., administered i.v., 3 times at 48-hour intervals; calf 500 was given oxytetracycline at the dose of 22 mg./kg. and 356C61 at the dose of 10 mg./kg., administered i.v., 3 times at 24-hour intervals.

Complement-fixation (cf) tests to determine the presence and titer of specific *A. marginale* serum antibodies, pcv, and parasitemia, as determined by examination of Giemsa-stained blood smears, were done to determine existence of *A. marginale* infection in treated calves. A recrudescence of anaplasmosis was assumed when parasitemia (1% of red blood cells were infected)

recurred. In the absence of relapsing parasitemia, treated calves 141, 197, and 188 were tested for infectivity by inoculating 200 ml. of their whole blood into each of 3 *A. marginale*-susceptible, splenectomized calves.

## Results

The response of infected calves treated with oxytetracycline and 356C61, separately and together, is presented (Table 1). Those calves given 356C61 or oxytetracycline separately had evidence of relapsing infection. Based on results of examination for parasitemia, calves treated with 356C61 had an average relapse period of 47 days, which was significantly longer than the average of 15 days occurring in calves treated with oxytetracycline.

When both drugs were injected simultaneously, signs of relapse were not evident in any of 6 calves for 120 days. Calves 141, 188, and 197, treated with both 356C61 and oxytetracycline, were apparently free of infection as determined by inoculation of blood in 3 susceptible, splenectomized calves.

The results of treatment as reflected by pcv and cf titers are presented (Table 2). All calves had marked increases in pcv 40 days after treatment. This increase was significantly greater in calves of groups I and III. A positive cf titer (1:5 or over) disappeared in group III calves on an average of 61 ± 28 days

after treatment. Decrease in antibody titer was evident in calves of groups I and II.

### Discussion

In previous studies,<sup>7</sup> i.v. administration of 356C61 on 5 successive days at the dose level of 5 mg./kg. did not eliminate infection from splenectomized calves. Administration of oxytetracycline each day at the dose level of 11 mg./kg. for both 5 and 10 days gave similar results. It was not surprising that, in the present experiment, administration of 356C61 and oxytetracycline separately also did not remove infection. In 1 instance (calf 140), the dose level of 356C61 was doubled to 10 mg. kg., but this did not alter the relapse time.

In all instances, 3 injections of both drugs at either 48- or 24-hour intervals were successful in eliminating evidence of infections for as long as 120 days. The absence of infection in the 3 calves tested for infectivity, plus the prolonged test-negative status of others, would indicate that carrier infections were removed by this treatment.

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