Evaluation Of A Long-Acting Oxytetracycline For Treatment Of *Pasteurella* Pneumonia In Calves

R. G. Breeze, *B.M.V.S., Ph.D., M.R.C.V.S.*
Department of Microbiology and Pathology
Washington State University
Pullman, Washington 99164

L. H. Lauerman, *D.V.M., Ph.D.*
Veterinary Diagnostic Laboratory
Colorado State University
Ft. Collins, Colorado 80521

J. A. Schmitz, *D.V.M., Ph.D.*
Veterinary Diagnostic Laboratory
Oregon State University
Corvallis, Oregon 97330

R. A. Magonigle, *M.S.*
Animal Health Research Department
Pfizer Inc.
Groton, Connecticut 06340

Introduction

A series of experiments was conducted at 4 different research facilities in the United States. The purpose of these experiments was to compare the therapeutic efficacy of a single intramuscular treatment with a long-acting oxytetracycline injectable (T-200, Liquamycin/LA 200; 200 mg oxytetracycline/ml; Pfizer, Inc. New York, New York) against two or three treatments with a conventional oxytetracycline (T-50, Liquamycin 50, 50 mg oxytetracycline/ml; Pfizer Inc.) in an induced *Pasteurella* pneumonia model in calves.

Materials and Methods

Animals

Holstein steer calves aged 4-9 weeks were allocated to 3 groups equally according to body weight before experimental infection. In each experiment, Treatment 1 was control, nonmedicated calves; Treatment 2, calves given T-50; and Treatment 3, calves given T-200. None of the calves had any history or clinical signs of respiratory disease prior to infection, and none received any antibacterial drug for 3 weeks before the experiment.

Calves were offered water, milk substitute and calf starter ration *ad libitum;* the quantities consumed by each group were measured daily.

Infection

Challenge inoculum of *Pasteurella multocida* was prepared from stock rabbit liver suspension culture (Pfizer Inc.) diluted 1:5 with tryptose phosphate broth and incubated at 37°C for 4-5 hours on a shaker. The culture was washed 3 times in fresh tryptose phosphate broth and standardized spectrophotometrically at 600 nm against a broth blank. Cultures were streaked on blood agar plates to check growth and purity.

Each animal was given 20 infective units in 10 ml culture suspension (1 infective unit was 0.25 ml at 59% transmission) further diluted with 10 ml of sterile broth for a total inoculum of 20 ml by endotracheal tube. Four to six times in the 36 hours prior to the *Pasteurella* challenge, calves were stressed by wetting alternately with hot and cold water for several minutes. At 24 and 6 hours before challenge, each calf received a 0.6 ml intratracheal injection of 8% acetic acid, the injection being given through a 1 inch 22 gauge needle inserted just cranial to the thoracic inlet.

Clinical observations

Daily clinical observations of body temperature, respiratory rate and type, demeanor, appetite and degree of gauntness were begun 2-4 days before infection and continued until necropsy at 7 days post-challenge. Weight gain and feed consumed daily were also noted.

Pathological examination

Seven days after challenge, or at death, all animals were examined post mortem and final body weights were taken. Lung lesions were then scored on a simple grading system and samples of lung tissue were taken for bacteriological culture.

Treatment

Treatment was initiated 2-6 hours after challenge, when calves first exhibited a febrile response and marked depression. All medicated groups received treatment at this time. T2 was given T-50 at either 3 mg/lb BW 3 times at daily intervals or 5 mg/lb BW twice at daily intervals. T3 was given one injection of T200 at 9 mg/lb BW.

Statistical Analysis

Results were analysed by a 2 way analysis of variance, except for mortality data subjected to the Fisher exact test and the Mantel-Haenszel test.

Results

Clinical observations

On the day of infection all calves were clinically normal, without nasal discharge or cough and with consistent rate and depth of breathing.

Two to six hours after infection almost all calves (53/59) were in sternal or lateral recumbency. All were dull, and many had increased rate and/or depth of breathing. Increased breathing sounds were heard on auscultation and spontaneous coughing was very frequent. Some calves had a slight to moderate expiratory grunt. None were interested in feeding. Body temperatures were generally elevated (103-106°F). There was no doubt that a severe response had occurred and so the two medicated groups were given antibiotics during this period in all experiments.

The results are summarized in Table 1. In surviving nonmedicated animals, the clinical signs persisted at about the same level for 24-72 hours following infection. These calves gradually improved but still had demonstrable respiratory disease at slaughter on experiment day 7. Seven of 19 calves in the T1 group became severely ill with

Location	Treatment	No. Cattle	Depression Index* at Day Onset	3	Final	Lung Lesion Score**	Mortality %	Av. Daily Gain, lb.
1	T1	5	3.2	1.6	1.9	2.2	0	0.88
	T2x	5	4.3	1.0	1.0	0.8	0	1.44
Oregon	T3	5	4.4	1.1	1.0	1.2	0	1.66
2	T1	5	4.0	4.6	2.4	2.0	20	−0.20
	T2x	5	4.0	2.2	1.4	1.2	0	0.20
Colorado	T3	5	4.6	1.6	0.0	0.8	0	0.31
3	T1	5	4.8	5.6	5.4	3.8	80	−1.57
	T2y	5	3.8	1.0	0.6	1.8	0	1.03
Indiana	T3	5	4.0	0.6	0.2	1.2	0	2.57
4	T1	4	6.5	4.8	3.5	3.4	50	0.05
	T2y	5	6.6	0.0	0.0	1.0	0	1.34
Washington	T3	5	7.0	1.6	0.0	0.5	0	1.61
Summary	T1	19	4.6^a	4.2^d	3.3^a	2.9^a	37^a	-0.21^a
Four Expts.	T2x&y	20	4.7^a	1.1^b	0.8^b	1.2^b	0^b	1.00
	T3	20	5.0^a	1.0^b	0.3^b	0.9^b	0^b	1.54^b

Table 1: Effects of experimental *Pasteurella multocida* challenge in control (T1) and treatment groups (T2, T3). Treatment description: T1, *Pasteurella* infected, nonmedicated; T2, *Pasteurella* infected and given conventional oxytetracycline (50 mg/ml) intramuscularly in 3 daily injections of 3mg/lb body weight (T2x) or 2 daily injections of 5 mg/lb bodyweight (T2y); T3, *Pasteurella* infected and given longacting oxytetracycline (200 mg/ml) in a single intramuscular injection of 9 mg/lb bodyweight.

** Depression based upon index 0 through 7 (0 = normal; 7 = moribund). Where mortality occurred, index means were derived using last recorded value.*

*** Lung lesions based upon score at necropsy of 0 through 4 (0 = no lesions; 4 = extensive consolidation).*

ab Means which do not share a common superscript are significantly different ($p < 0.05$).

respiratory disease, as evidenced by persistent fever, cough, depression, increasing respiratory adventitious sounds and refusal to stand or take feed and water. Of the 7 T1 calves that died during the experiment, 3 were dead on or before experiment day 3 while 4 calves died between experiment days 4 and 6.

Twelve to 16 hours following the initiation of therapy there was obvious clinical improvement in calves in both of the medicated groups. The overall response to therapy was essentially equal in both T2 and T3 calves and was characterized by reduced depression and fever, remission of cough, resumption of a more normal respiratory pattern and improved appetite.

Pathology and Bacteriology

Lung involvement in nonmedicated calves was moderate to severe. Lesions were observed in all T1 calves, most often in cranial segments of the lung lobes. The lesions were characterized by the presence of serofibrinous or purulent exudate in the bronchi and bronchioles and lobular congestion with areas of consolidation and collapse. In some individuals more than 50% of the lung tissue was consolidated while fibrinous pleuritis and/or pericarditis was also noted.

Lesions in calves from both of the oxytetracycline medicated groups were more scattered and less severe than those in T1. Six calves in T2 and 7 calves in T3 had no evidence of lung lesions at the time of necropsy.

The infecting *P. multocida* organism was recovered from 51% of the nonmedicated calves sampled but was not isolated from any of the samples from medicated calves in groups T2 and T3.

Conclusions

The *P. multocida* endotracheal challenge compounded by the stress procedure produced a severe and sometimes fatal respiratory infection. A high incidence and severity of disease were observed among nonmedicated controls, while cattle given a single injection of T-200 or multiple doses of T-50 quickly responded to treatment with significant reduction of clinical signs and mortality and significantly improved performance. Necropsy observations of all animals at the trial termination confirmed that therapy significantly diminished the incidence and severity of pathological lesions resulting from the infection. One therapeutic treatment with T-200 was equally effective to 2 or 3 daily doses of T-50 in each of the four experiments. **The advantage afforded by a single treatment in reducing labor, handling and stress in penumonic animals will be beneficial under field conditions.**

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