A Long-Acting Tetracycline for Treatment of *Pasteurella* Pneumonia in Calves

R. G. Breeze, *B.V.M.S., Ph. D., M.R.C.V.S.*
Department of Microbiology and Pathology
Washington State University
Pullman, WA 99164
R. A. Magonigle, *M.S.*
Animal Health Researth Department
Pfizer Inc.
Terre Haute, IN 47808

Introduction

The purpose of this experiment was to compare the therapeutic efficacy of a single intramuscular treatment with a long-acting tetracycline (T-200, Terramycin/LA-200; 200 mg oxytetracycline/ml; Pfizer, Inc., New York, New York) against two treatments with a conventional tetracycline (T-50, Liquamycin 50, 50 mg oxytetracycline/ml; Pfizer Inc.) in an induced *Pasteurella* pneumonia model in calves.

Materials and Methods

Animals

Fourteen Holstein steer calves aged 32-64 days were allocated to 3 groups equally according to body weight 4 days before experimental infection. Group A was 4 control, nonmedicated calves, group B, 5 calves given T-50, and group C, 5 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, rolled oats and calf pellets *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 phospate 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. Thirty, 28, 24 and 8 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, adventitious lung sounds, demeanor, appetite and degree of gauntness were begun 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 scored on a simple grading system and the lungs were weighed. Samples of lung tissue were taken for bacteriological culture.

Serology

A serum sample was taken from each calf before infection and before slaughter on day seven. Samples were submitted to the Washington State Animal Disease Diagnostic Laboratory for examination for viral antibodies.

Treatment

Treatment was initiated 2 hours after challenge, when calves first exhibited a febrile response and marked depression. All medicated groups received treatment at this time. Group B was given T-50 at 5 mg/lb BW and this was repeated at 26 hours. Group C was given one injection of T200 at 9 mg/lb BW.

Results

Clinical Observations

Most of the calves had had an episode of diarrhea in the

period before experimentation. This was overcome by fluid and electrolyte supportive therapy without addition of any antibiotics or chemotherapeutic agent. Several calves had lost weight but all were bright and eating well before experimental infection.

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

Two hours after infection all calves 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 (103-105° F). There was no doubt that a severe response had occurred and so the two treatment groups were given antibiotics.

In group A (nonmedicated control) the clinical signs persisted at about the same level for the first 24 hours postinfection, except for one calf which remained dyspneic and in sternal recumbency until it died at 20 hours. Another calf became very dull at 72 hours and died in respiratory distress about 110 hours after infection. The other two calves gradually improved and had only a mild clinical respiratory disease at slaughter, although coughing was easily induced by exercise.

Group B (T-50 treated) calves were very sick 2 hours postinfection. By 16 hours, however, all were greatly improved. All were seen to take hay, concentrate, milk substitute and water on the morning after infection. Clinical signs were relatively mild at this time time and thereafter. Appetite soon returned to normal.

Group C (T-200) treated) calves were also very sick 2 hours post-infection. By 16 hours, there was no obvious clinical improvement but this was not so marked as in group B. However, all calves ate and drank from 16 hours postinfection and gradually improved each day. By day 2 there was no apparent difference clinically between groups B and C and this remained true through the rest of the study. During the experimental period, the average daily weight gain (lb) and feed consumption/head were: 0.06 and 2.8 in group A, 1.34 and 4.5 in group B, and 1.61 and 4.4 in group C.

Local tissue swelling and pain were noted at the sites of antibiotic injection. These were not severe in any animal and were most obvious in group B.

Pathology

In the control calf which died 20 hours after infection, there was a severe fibrinous pleuritis and pneumonia. Approximately 1 liter of yellow fluid containing fibrin was recovered from the pleural cavity. The left caudal lung lobe and segments in the right caudal and middle lobes were dark red and edematous; smaller subsegmental or lobular foci with a similar appearance were scattered through the rest of the lung. The red areas were clearly "marbled" by interlobular edema macroscopically and histologically had typical changes of an early fibrinous pneumonia. The control calf which died at 110 hours had subsegmental areas of consolidation scattered throughout both lungs. There was less edema and congestion than in the previous control.

Animal	Drug Pretreatment	Time from 3 methylindole dose to death (Hours)	Severity of Main Pulmonary Lesions at Necropsy		
			Edema	Interstitial Emphysema	Alveolar Epithelial Hyperplasia
1	None	30	++++	+++	++
2		94	+++	++	++++
3	Acetylsalicylic acid	65	++++	++	+++
4		94	+	++	++
5	Mepyramine maleate	58	++++	+++	++++
6		96	+	-	+
7	Sodium Meclofenamate	35	++++	+++	++++
8		40	++++	++	++
9	Diethylcarbamazine citrate	14	++++	-	-
10		96	++	++	++
11	Betamethasone	12	++++	-	-
12		96	++	++	+++

Table I. The extent of pulmonary lesions in 12 cattle given a single oral dose of 0.2 g 3 methylindole/kg BW with or without pretreatment with other drugs. (- absent; + mild; ++ moderate; +++ severe; ++++ very severe).

Fibrinous pleuritis was noted over affected areas. *P. multocida* was recovered in pure culture from lung lesions of both calves.

The extent of lung lesions, if any, in the other 12 animals is indicated in Table 1. The lesions were all examined histologically to verify that they were consistent with those of a fibrinous pneumonia and that virus inclusion bodies were absent. No evidence of any pre-existing or other pneumonic condition was found nor did any calf have any other obvious disease condition that could have caused or contributed to death. One calf in group C had a 1 cm diameter tracheal ulcer, apparently at a site of acetic acid injection. *P. multocida* was not recovered from any of the remaining calves in groups A, B, or C.

Serology

Preinfection and post-infection serum samples were negative for antibodies to bovine rotavirus and coronavirus, bovine viral diarrhea, parainfluenza 3, bovine adenovirus and infectious bovine rhinotracheitis. Seven day samples were not obtained from the two control calves which died.

Conclusions

The *P. multocida* endotracheal challenge compounded by the stress procedure produced a severe and sometimes fatal respiratory infection. Treatment with oxytetracycline, instituted at a time when marked clinical signs were clearly apparent, resulted in a dramatic clinical improvement in all treated animals, whereas 2 of the 4 nonmedicated calves died. Calves given conventional oxytetracycline (50 mg/ml) made a more rapid recovery initially but the 2 treatment groups wre similar clinically and pathologically in the later experimental period. Extensive lesions were found in control calves but were generally scattered and mild in treatment groups. The two drugs were equally effective in the therapeutic treatment of induced *Pasteurella* pneumonia but the long-acting formulation has the advantages of less tissue reaction and fewer injections. This should be beneficial in reducing labor, handling and stress in pneumonic animals.

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