Treatment of Bovine Respiratory Disease with Erythromycin and Amoxicillin

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Summary

The sequence of drugs used for the treatment of bovine respiratory disease in feedlot cattle in trials conducted in 1984 and 1985 was erythromycin, amoxicillin, and spectinomycin. If the clinical condition of a steer had not improved after 24 hours the next drug in the sequence was given. The combined response rate to erythromycin and amoxicillin was 82% in 1984 and 87.5% in 1985. Only a single animal died (0.52%) of respiratory disease each year further, indicating a satisfactory response to the antimicrobic treatment regimen.

Antimicrobic susceptibility tests indicated that all strains of *Pasteurella haemolytica* isolated were sensitive to erythromycin. However, the clinical response rate to erythromycin was only 60% in 1984 and 53% in 1985. Susceptibility testing revealed resistance to other approved antimicrobics for use in feedlot cattle, ie., tetracycline, penicillin, streptomycin and sulfonamides, suggesting that clinical response to these drugs would not have been acceptable.

History or prior clinical response of cattle from a given source to treatment combined with antimicrobic susceptibility testing provides a sound basis for establishing a sequence of drugs to be used. The compliance policy guides for extra-label use of new animal drugs in food-producing animals should be meticulously followed when response to treatment is not acceptable.

Even though *P. haemolytica* can only be recovered sporadically from the nares of normal cattle it is considered an important etiologic agent of bovine respiratory disease (BRD).[1] An isolation rate of 78.5% has been reported for *P. haemolytica* from nasal swabs taken from cattle with clinical BRD.[2] Multiple antimicrobial resistance of strains of *P. haemolytica* to common antimicrobials approved for use in feedlot cattle has been reported.[2 3 4 5] Amstutz et al reported 46 of 51 strains of *P. haemolytica* resistant to streptomycin and tetracyclines but only 12 of 51 to sulfonamides.[2] All 25 strains of *P. haemolytica* isolated in a 1982 trial were resistant to sulfonamides and 24 to tetracyclines.[5] Resistance to tylosin has also been reported.[2 7]

Conversely, nearly all of the strains of *P. haemolytica* studied have been found susceptible to antimicrobials not approved for systemic treatment of feedlot cattle, eg. chloramphenicol, gentamicin, or neomycin.[2 4] However, these drugs do not provide an alternative for treatment of BRD. Chloramphenicol has been withdrawn from all veterinary use. Gentamicin and neomycin are both associated with persistent tissue residues, particularly in the kidney, making these drugs unacceptable for the treatment of BRD.

We report on the results of the sequential use of three drugs, erythromycin, amoxicillin, and spectinomycin in the treatment of BRD in trials conducted in 1984 and 1985. The first two antibiotics are approved for use in feedlot cattle. Other antimicrobial drugs approved for use in feedlot cattle were not included in the sequence due to history of resistance of *P. haemolytica* and lack of clinical response in cattle from the same source in prior years. The extra-label use of spectinomycin occurred only in life threatening situations when cattle did not respond to treatment with either of the two approved drugs.

Submitted as Journal Paper # 10,703, Purdue Agriculture Experiment Station, West Lafayette, IN 47907.

Materials and Methods

Cattle were procured through an order buyer from 3 different markets in Kentucky, 192 steers each year. Cattle obtained from this source for several years have had a predictable incidence of BRD in excess of 30%. Histories of place of origin, preconditioning and other health practices were not available.

Processing on arrival at the feedlot included individual identification by ear tag and administration of 2.5 M units of vitamin A IM, a 7-way clostridial bacterin-toxoid,

intranasal infectious bovine rhinotracheitis vaccine, intramuscular bovine virus diarrhea - parainfluenza 3 vaccine, a bovine respiratory syncytial virus vaccine, a *Haemophilus somnus* bacterin, a 5-way leptospiral bacterin, and 0.22 mg/kg ivermectin.

The receiving ration was good quality mixed orchard grass-alfalfa hay to appetite plus 0.45 kg/head each of cracked corn and natural protein supplement. Seven days post-processing the hay was top dressed with corn silage. The amount of silage was increased incrementally and the hay decreasd over a 4 day period. The ration for the duration of the trials was corn silage to appetite plus 1 kg corn and 0.7 kg supplement per head per day.

During daily observation, any cattle with clinical signs of BRD were restrained and evaluated to determine if treatment was indicated. The arbitrary rectal temperature of 40°C or greater was not the sole criterion for the initiation of therapy. Rectal temperature plus signs of loss of herding instinct, rear leg weakness, shallow and rapid respirations, frequent cleaning of the muzzle and somnolence were the criteria used to determine if antibiotic therapy was indicated. A sequence of three antibiotics was followed depending on the response of the animals to treatment. First, erythromycin at 13 mg/kg IM was given once daily until the rectal temperature was less than 39.5°C for 2 days, as well as marked clinical improvement. If the clinical condition of a steer had not improved after 24 hours the second drug, amoxicillin 11 mg/kg IM was given. The steers that did not respond to treatment with amoxicillin were subsequently treated with spectinomycin, 11 mg/kg IM.

Sterile swabs thrust deeply into the nares at the time of the initial treatment of BRD provided specimens for isolation and identification of pasteurellae. Isolates of *P. haemolytica* were analyzed for antimicrobic susceptibility by the disc diffusion method using Mueller-Hinton agar plates supplemented with 5% sheep blood and standard assay procedures.[8]

Results

The incidence of BRD was 40.6% (78/192) in 1984 and 37.5% (72/192) in 1985. Seven steers in 1984 and 12 in 1985 that responded initially, relapsed and required a second course of treatment. The average number of days of treatment per animal was 4.1 in 1984 and 4.8 in 1985. One steer died due to pasteurella pneumonia during each trial. During the 1984 trial 60% (47/78) of the cases of clinical BRD responded to treatment with erythromycin. Sixteen of 31 (52%) that did not respond to erythromycin responded to amoxicillin therapy. Fourteen subsequently responded to spectinomycin. Thirty eight of 72 (53%) responded to erythromycin in the 1985 trial. Of the 34 subsequently treated with amoxicillin 25 (74%) responded and nine required treatment with spectinomycin.

Twenty seven of the 31 strains of *P. haemolytica* isolated in 1984 were serotype 1 and 4 serotype 2. Serotyping of the 35 strains isolated in 1985 identified 34 serotype 1 and only 1 serotype 2. The level of resistance of the strains to both ampicillin and penicillin was the same each year, 87% in 1984 and 60% in 1985. The resistance to other antimicrobials approved for use in feedlot cattle for 1984 and 1985 was: erythromycin 0 for both years, streptomycin 97% and 83%, triple sulfonamides 52% and 94%, and tetracyclines 74% and 91% respectively. (Table 1)

TABLE 1 - In vitro susceptibility of bovine strains of *Pasteurella haemolytica* to antimicrobics approved for feedlot cattle

Year isolated	Number of strains	Antimicrobics					
		pen	amp	strep	tet	sulfa	eryth
1984	31	4*	4	1	8	15	31
1985	35	14	14	6	3	2	35

* Number susceptible

Discussion

Effective treatment of BRD depends on using criteria that discriminate between normal and affected cattle early in the course of the disease. The clinical signs listed above identify BRD early. The frequently listed clinical signs of labored breathing, encrusted muzzle, gaunt and depressed decribe the animal that has had clinical BRD for 24 to 48 hours. If treatment is not initiated until these signs are apparent the response is frequently poor.

Success of treatment also depends on selecting antimicrobials effective against the major pathogenic bacteria involved. The susceptibility or resistance of a given bacterial population influences the response to therapy. The in vitro sensitivity of bacteria isolated during an outbreak of BRD provides a basis for selecting effective antimicrobials. However, in vitro resistance does not necessarily predict results of treatment. During a 1982 trial 96% of *P. haemolytica* isolates were resistant to tetracycline but 13 of 49 (26.5%) of the animals treated with oxytetracycline responded clinically to therapy.[6]

A sequence of drugs should be established and adhered to when antimicrobial resistance is anticipated or encountered. The decision to shift to the next drug in the sequence should be made on the lack of clinical improvement and/or a decline in rectal temperature at the end of 24 hours. The first drugs in the sequence should be those approved for use in feedlot cattle. Prior experience with cattle from a given source or antimicrobic susceptibility test results on isolates from the first cases of BRD in a group of cattle can identify patterns of antimicrobial resistance. This provides a sound medical basis to exclude some approved drugs when establishing a sequence of treatment. Prior years experience with in vitro resistance and lack of clinical response to treatment of BRD in cattle from the same order buyer provided the basis for not including tetracyclines or

sulfonamides in these trials.

The compliance policy guides of the Center for Veterinary Medicine for the extra-label use of new animal drugs in food producing animals must also be considered in the selection of drugs and doses. The guide states that: 1) a careful diagnosis has been made within the context of a valid veterinarian-client-patient relationship, 2) therapy with a given drug or dose is clinically ineffective, 3) the identity of animals can be maintained and 4) an extended time period for drug withdrawal is established prior to marketing to assure that no illegal residues occur. Records of any such treatment must be maintained.[9]

The rate of response to either erythromycin, 60% and 53% or amoxicillin, 52% and 74% respectively for 1984 and 1985 could be considered unacceptable. However, the combined response rate was 82% in 1984 and 87.5% in 1985. Only a single animal died each year, a rate of 0.52%, an indication of a satisfactory response to treatment of BRD. The average of 4.12 days on treatment per steer on 1984 and 4.8 days in 1985 reflects the clinical nonresponsiveness to the approved drugs. Few, if any, animals that have not responded within 24 hours to antibiotic therapy, will respond if treatment with the same antibiotic is continued. The duration of treatment would have averaged 4.7 days if the decision to shift from erythromycin to amoxicillin has been made at 48 hours rather than 24 requiring an additional 45.6 days of treatment. The cost of treatment would have been increased $205.00 basd on an average drug cost of $2.00 and a chute cost of $2.50 per head.

Antimicrobic susceptibility tests indicated that all strains of *P. haemolytica* were sensitive to erythromycin. Treatment of BRD with erythromycin did not bear this out with clinical response rates of 60% and 53%. The discrepancies between the susceptibility testing and clinical response could be multifactorial. The MIC breakpoint selected for determining susceptibility and resistance may not reflect the pharmacokinetics of erythromycin in cattle with BRD. Strains of *P. haemolytica* of known clinical responsiveness to a dose of 13 mg/kg of erythromycin have not been tested to determine the MIC breakpoint for susceptibility and resistance. The breakpoint is extrapolated from the MIC established for bacteria of other genera isolated from man. The colonies selected for the inoculum may not have included the more resistant strains. However, the resistance patterns and clinical response to the tetracyclines and sulfonamides were very similar in prior years. Further studies with strains of *P. haemolytica* of known clinical responsiveness are necessary to clarify apparent discrepancies between in vitro antimicrobic susceptibility and clinical response in cattle treated for BRD.

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