Sodium Bicarbonate Does Not Prevent Acute Bovine Pulmonary Edema and Emphysema

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Some ranchers, researchers and veterinarians in the western USA believe that sodium bicarbonate is an effective preventative for acute bovine pulmonary edema and emphysema (ABPE). This belief may arise in part from the fact that sodium bicarbonate is a widely used ruminal buffering agent, and that 3-methyl-indole (3MI), the pneumotoxic fermentation product of tryptophan (TRP) is formed in the rumen from indoleacetic acid (IAA), by a *Lactobacillus sp.* (9). Even though *Lactobacillus* organisms can often grow at a lower pH than many other bacteria, the formation of 3MI involves at least 2 types of organisms (8). The first step is the degradation of TRP to IAA which can be accomplished by a variety of ruminal organisms, and the second step is decarboxylation of IAA to 3MI by the *Lactobacillus sp. In-vitro* studies with ruminal fluid have shown that maximum conversion of TRP to 3MI occurs at pH 6.5-7.0, and that conversion is markedly reduced below pH 6.5 (7). *In-vitro* conversion of TRP to 3MI and actual ruminal 3MI concentrations after an oral dose of TRP are also lower in cattle consuming concentrate diets (Ruminal pH 5.0-6.0) than in cattle consuming hay diets (ruminal pH 6.5-7.0) (Kowalczyk and Carlson, *unpublished data*). Ruminal buffering agents such as sodium bicarbonate are usually used to increase ruminal pH in cattle fed concentrate rations (6).

These findings suggest that sodium bicarbonate may not be effective in reducing 3MI production and the incidence of APBE. Since there is no published data available, we tested the effectiveness of sodium bicarbonate in preventing ABPE. We have found that monensin will prevent tryptophan-induced ABPE by reducing ruminal formation of 3-methylindole (3, 4). But, monensin is not presently approved by the Food and Drug Administration (FDA) for use in brood cows, the animals most likely to develop ABPE. If sodium bicarbonate could prevent the disease, ranchers would have a readily-available, cheap preventative which would not require FDA approval.

Materials and Methods

Animals

Four Hereford heifers, 6-8 months old, were used in pairs in a switch-back design. Four calves were fed chopped hay (group 1) and 8 calves were fed chopped hay containing 4% $NaHCO_3$ for 2 weeks, followed by an oral dose of TRP (0.35 g L-TRP/kg body weight) in gelatin capsules. $NaHCO_3$ administration was continued in the feed at 4% of dry matter (group 2) or an an equivalent daily oral dose in gelatin capsules (group 3) after TRP dosing.

Samples of ruminal fluid were taken from all calves at the beginning of the experiment and after 2 weeks of hay or of hay and $NaHCO_3$ pretreatment. These samples were incubated *in vitro* with TRP to determine the capacity of ruminal microflora to form 3MI and indole (3, 4). Ruminal fluid samples were also taken at 0, 6, 12, 24, 48, 72, and 96 hours after TRP dosage and analyzed for pH, 3MI and indole (1). Clinical signs were monitored twice daily for 96 hours after TRP dosage.

Statistical analysis was by student's "t" test.

Results

Ruminal fluid analysis

Ruminal 3MI levels in the three groups are given in Figure 1 and Table 1. There were no significant differences ($P > 0.05$) in ruminal 3MI levels between groups 1 and 2 at any sampling time. Peak ruminal 3MI concentrations ranged from 85-143 μg/ml in both groups. Between 6 and 24 hours, ruminal 3MI was significantly lower ($P < 0.05$) in group 3 than in group 1, but levels were still high enough to cause lung disease in each group.

Ruminal indole concentrations in all groups peaked at 8-11 μg/ml at 6 hours and then fell below the limits of detection by 48 hours.

Ruminal pH was variable and ranged from 6.8 to 7.3 at the time of the TRP dose (Figure 2). Except for a slight decrease in pH to 6.5-6.6 at 12-18 hr, most values ranged rom 6.9 to 7.3 for the duration of the experiment. There were no significant differences ($P > 0.05$) in ruminal pH among the groups.

$NaHCO_3$ had no effect ($P > 0.05$) on *in vitro* conversion of TRP to 3MI or indole by ruminal fluid taken at the beginning and end of the pretreatment period (Figure 3).

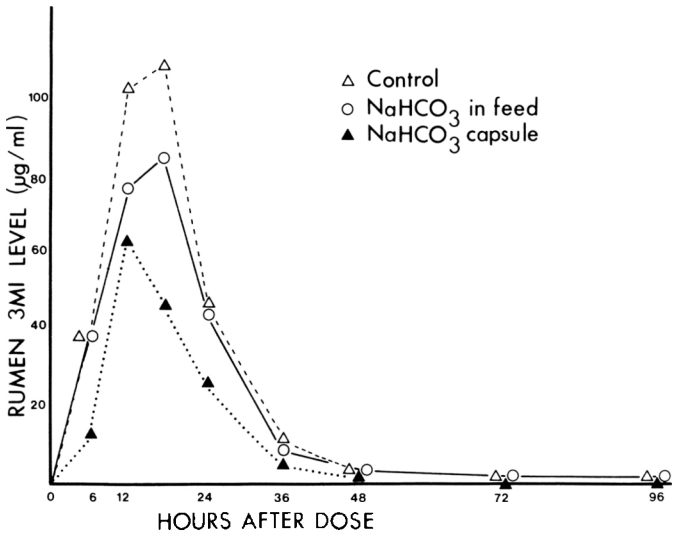

Figure 1. Ruminal 3-methylindole levels in calves given an oral dose of 0.35 g L-tryptophan/kg body weight after no pretreatment or with a supplement of 4% sodium bicarbonate in the feed or by daily capsule.

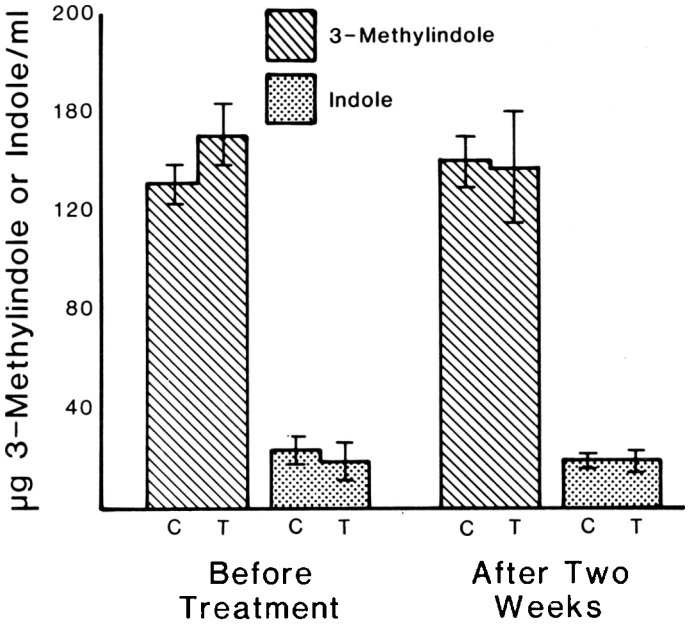

Figure 2. Formation of 3-methylindole and indole by *in vitro* incubation of L-tryptophan with ruminal fluid from calves before and after two week of feeding on hay (control, C) or on hay containing sodium bicarbonate (test, T). Bars are ± SEM.

Table One

TREATMENT GROUP AND ANIMAL		RUMINAL 3-METHYLINDOLE CONCENTRATION AFTER TRYPTOPHAN DOSING								
		Hours after tryptophan dose								
		0	6	12	18	24	36	48	72	96
		(3-methylindole, ug/ml)								
(1)	1	2.7	59.1	138.0	143.4	85.2	8.4	3.1	0.8	1.9
Control	2	1.1	47.0	123.5	119.2	47.9	9.3	2.6	0.5	0.5
	3	0.6	18.7	92.0	81.3	25.1	10.1	6.2	2.0	NS[1]
	4	1.3	36.1	50.0	96.7	49.6	13.5	6.3	2.6	NS
Mean ± SEM		1.4 ± .5	40.3[a,2] ± 8.6	103.4[b] ± 17.4	110.9[c] ± 14.2	44.5[d] ±13.1	10.3 ± 1.1	4.6 ± 1.0	1.5 ± .5	1.2 ± .7
(2)	5	1.8	56.6	85.8	58.7	22.7	2.5	0.7	0.5	0.8
$NaCHO_3$	6	2.9	73.5	72.2	56.4	46.3	2.6	0.7	0	1.5
in	7	0.4	9.7	68.7	96.5	37.6	3.0	1.7	0.9	NS
feed	8	0.6	19.7	78.0	132.0	76.8	22.6	6.4	2.4	NS
Mean ± SEM		1.4 ±0.6	39.9 ±15.1	76.2 ± 3.7	85.9 ± 17.9	45.8 ±11.4	7.7 ± 5.0	2.4 ± 1.4	0.95 ± 0.6	1.6 ±0.4
(3)	9	0.58	19.3	82.1	33.4	27.9	8.1	0	0.8	3.5
$NaCHO_3$	10	0	13.3	67.4	30.5	10.3	1.4	0	0	1.4
by	11	1.0	6.8	47.8	45.9	9.8	1.1	0.6	1.0	0.6
capsule	12	0	11.8	62.3	79.6	62.5	16.2	13.8	0.6	0
Mean ± SEM		0.4 ±0.2	12.8[a] ± 2.6	64.9[b] ± 7.1	47.3[c] ± 11.2	27.6[d] ±12.4	6.7 ± 3.6	3.6 ± 3.4	0.6 ±0.2	1.4 ±0.8

[1]NS - not sampled, calf too sick.

[2]Means with same superscripts are significantly different ($P<0.05$).

Ruminal 3-methylindole levels in control calves fed hay (group 1), test calves fed hay containing 4% sodium bicarbonate (group 2), or test calves fed hay and given the 4% bicarbonate supplement in gelatin capsules (group 3).

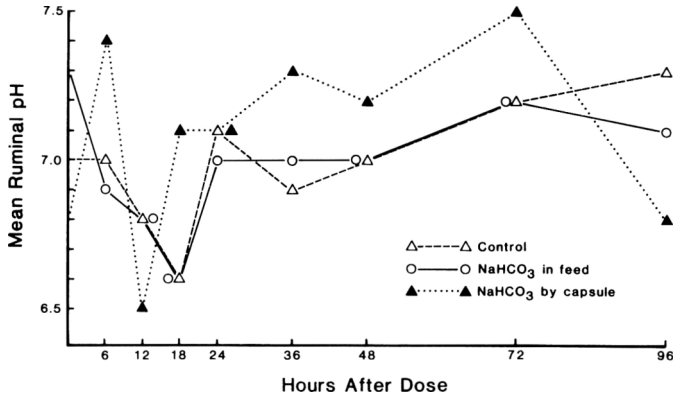

Figure 3. Effect of sodium bicarbonate on ruminal pH in calves after a tryptophan dose.

Clinical Signs

Calves in all three groups developed clinical signs of ABPE, including increased rate and depth of breathing, labored breathing and expiratory grunt. The first signs were noticed 12 to 18 hours after dosing. Three of the control calves became very sick -- two were so severe that ruminal incubation was not attempted at 96 hours in case the animals should die. One calf in group 2 was mildly affected, but two others were severely ill and were not sampled at 96 hours. All the calves in group 3 became sick, one mildly, two moderately, and one severely.

All calves that were severely ill assumed sternal recumbency and showed a marked expiratory grunt and labored breathing. These were all given furosemide (0.5-1.0 mg/kg intravenously b.i.d.) from 48 to 96 hours, during which period they ate and drank very little. After 96 hours, furosemide was discontinued and the animals were rehydrated. Administration of furosemide did not appear to influence the clinical course. Clinical signs gradually abated over the next 7 days, without further treatment other than close confinement and hand feeding.

Discussion

The results of this study demonstrate that sodium bicarbonate is not an effective prophylactic agent for ABPE, even when given at the high level of 4% dry matter intake for 2 weeks before TRP challenge.

The animals of group 2, especially those severely ill, did not eat all of their allotted feed after TRP dosage, and this might explain the failure of sodium bicarbonate to protect against ABPE. However, the apparent reason for the reduced appetite was the developing respiratory signs of ABPE, as noted also in the control group. The clinical signs in group 2 were not preceded by a period of reduced feed and sodium bicarbonate intake. Rather, the failure of the treatment regimes to prevent 3MI production was responsible for development of a severe clinical episode of ABPE, during which eating took second place to breathing. To confirm this, and to get around the problem of lowered feed consumption, the bicarbonate supplementation was continued by gelatin capsule after TRP dosage in group 3. Ruminal 3MI levels were significantly lower in this group than in the controls between 6 and 24 hours, indicating that sodium bicarbonate can have a suppressive effect on ruminal 3MI production. However, this effect was not sufficient to prevent clinical signs, which were seen in all the animals. It is unlikely that bicarbonate intake could feasibly be increased beyond 4% of dry matter, and daily oral bolus administration is quite impractical under range conditions. Since it appears pointless to incorporate bicarbonate into feed, we conclude there is no value in this form of ABPE prevention.

At the present time, there is no alternative to good herd management and monensin supplementation in the prevention of ABPE. Herd management should include procedures to reduce consumption of lush forage immediately after pasture change. Examples would be minimizing the difference between pastures during grazing transition, feed hay prior to pasture change, or supplementary feeding during the first few days after pasture change. We have been investigating various means to deliver monensin at about 200 mg/head/day in the critical days just before and just after pasture change. Cattle will accept monensin in pelleted feed supplements, in range blocks or in salt, provided they become familiar with the forms of supplementation before pasture change. On our experimental pasture, we supplement with monensin from the day before to about 10 days after pasture change. We *do not recommend* supplementation with monensin for a longer period *before* each pasture change, since it is not yet clear how long the suppressive effect on 3MI production lasts. Our preliminary data indicate this may not be longer than two weeks each occasion monensin is added to the diet. We should also point out that our field experiments are designed to *increase* the likelihood of ABPE occurring in test animals and so both cattle and pastures are managed in a manner calculated to precipitate disease. We have stressed previously (2) the importance of herd and pasture management in helping to limit losses from ABPE in the field. Monensin supplementation should be considered part of an overall prevention strategy, along with management schemes developed by the individual rancher and his local veterinarian.

Acknowledgments

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of Agriculture (project 901-15-169). Scientific paper no. 5978, Agricultural Experiment Station, Washington State University, Pullman, WA 99164.

References

1. Bradley, B. J. and J. R. Carlson. A gas-liquid chromatographic procedure for the determination of indole and 3-methylindole in bovine plasma. Anal. Biochem. 59:214 (1974). - 2. Breeze, R. G. and J. R. Carlson. Acute bovine pulmonary emphysema. *In* "Current Veterinary Therapy, Food Animal Practice" (editor J. L. Howard), pp. 832-835. W. B. Saunders, Philadelphia (1980). - 3. Hammond, A. C., J. R. Carlson and R. G. Breeze. Monensin and the prevention of tryptophan-induced acute bovine pulmonary edema and emphysema. Science. 201:153 (1978). - 4. Hammond, A. C., J. R. Carlson. Inhibition of ruminal degradation of L-tryptophan to 3-methylindole, *in vitro* J. Anim. Sci. 51:207 (1980). - 5. Hammond, A. C., J. R. Carlson and R. G. Breeze. Prevention of tryptophan-induced acute bovine pulmonary edema and emphysema (fog fever). Vet. Rec. 107:322 (1980). - 6. Weinberg, M. S., and A. L. Sheffner, Editors. *Buffers in Ruminant Physiology and Metabolism,* Church and Dwight Co., Inc., New York, NY (1976). - 7. Wong, L. P. Factors affecting three-methylindole production by *Lactobacillus sp.* from the rumen. M. S. Thesis, Washington State University, (1979). - 8. Yokoyama, M. T. and J. R. Carlson. Dissimilation of tryptophan and related indolic compounds by ruminal microorganisms, *in vitro.* Appl. Microbiol. 27:540 (1974). -9. Yokoyama, M. T., J. R. Carlson and L. V. Holdeman. Isolation and characterization of a skatole-producing *Lactobacillus sp.* from the bovine rumen. Appl. Environ. Microbiol. 34:837 (1977).