Effects of Lasalocid on Selected Ruminal and Blood Metabolites in Young Calves

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ABSTRACT

Twelve Holstein bull calves were ruminally cannulated at 5 d of age and assigned to 0 or 1 mg of lasalocid/kg of BW daily, administered postruminally via milk replacer or into the ruminal cannula. Calves were fed milk replacer for 8 wk and calf starter for 12 wk. Lasalocid administration was terminated at weaning in calves fed lasalocid in milk replacer. Ruminal pH tended to be higher in calves fed lasalocid ruminally than in calves on control treatment and averaged 5.9 and 5.6 and 5.4 and 5.1 during wk 1 to 8 and 9 to 12, respectively. Molar proportion of ruminal butyrate tended to be lower when lasalocid was added to the rumen, particularly after weaning. Blood β-hydroxybutyrate and acetoacetate were lower when lasalocid was administered into the rumen after weaning and averaged .897 and .646 and .026 and .015 m*M* in calves on control and ruminal treatments, respectively. No effects of lasalocid administered via the milk replacer were observed, except for plasma NEFA, which were reduced postweaning. These data suggest that lasalocid reduces blood β-hydroxybutyrate by changes in ruminal fermentation and subsequent metabolism of butyrate by ruminal epithelium.

(**Key words**: calves, lasalocid, ketones, ruminal development)

Abbreviation key: **ACAC** = acetoacetate, **ADG** = average daily gain, **BHBA** = β-hydroxybutyrate, **MR** = lasalocid administered via milk replacer, **RC** = lasalocid administered via ruminal cannula.

INTRODUCTION

Development of ruminal function typically has been characterized by increased size of the reticulorumen (26), metabolic activity of ruminal epithelium (25), and concentration of fermentative end products in the rumen (1, 2) and in blood (15, 17, 19). Recently, we (16) reported rapid increases in concentrations of blood β-hydroxybutyrate (**BHBA**) and acetoacetate (**ACAC**) with weaning and increasing starter intake in young calves sampled 2 h after feeding. By 12 wk of the study, concentration of blood ketones exceeded 1.0 m*M*, a level typical of subclinical ketosis in mature cattle. The high correlation between starter intake and blood BHBA (r = .71) suggested that much of the increase in ketones resulted from alimentary ketogenesis; however, no data were collected to document changes in the rumen associated with increasing DMI and blood ketones.

Monensin reduced the concentration of ketones in blood of lactating dairy cows (21), possibly by increased production of ruminal propionate (3, 14, 20, 27), which, in turn, provided gluconeogenic precursors and might have reduced hepatic ketogenesis. Also, ionophores may alter the site of starch digestion, which may increase absorption of glucose (23) or possibly alter gut usage of propionate, thereby sparing glucose (8).

Most data suggest that responses to ionophores are mediated through alteration of ruminal fermentation; however, Armstrong and Spears (4) reported changes in concentration of blood metabolites in response to intravenous infusion of monensin. Ilan et al. (11) reported

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that monensin fed to young calves in milk replacer (to bypass the rumen) or added directly to the rumen improved DM digestibility slightly and altered fecal excretion of digestive enzymes. Anderson et al. (2) also suggested that effects of ionophores may be, in part, mediated through a postruminal response, including reduced numbers of intestinal coccidia.

The objective of this study was to determine the effects of lasalocid on concentrations of blood ketones and other selected blood metabolites in calves and to determine the relationship between blood ketones and ruminal VFA profiles.

MATERIALS AND METHODS

Calf Assignment and Feed Management

Twelve Holstein bull calves were equipped surgically with ruminal cannulas at 5 d (SE = .5) of age and housed individually in 1.8-m^2 pens bedded with shavings. Calves were assigned to treatment in a completely randomized experimental design for a 12-wk study after 3 d of recuperation from surgery. Treatments were lasalocid sodium (Hoffman-LaRoche, Inc., Nutley, NJ) at 0 (control) or 1 mg/kg of BW daily added to milk replacer (**MR**) or administered to the rumen via ruminal cannula (**RC**). Lasalocid dosage was based on BW of the previous week and was administered twice daily in equal doses during a.m. and p.m. feeding. Addition to the rumen was accomplished by mixing lasalocid (calcium carbonate carrier) with distilled water. The water-lasalocid suspension was injected into the ruminal cannula immediately after mixing. After calves were weaned (8 wk of the study), lasalocid was not fed to calves on MR treatment.

Calves were fed 1.8 kg of commercial milk replacer that contained 13% solids twice daily (approximately 0800 and 1630 h) from nipple bottles until weaning. Calves were offered a pelleted calf starter (Table 1) once daily (0800 h) for ad libitum consumption to a maximum of 4.5 kg/d. Starter was sampled once per shipment and analyzed for DM, CP, ether extract (5), ADF, NDF (7), and minerals.

TABLE 1. Ingredient composition of experimental calf starter.

Item	(% as fed)
Corn, ground	20.0
48% CP soybean meal	7.5
Soybean hulls	20.0
Wheat middlings	25.0
Cottonseed hulls	7.5
Cottonseed meal	5.8
Alfalfa meal	5.0
Molasses	3.0
Vitamins plus minerals[1,2]	6.2

[1]Including bentonite, limestone, binder, dicalcium phosphate, salt, and vitamin and mineral premix.

[2]To provide (minimum): 2200 IU/kg of vitamin A, 300 IU/kg of vitamin D, 25 IU/kg of vitamin E, 50 ppm of Fe, .10 ppm of Co, 10 ppm of Cu, 40 ppm of Mn, 40 ppm of Zn, .25 ppm of I, and .20 ppm of Se.

Sampling and Analysis

Blood was obtained once weekly by jugular venipuncture into evacuated tubes approximately 2 h after a.m. feeding. A 2-ml subsample was deproteinated immediately by addition to 2 ml of 1 *M* perchloric acid. Remaining blood was added to anticoagulant, placed on ice, and transported to the laboratory. Plasma was harvested by centrifugation (3000 × *g*) and stored (–20°C) prior to analysis for glucose, NEFA, plasma urea N (16), and VFA (17). Deproteinated blood was centrifuged, and supernatant liquid was analyzed for BHBA and ACAC (28). A second blood sample was collected and allowed to coagulate at room temperature. Serum was separated by centrifugation and stored (–20°C) prior to analysis of Ca, Mg, K, and Na (atomic absorbance spectrophotometry).

Approximately 40 ml of ruminal fluid were collected immediately after blood collection via vacuum pump from the ruminal cannula. Ruminal pH was measured immediately, and the sample was frozen quickly in liquid N. Sample was placed on ice, transported to the laboratory, and stored (–20°C) until analyzed for VFA (18) and NH_3 N (Sigma 640 kit; Sigma Chemical Co., St. Louis, MO).

Statistical Analyses

Data (except intake of DM and nutrients) were analyzed according to analysis of covariance as a split-plot experimental design using a general linear mixed model algorithm (6).

TABLE 2. Chemical composition of feeds.

Item	Calf starter[1]		Milk replacer[2]	
	$\bar{X}$	SD	$\bar{X}$	SD
DM, %	89.4	.6	92.0	3.1
	(% of DM)			
CP	20.0	1.5	22.3	.3
NDF	35.7	1.0	.0	
Ether extract	3.8	.8	7.7	1.3
	(mg/g of DM)			
Ca	8.9	.7	10.2	.7
P	6.4	.4	10.3	.4
Mg	3.5	.5	1.9	.1
K	12.1	1.6	33.1	1.2
Na	4.1	.7	19.6	.8

[1]n = 6.

[2]n = 4.

However, because treatment application changed during the study (i.e., calves on MR treatment did not receive lasalocid after weaning), analyses were conducted by period: preweaning (1 to 8 wk) and postweaning (9 to 12 wk). Random effect in the model was animal within treatment, which was used as whole-plot error. Variance components were estimated using LaMotte or EMREML procedures (6). Weekly starter intake was included in the model as a covariable to remove variation associated with dry feed intake. Single degree of freedom contrasts compared MR and RC treatments with control. Significance was declared at $P < .05$ unless otherwise noted.

RESULTS AND DISCUSSION

All calves were generally healthy throughout the study. Three cases of bloat (control) and one incidence of noncoccidial scours (control) were observed during the study. Two calves were removed during the last 2 wk of the study because of management factors unrelated to treatment.

Chemical composition of experimental starter (Table 2) was consistent with starters fed as the sole dry feed to young calves. Starter contained high fiber by-products (cottonseed and soybean hulls) to stimulate ruminal development. Composition of milk replacer was slightly lower in fat than expected but otherwise corresponded to recommended nutrient composition (13). Intake of DM and nutrients (Table 3) increased during the study ($P < .01$) but were unaffected by treatment. During the last 2 wk of the study, only two calves consumed 4.5 kg/d of starter, the maximum allowed throughout the study. Intake of CP and TDN generally exceeded NRC recommendations (13) for calves of this age, which resulted in acceptable rates of average daily gain (ADG). Small amounts of coagulated milk occasionally were observed in samples of ruminal fluid from calves on all treatments prior to weaning, indicating some backflow of milk into the rumen or incomplete esophageal groove closure. Therefore, some lasalocid given to calves on MR treatment probably did not bypass the rumen completely.

Covariately adjusted least squares means of BW and ADG (Table 3) compared favorably with growth rates of intact calves (15, 16),

TABLE 3. Least squares means of BW, average daily gain (ADG), intake, and feed efficiency in calves fed 0 (control) or 1 mg of lasalocid/kg of BW daily in milk replacer (MR) or via ruminal cannula (RC) during 1 to 8 wk (preweaning) or 9 to 12 wk (postweaning).

Item	Treatment			SE
	Control	MR	RC	
BW,[1] kg				
Preweaning[a]	55.5	53.7	52.6	2.7
Postweaning[a]	93.8	88.8	84.0	6.9
ADG,[1] kg				
Preweaning[a]	.53	.51	.62	.07
Postweaning	.89	.92	1.00	.10
DMI, kg/d				
Preweaning[a]	1.36	1.32	1.04	.14
Postweaning[a]	3.13	2.68	2.68	.26
CP Intake, kg/d				
Preweaning[a]	.293	.286	.231	.028
Postweaning[a]	.618	.530	.530	.052
NDF Intake, kg/d				
Preweaning[a]	.35	.34	.24	.05
Postweaning[a]	1.10	.94	.95	.09
TDN Intake,[2] kg/d				
Preweaning[a]	1.26	1.24	1.01	.11
Postweaning[a]	2.50	2.14	2.15	.21
Gain:feed[1]				
Preweaning	.380	.349	.413	.100
Postweaning	.310	.309	.347	.043

[a]Significant week effect ($P < .05$).

[1]Adjusted for weekly starter intake by analysis of covariance.

[2]Predicted from NRC (13).

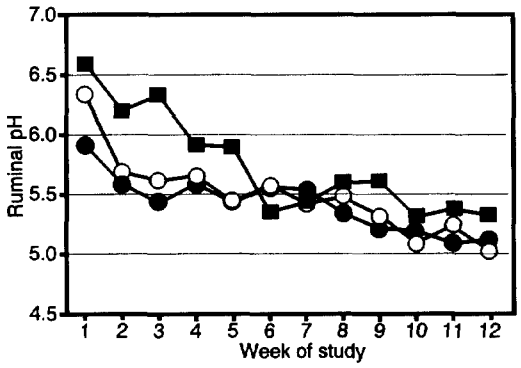

Figure 1. Least squares means of ruminal pH in calves administered 0 (●) or 1 mg of lasalocid/kg of BW daily in milk replacer (○) or into ruminal cannula (■). SE = .17.

indicating that cannulation had little effect on normal growth. However, ADG was low during the first few weeks, which is attributable to stress of cannulation. No effects of treatment on BW, ADG, or feed efficiency were observed.

Ruminal pH (Figure 1) fell from near neutrality during the early weeks of study to approximately 5 by the last 4 wk. Clearly, rapid ruminal fermentation of ingested calf starter caused the low ruminal pH. Ruminal pH tended to be greater when lasalocid was administered ruminally during wk 1 to 8 and 9 to 12 (Table 4; $P < .10$). Higher pH suggests an inhibition of ruminal bacteria by lasalocid during the first few weeks of life, as reported by Anderson et al. (2). Also Schelling (22) suggested that ruminal pH was higher with monensin both in vivo and in vitro, which may be attributed to depression in lactate production at low pH. Although not measured in this study, lasalocid also may have inhibited lactate production, thereby reducing the postprandial pH depression.

Ruminal VFA increased with increasing starter intake during the preweaning period (Table 4). After weaning, increases in VFA were not significant, although DMI continued to increase. Peak VFA concentration reached 188 m*M*, which is indicative of rapid fermentation by ruminal bacteria immediately after feeding. Molar proportions of individual VFA were unaffected by treatment except for butyrate, which tended to be lower in calves on RC treatment during the postweaning period ($P < .10$). Acetate to propionate ratio tended to be reduced during the preweaning period ($P < .10$) in calves on RC treatment also. Low acetate to propionate ratio (less than 2) generally reflects intake of high grain diets by young calves (1, 2). Previous reports (14, 27)

TABLE 4. Least squares means[1] of ruminal pH, NH_3 N, and VFA in calves fed 0 (control) or 1 mg of lasalocid/kg of BW daily in milk replacer (MR) or via ruminal cannula (RC) from 1 to 8 wk (preweaning) or 9 to 12 wk (postweaning).

	Treatment			
Item	Control	MR	RC	SE
pH				
Preweaning[a]	5.55	5.65	5.91[b]	.12
Postweaning[a]	5.10	5.18	5.42[b]	.12
NH_3 N, mg/dl				
Preweaning	14.9	13.1	15.0	2.2
Postweaning	18.2	15.7	21.4	4.2
VFA, m*M*				
Preweaning[a]	133.2	124.4	120.4	15.9
Postweaning	178.7	178.7	187.7	17.2
Acetate, mol/100 mol				
Preweaning	54.1	56.2	52.7	1.5
Postweaning	48.4	51.7	48.6	2.0
Propionate, mol/100 mol				
Preweaning	29.0	29.2	32.4	1.7
Postweaning	33.3	31.6	37.1	1.9
Butyrate, mol/100 mol				
Preweaning	13.2	11.3	10.8	1.9
Postweaning	12.8	11.7	9.7[b]	1.1
Isobutyrate, mol/100 mol				
Preweaning	.1	.1	.3	.1
Postweaning	.1	0	.1	.1
Isovalerate, mol/100 mol				
Preweaning	.5	.5	.6	.2
Postweaning	.4	.2	.5	.1
Valerate, mol/100 mol				
Preweaning	3.2	3.0	2.9	.5
Postweaning	4.8	4.8	4.1	.4
Acetate:propionate				
Preweaning	2.02	2.10	1.70[b]	.16
Postweaning	1.52	1.72	1.32	.16

[a]Significant week effect ($P < .05$).

[b]Mean differs from control ($P < .10$).

[1]Adjusted for weekly starter intake by analysis of covariance.

have shown that ionophores increase concentration of ruminal propionate at the expense of acetate and butyrate. Rates of VFA production, however, have been less well documented. Rogers and Davis (20) reported no significant effect of monensin on ruminal butyrate production when using isotope dilution procedures, but molar proportion was reduced from 11.0 to 8.7%. Production of butyrate averaged .41 and .37 mol/d for each kilogram of DMI consumed by steers fed control and monensin diets, respectively. However, DMI was reduced by addition of monensin, which increased ruminal retention and altered total VFA production rates. Conversely, Armentano and Young (3) reported increased ruminal butyrate (and propionate) production and decreased acetate production in steers fed monensin. Data from animals with multiple catheters (8, 9, 10) indicated no significant effect of ionophores on net portal flux of BHBA. In all studies, cattle were fed 12 times daily to minimize effects of feeding.

Administration of lasalocid in calves on RC treatment caused nonsignificant increases in molar proportion of propionate both preweaning and postweaning. The generally small response to ionophores in young, preruminant calves may be attributed to incomplete development of ruminal function (11). Anderson et al. (2) reported small but significant increases in ruminal propionate and decreases in acetate with lasalocid feeding, and Marounek et al. (12) reported a reduction in molar proportion of butyrate in young calves fed monensin.

Concentration of ruminal NH_3 N (Table 4) was unaffected by lasalocid administration and averaged 14.3 and 18.4 mg/dl at wk 1 to 8 and 9 to 12, respectively. Elevated NH_3 N concentration resulted from rapid degradability of protein sources (soybean meal and wheat middlings) used in the formulation (Table 1).

TABLE 5. Least squares means[1] of selected blood metabolites in calves fed 0 (control) or 1 mg of lasalocid/kg of BW daily in milk replacer (MR) or via ruminal cannula (RC) during 1 to 8 wk (preweaning) or 9 to 12 wk (postweaning).

Item	Treatment			SE
	Control	MR	RC	
β-Hydroxybutyrate, m*M*				
Preweaning[a]	.356	.311	.314	.047
Postweaning	.897	1.011	.646[b]	.072
Acetoacetate, m*M*				
Preweaning	.009	.010	.010	.002
Postweaning	.026	.024	.015[c]	.003
NEFA, m*M*				
Preweaning	.158	.159	.151	.013
Postweaning	.133	.088[c]	.101[c]	.008
Glucose, m*M*				
Preweaning[a]	5.09	4.85	5.10	.18
Postweaning	4.75	4.57	5.03	.12
Urea N, mg/dl				
Preweaning[a]	3.36	3.22	3.38	.29
Postweaning	4.16	3.33	3.94	.31
VFA, m*M*				
Preweaning	.53	.63	.54	.05
Postweaning[a]	.97	.99	.94	.09
Acetate, mol/100 mol				
Preweaning[a]	92.5	94.3	92.9	1.0
Postweaning	94.1	93.3	93.8	.8
Propionate, mol/100 mol				
Preweaning	3.5	3.8	4.3	.7
Postweaning	4.1	4.3	4.9	.6
Butyrate, mol/100 mol				
Preweaning	3.7	1.9	2.0	.7
Postweaning	2.0	2.6	1.0	.6

[a]Significant week effect ($P < .05$).

[b]Mean differs from control ($P < .05$).

[c]Mean differs from control ($P < .01$).

[1]Adjusted for weekly starter intake by analysis of covariance.

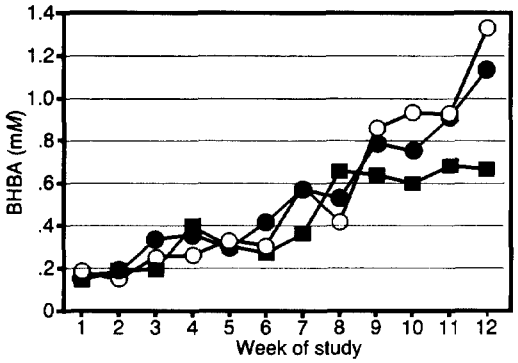

Figure 2. Least squares means of blood β-hydroxybutyrate (BHBA) in calves administered 0 (●) or 1 mg of lasalocid/kg of BW daily in milk replacer (○) or into ruminal cannula (■). SE = .09.

TABLE 6. Least squares means[1] of serum Ca, Mg, K, and Na in calves fed 0 (control) or 1 mg of lasalocid/kg of BW daily in milk replacer (MR) or via ruminal cannula (RC) during 1 to 8 wk (preweaning) or 9 to 12 wk (postweaning).

Item	Treatment			SE
	Control	MR	RC	
Ca, mg/dl				
Preweaning[a]	11.30	11.27	11.15	.17
Postweaning	11.80	11.47	11.60	.26
Mg, mg/dl				
Preweaning	2.20	2.18	2.32	.05
Postweaning	2.26	2.15	2.30	.04
K, mg/dl				
Preweaning	21.90	22.44	22.66	.67
Postweaning	20.52	19.53	21.07	.49
Na, mg/dl				
Preweaning	382.51	381.73	386.82	3.30
Postweaning	379.52	382.40	372.35	4.40

[a]Significant week effect ($P < .01$).

[1]Adjusted for weekly starter intake by analysis of covariance.

Blood BHBA (Table 5) increased with time on study within 1 to 8 wk ($P < .01$) and 9 to 12 wk ($P < .10$) and reached highest concentration at 12 wk in calves on control and MR treatments (Figure 2). Concentration did not increase with weaning in calves on RC treatment, which was 28% lower than control during wk 9 to 12. Acetoacetate was reduced ($P < .01$) in calves on RC treatment during the postweaning period also. As in previous studies (16, 18), the correlation between DMI and blood BHBA (unadjusted means) was high (r = .78), which suggests that most BHBA originated from alimentary ketogenesis. Reduced BHBA and ACAC in calves on RC treatment was consistent with the trend for lower ruminal butyrate. The concentration of ruminal butyrate, although not significant, was 18% lower in calves on RC treatment than in calves on control treatment (18.4 vs. 22.2 m*M*) during wk 9 to 12.

The antiketogenic effect of ionophores fed to lactating cows (21) has been attributed to increased production of propionate in the rumen, which provided gluconeogenic precursors and reduced the need for lipid mobilization and hepatic ketone synthesis. High BHBA to ACAC ratios, low plasma NEFA, and normal glucose concentrations (Table 4) indicated little hepatic ketogenesis and suggested that alimentary ketogenesis was the primary source of blood ketones in our study. That rates of gain approached 1 kg/d during the postweaning period further obviated the need for long-term lipid catabolism and ketone synthesis. Lack of response in calves on MR treatment suggests that lasalocid did not impact hepatic ketogenesis. Apparently, the observed reduction in ruminal butyrate with lasalocid administration in calves on RC treatment caused reduced alimentary ketogenesis, thereby reducing blood ketones. However, direct effects of lasalocid on ketone production by ruminal epithelium and liver and utilization by peripheral tissues cannot be excluded based on our data. It is possible that pH also influenced blood ketone concentration, because ruminal pH can influence rate of VFA absorption, particularly butyrate, from the rumen (24). Higher ruminal pH in calves on RC treatment may have reduced the rate of butyrate absorption, thereby reducing blood BHBA at 2 h postprandial.

Plasma VFA (Table 5) increased with increasing DMI (r = .62) and were unaffected by treatment. As expected, plasma VFA were mostly acetate; propionate and butyrate constituted only 1 to 5% of VFA. Serum minerals (Table 6) also were unaffected by treatment.

CONCLUSIONS

Results of this study indicate that lasalocid introduced into the rumen reduces concentration of blood BHBA and ACAC, particularly during the postweaning period. Slightly lower ruminal butyrate and higher ruminal pH suggest that changes in ruminal fermentation after weaning of calves caused the reduction in blood ketones. Blood glucose and NEFA were within normal concentrations, which suggests that ketones were of alimentary origin.

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