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Efficacy of Sodium Borate in the Prevention of Fatty Liver in Dairy Cows

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The effects of sodium borate (100 mg/kg body weight, PO, 15 days) from a month before expected calving until a month after calving were evaluated in dairy cows susceptible to fatty liver. Cows received either sodium borate (n = 13) or no treatment (n = 10). All cows had mild fatty livers and increased plasma triglycerides and very low density lipoprotein (VLDL) concentrations at the beginning of the experiment. The control group of cows developed significant fatty liver after calving, and 2 of them had severe fatty liver associated with clinical and biochemical abnormalities. There were no clinicopathological signs related to sodium borate administration. Serum triglycerides and VLDL concentrations before calving decreased significantly at calving and after calving in controls, and they were within the normal range only after calving. There were significant alterations during the experiment in some hematological and chemical variables between groups, within period, but they were within the normal range. Unlike treated cows, serum triglycerides and VLDL concentrations correlated with liver fat content after calving in untreated cows. Our results document that sodium borate decreases the degree of fatty liver in dairy cows during early lactation.

Key words: Borax; Cattle; Hepatic lipidosis.

Fatty liver (hepatic lipidosis) is a metabolic disorder affecting one third of periparturient, high-yielding dairy cows,[1] and its prevalence and incidence are high in dairy farms.[2,3] The negative energy balance attributable to initiation of milk production, reduction in feed intake, stress at calving, and hormonal changes during the pre- and postpartum periods are the main causal factors for development of fatty liver.[1–4] Negative energy balance is essentially universal among dairy cows in the first few weeks of lactation. Fatty liver occurs not solely because of negative energy balance but also because of the failure of appropriate adaptive mechanisms.[5] Although cause and effect have not been established, severe fatty liver can be associated with clinical disease. Although cows with mild and moderate fatty liver do not have clinical signs, the condition has been associated with other health and production problems.[4,6–8] Despite advances in the understanding of the hepatic biochemistry and sequence of metabolic events during the development of hepatic lipidosis, incidence rates of this disease, even in well-managed herds, remain similar to rates published decades ago.[9]

Reducing the severity and duration of negative energy balance is crucial in the prevention of fatty liver, for which there is no proven effective treatment. In theory, effective treatment would enhance lipoprotein triglyceride export from the liver. However, compounds that are known lipotropic agents in nonruminants have not been proved to be effective in ruminants.[10]. Choline, inositol, methionine, somatotrophin, glucagon, and vitamin B_{12} are often suggested as treatments,[10–17] but there is insufficient scientific data to support their use. In essence, treatment is the same as prevention; attempts should be made to avoid negative energy balance and minimize fatty acid mobilization from adipose tissue.[10]

Borax (sodium borate, $Na_2B_4O_7$) is known as a toxic material in veterinary and human medicine.[10,18] The effect of sodium borate on lipid profiles was investigated in dogs fed a fatty diet in our previous study,[19] where it was suggested that sodium borate could be worth investigating as a drug to lower plasma lipid in humans and animals. Therefore, we speculated that borax might prevent fatty liver in dairy cows. This present study was designed to evaluate the effects of sodium borate in the prevention of fatty liver in dairy cows.

Material and Methods

Animals, Diets, and Sodium Borate Administration

The experimental design was approved by the Committee on Use of Animals in Research of the Selcuk University, Faculty of Veterinary Medicine.

A total of 23 pregnant, multiparous Holstein cows in the dry cow herd belonging to the Farm of Faculty of Veterinary Medicine were enrolled; mean age was 5.5 years, mean 305-day milk production was 7,500 kg, and mean body weight was 450 kg at the start of the experiment. Cows were fed individually and had free access to tap water. During the entire experiment, all cows were fed for ad libitum intake (Table 1). The cows were studied from a month before predicted calving until a month after calving. The cows were randomly allocated to 2 groups: 10 to the control group and 13 to the experimental group. Sodium borate (100 mg/kg body weight dissolved in 1 L of warm water, by stomach tube, 15 days) was administered to the experimental group for a month before expected calving until a month after calving. The anticipated calving dates (30 days ± 1 day) and the days of gestation (280 days ± 1 day) were similar between groups.

Blood Sampling and Hematological and Biochemical Analyses

Blood samples were collected at 1 month before expected calving, at calving, and at 1 month after calving. Blood samples were taken from the jugular vein just before the liver biopsies were obtained. Hematological analysis included CBC. Serum was harvested within an hour by centrifugation for 15 minutes at 3,000 rpm. Serum was stored at −20°C before analysis. Serum was analyzed for glucose, cholesterol, triglycerides, urea, total protein, albumin, HDL (high-density lipoprotein) cholesterol concentrations, and aspartate aminotransferase (AST), gamma glutamyltransferase (GGT), and creatine kinase (CK)

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Table 1. Prepartum and postpartum rations as fed.

Ingredient	Consumption (kg/d)	
	Prepartum	Postpartum
Corn silage	10	12
Sugar beet pulp	—	10
Wheat straw	4	4.5
Hay	4	—
Concentrate[a]	2	8.5

[a] The concentrate consisted of 35% barley, 19.85% wheat, 15% wheat bran, 25% cotton seed meal, 3% limestone, 0.3% salt, and 0.35% vitamin-mineral mixture. It contained 21.5% crude protein and 2,850 kcal/kg metabolizable energy.

activities. All analyses were performed with commercial test kits.[a] LDL cholesterol was calculated from [total cholesterol − (HDL cholesterol + Triglyceride/5)], and very low density lipoprotein (VLDL) was calculated from [Triglyceride/5].[20]

Liver Biopsy

Liver biopsies were collected at 1 month before expected calving and at 1 month after calving and were performed via the right, 11th to 12th intercostal space.[21] Liver samples were put in Baker's formol-Ca solution and fixed 16 hours. Thin sections (12 μm) were cut from each sample, stained with oil Red O and Sudan Black B, and examined under light microscopy. The percent volume of visible fat in hepatic parenchymal cells was estimated by the stereological point-counting method.[22] Five fields from each animal were examined at 1,100× through the oil immersion lens of a light microscope and a 100-point eyepiece graticule. The average volume fraction of liver cell parenchyma occupied by oil Red O–positive droplets was recorded. Cows with <20% of fat in the liver were classified as mild fatty liver (normal) on the basis of histological analysis of liver biopsy samples. Those with 20–40% fat were considered moderately fatty, whereas cows with >40% fat were considered severely fatty.[23]

Statistical Analyses

The statistical significance of differences between experimental and control groups was evaluated by 2-sample *t*-tests. To compare the differences between the pre- and postcalving periods within the groups, paired *t*-tests were performed by the SPSS statistical software package.[b] A Spearman correlation analysis was performed to compare the measurements at each sampling period.

Table 2. Liver fat content (mean ± SD, range).

	Liver Fat (μm³/100 μm³)		
	Before Calving	After Calving	*P*
Experimental group	9.8 ± 7.6 (1–20)	6.3 ± 5.39 (1–18)	.056
Control group	6.4 ± 6.7 (1–17)	29.1 ± 30.7 (7–62)	<.001
P	.828	<.001	

Results

All cows were apparently healthy and had mild fatty liver (normal) and increased serum triglycerides and VLDL concentrations at the beginning of the experiment. The control group of cows developed significant fatty liver after calving (Table 2), and 2 of them had severe fatty liver associated with clinical signs such as anorexia, depression, weakness, ketonuria, and decrease in milk production. The affected cows had leukopenia, higher AST, and lower GGT activities and lower albumin concentrations than did cows with mild to moderate fatty liver. The remaining cows with moderate (7) and mild (1) fatty liver were clinically normal and had nearly normal milk production. The serum triglycerides and VLDL concentrations before calving decreased significantly at calving and after calving periods in controls, and they were within the normal range only after calving. There was significant negative correlation between the liver fat and triglyceride level ($r = -.811$, $P = .027$) and between the liver fat and VLDL level ($r = -.811$, $P = .027$). There were no clinicopathological signs related to borax administration during the experiment (Table 3), and the fat infiltration of the liver tended to decrease after calving in the experimental group of cows.

Discussion

The present results indicate that healthy cows fed balanced ration develop marked fatty liver after calving and that sodium borate decreases fat infiltration of the liver in dairy cows during early lactation. Sodium borate seems to be effective on lipid metabolism, especially serum triglycerides and VLDL secretion of the liver.

Diagnosis of fatty liver based on clinical signs and rou-

Table 3. Median of hematology and chemistry results.

	Reference Range	Before Calving			Calving			After Calving		
		Treatment	Control	*P*	Treatment	Control	*P*	Treatment	Control	*P*
MCHC (g/dL)	26–36	31.6	31.8	.11	32.1	33.7	.072	32.0	33.4	.005**
RDW (%)	13–18	17.0	16.9	.263	18.9	16.8	.001**	18.3	19.7	.047*
WBC (10^3/mm³)	4–12	8.5	10.1	.048*	9.3	9.9	.74	7.8	9.1	.016*
Triglycerides (mg/dL)	0–14	16	19.5	.160	15	17.5	.287	16	12.0	.334
Cholesterol (mg/dL)	80–180	131	115.0	.196	112	96.5	.133	151	125.0	.876
Glucose (mg/dL)	45–75	59	65.0	.349	70	46.5	.044	62	52.0	.545
TP (g/dL)	6.7–7.5	7.6	7.7	.438	7.2	6.9	.272	7.6	7.4	.166
Urea (mg/dL)	20–30	16	21.0	.179	23	17.0	.003**	21	15.0	.813
GGT (U/L)	11–24	22	24.0	.920	23	28.5	.196	23	22.5	.239
HDL (mg/dL)	60–70	62	50.0	.736	69	48.0	.028*	68	57.5	.467
VLDL (mg/dL)	0–2.8	3.2	3.9	.160	3	3.5	.287	3.2	2.4	.334

GGT, gamma glutamyltransferase; HDL, high-density lipoprotein; MCHC, mean cell hemoglobin concentration; RDW, red cell distribution width; TP, total protein; VLDL, very low density lipoprotein; WBC, white blood cell.

tine clinicopathological findings is inadequate for several reasons.[7] Mild and moderate fatty liver can result in changes in liver function that are not accompanied by hepatocyte destruction and increases in liver-specific enzyme activities.[6,24–33] There are significant alterations in the results of specific tests for liver function, particularly in dairy cows with severe fatty liver; however, it is emphasized that they should be interpreted with caution because of considerable individual variation. The present study is consistent with previous work.[33]

Accumulation of fat in the liver cells and development of fatty liver is caused by reduced synthesis of VLDL.[34–36] A major factor contributing to the development of fatty liver is the low output of hepatic triacyl-glycerols, which form part of the VLDL particules. The amount of total lipids in serum, VLDL, and high-density lipoproteins decreased significantly by 0.5 weeks after parturition.[36] The lowest serum lipoprotein concentrations occurred in cows with severe steatosis or during the evaluation of moderate steatosis.[35] Yomamoto et al[37] also reported that serum triglycerides concentration peaked (21 mg/dL) during the nonlactating stage and remained decreased during the lactating stages. Disorders in the liver lipotropic function can lead to diseases: overproduction of VLDL and coronary artery disease (in humans) and defects in VLDL production and liver steatosis-ketoacidosis (in cows).[34] Similarly, our study revealed that the triglycerides and VLDL concentrations decrease significantly at calving and after calving in controls and that there is significant negative correlation between the liver fat and these variables. Contrary to the controls, increased triglycerides and VLDL concentrations and mild fatty liver in the experimental group of cows can be considered striking clinicopathological findings. Furthermore, mild fatty liver in the experimental group tended to decrease after calving.

Signs associated with fatty liver in cows can be difficult and expensive to treat. Prevention of fatty liver is more rewarding than treatment. Prevention of fat cow syndrome is based on the coordination of feeding and reproductive management.

Apart from the classical treatments, we used sodium borate in the prevention of fatty liver in dairy cows. Sodium borate has been used as a herbicide, an insecticide, and a soil sterilant. It is toxic to animals if consumed in >0.5 g/kg. Poisoning has not been reported when sodium borate was used at lower doses but has occurred when it was accidentally added to livestock feed and when sodium borate powder was scattered openly for cockroach control. Principal signs with acute poisoning are diarrhea, rapid prostration, and, rarely, convulsions.[10] In humans, seizure disorders and anemia associated with chronic sodium borate intoxication developed.[38] There were no clinical and clinicopathological findings related to borax administration in any of the cows, likely because sodium borate was given at a nontoxic dose.

The precise mechanism of action of sodium borate is unclear, but it is known that borates are neither metabolized nor accumulated in the body, except for low deposits in bone.[39] Armstrong et al[40] reported that sodium borate could have beneficial effects on reproductive and bone characteristics. In addition, borates have been linked to the metabolism macrominerals,[41] energy metabolism,[42] and immune system.[43] In our previous study,[19] sodium borate altered the lipid profile when administered to dogs. The present study reveals that sodium borate might play a role on lipid metabolism, particularly serum triglycerides, and VLDL secretion of the liver in dairy cows.

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