PEER REVIEWED

Congenital Myopathy, Cardiomyopathy and Vitamin E and/or Selenium Levels in Cattle: A Retrospective Study of 1208 Abortion Cases

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Abstract

Congenital myopathy involving the myocardium, skeletal muscle and tongue was diagnosed in 58 of 1208 aborted bovine fetuses submitted for necropsy between February 1983 and June 1994. Microscopic characteristics of muscle lesions were consistent with segmental nutritional myopathy. Liver vitamin E and selenium (Se) concentrations in 40 of the 58 fetuses with myopathies were assayed, and 38 (95%) had either a deficiency of vitamin E (n=27), Se (n=2) or both micronutrients (n=9). Over this time period, 570 bovine fetal livers, including those from the 40 of the 58 cases with congenital myopathy, were assayed for vitamin E and Se concentrations. Vitamin E values varied from non-detectable to 57 μg/g of dry weight (DW), and Se values from 0.05-10.96 μg/g (DW), indicating placental transfer of both elements and fetal ability to sequester both nutrients in the liver. For 190 cases, deficiencies of liver vitamin E (n=119), Se (n=29), or both (n=42) were the only abnormal findings.

Résumé

La myopathie congénitale impliquant le myocarde, les muscles squelettiques et la langue a été diagnostiquée chez 58 fœtus bovins avortés parmi 1208 cas soumis à la nécropsie entre février 1983 et juin 1994. Les caractéristiques microscopiques des lésions musculaires étaient compatibles avec la myopathie nutritionnelle segmentaire. Les concentrations de vitamine E et de sélénium dans le foie ont été déterminées chez 40 des 58 fœtus avec myopathie et il en ressort que 38 (95%) avaient une déficience en vitamine E (n = 27) ou en sélénium (n = 2) ou au niveau des deux micronutriments (n = 9). Durant cette période, on a examiné les concentrations de vitamine E et de sélénium dans 570 foies de fœtus bovins incluant 40 des 58 cas avec myopathie congénitale. Les concentrations de vitamine E variaient de non détectables jusqu'à 57 μg/g de matières sèches alors que les concentrations de sélénium variaient entre 0.05 et 10.96 μg/g de matières sèches indiquant un transfert placentaire des deux éléments de même qu'une aptitude des fœtus à accumuler les deux éléments dans le foie. Dans 190 cas, des déficiences dans la concentration de vitamine E dans le foie (n = 119), ou du sélénium (n = 29) ou des deux (n = 42) étaient les seuls résultats anormaux.

Introduction

Vitamin E and selenium (Se) are essential nutrients which protect cellular membranes and organelles from endogenous peroxidation damage.[5,7,14,40] They have similar biochemical roles, although a deficiency of one of these elements cannot necessarily be resolved by supplementation with the other. However, sparing effects with regard to vitamin E and Se have been demonstrated.[16,33]

In 1922, vitamin E was first described as a nutrient essential for reproduction in the rat.[8] Subsequently, there have been numerous reports on the beneficial effects of vitamin E and/or Se on the maintenance of the central nervous, musculoskeletal, reticuloendothelial, and reproductive systems, and successful completion of pregnancy in a variety of species.[1,2,3,9,18,20,24,26,31,34,36,43,41,47,51,54,56,57,59]

The occurrence of congenital nutritional myopathy and cardiomyopathy in farm animals is not well described. Some reports associated selenium deficiency with fetal myocardial necrosis and abortion in cattle.[39,46,55] On the other hand, it is generally believed that vitamin E does not cross or poorly crosses the placenta.[33]

The purpose of this report is to describe vitamin E/Se levels in aborted fetuses with or without histologic lesions of congenital myopathy and cardiomyopathy.

Materials and Methods

A total of 1208 aborted bovine fetuses were submitted to the Diagnostic Center for Population and Animal Health (DCPAH) at the Michigan State University from February 1983 through June 1994 by cattle producers or veterinarians in Michigan, southern Wisconsin, northern Indiana, northern Ohio and Minnesota. The fetuses originated from 350 different farms which had experienced multiple abortions totaling approximately 8000 fetuses.

Pathologic Examination

Complete postmortem examination was performed on the fetuses, which were mostly in the third trimester of gestation. Tissues from major organs, including brain, tongue and skeletal muscle, and placenta when available, were fixed in 10% neutral-buffered formalin, embedded in paraffin, and stained with hematoxylin and eosin for light microscopic examination.

Microbiologic Examination

Samples from liver, lung, stomach contents and placenta (when available) from all fetuses were obtained aseptically and cultured aerobically, as well as for *Campylobacter*, *Leptospira*, *Mycoplasma*, *Ureaplasma*, *Listeria*, *Haemophilus* and *Chlamydia* species. Anaerobic culture was done on selected cases when aerobic culture did not yield significant bacterial growth, but sections from lung and placenta showed gram-positive or gram-negative organisms histologically. For virologic examination, fluorescent antibody testing (FAT) and virus isolation on fetal lung, liver, spleen and placenta were used to identify infectious bovine rhinotracheitis virus (IBRV), bovine viral diarrhea virus (BVDV), parainfluenza-3 (PI-3) and bovine respiratory syncytial virus (BRSV). When either single or paired serum samples from the dams were available, titers were obtained for IBRV, BVDV, *Brucella* and *Leptospira* spp.

Nutritional Examination

Samples from 570 fetal livers were randomly selected and assayed for vitamin E using a high performance liquid chromatographic (HPLC) procedure,[6] and for Se using a fluorescent spectrophotometry technique.[53]

The effect of autolysis on fetal liver vitamin E and Se concentrations was determined by incubating organ samples (150 g) at room temperature in sealed plastic bags, and assaying the samples at 12-hour intervals. There was no significant change in fetal liver vitamin E and Se concentrations over a 4-day (96-hr) postmortem period.

Livers with less than 4 μg/g dry weight (DW) vitamin E and less than 1.2 μg/g (DW) Se were considered deficient, based on the DCPAH's established reference ranges. Deficiency values were determined for fetal liver as values less than 50% of the means of all assays conducted on each specimen through 1985 in the clinical nutrition section. Normal vitamin E and Se concentrations for bovine fetal liver have been established to be 4-8 μg/g and 1.2-2.0 μg/g, respectively, on a dry weight basis.

Results

From the 1208 aborted bovine fetuses examined, infectious agents were identified as the cause of abortion in 296 (24.5%) of cases associated with placentitis, bronchopneumonia, meningitis and myocarditis. In addition, there were 10 cases of renal oxalosis, 33 cases of congenital malformations, 58 cases of fetal myodegeneration and cardiomyopathy, and 190 cases of deficiencies of liver vitamin E (n=119), Se (n=29), or both nutrients (n=42) with no other abnormal findings. The cause of abortion was not determined on 811 bovine fetuses.

Necropsy

Most of the 1208 aborted fetuses had variable degrees of postmortem autolysis. Serosanguineous fluids were present in the thoracic and abdominal cavities. Some of the 1208 aborted fetuses had interstitial edema in the cranial lobes of the lungs. The hearts of seven fetuses contained prominent pale yellow areas throughout the epicardium (Figure 1). These were later determined to have marked vitamin E and Se deficiency

Nutritional Examination

Vitamin E and Se concentrations were determined in 570 randomly selected fetal livers. Vitamin E concentrations ranged from undetectable (zero) to 57.0 μg/g (DW), while Se concentrations ranged from 0.05 to 10.96 μg/g (DW; Figures 2, 3). Of the 570 fetal livers assayed, 300 (52.6%) contained inadequate levels of vitamin E (less than 4 μg/g DW) and 129 (22.6%) contained inadequate Se concentration (less than 1.2 μg/g DW). Among 40 fetuses with myopathy and cardiomyopathy assayed for vitamin E and Se, 38 (95%) had livers with low to undetectable vitamin E concentration (n=27), low Se concentration (n=2), or both nutrients (n=9, Table 1). For 190 of the 570 cases, liver vitamin E deficiency (n=119), Se deficiency (n=29) or deficiency of both nutrients (n=42) was the only abnormal finding. For the remainder of these cases (n=201) the causes of abortion were primarily inflammatory conditions.

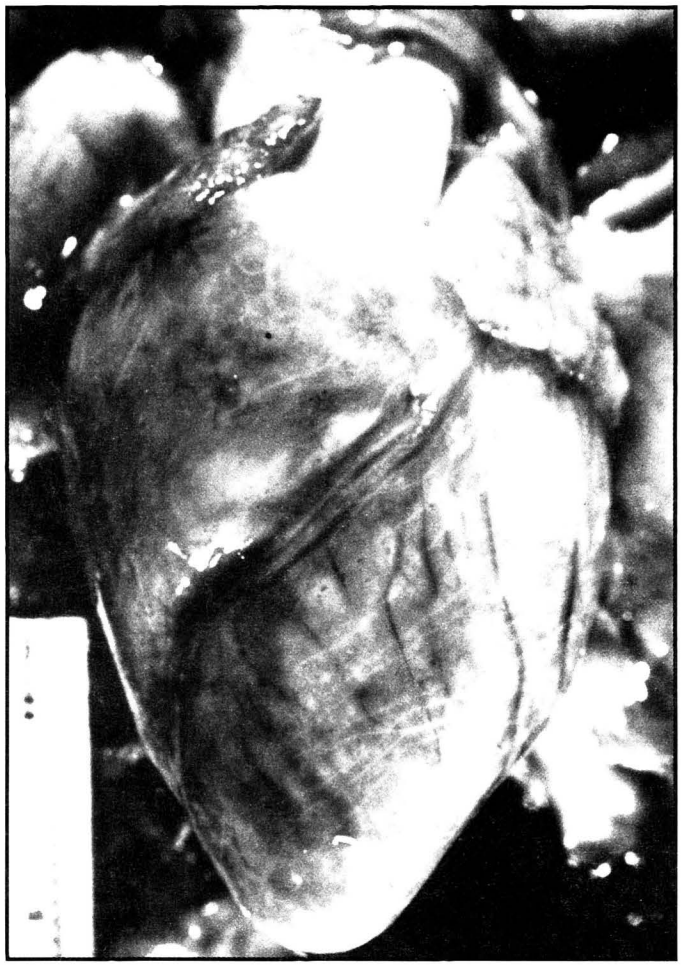

Figure 1. Heart from an 8-month-old aborted bovine fetus. Note prominent pale areas throughout the myocardium.

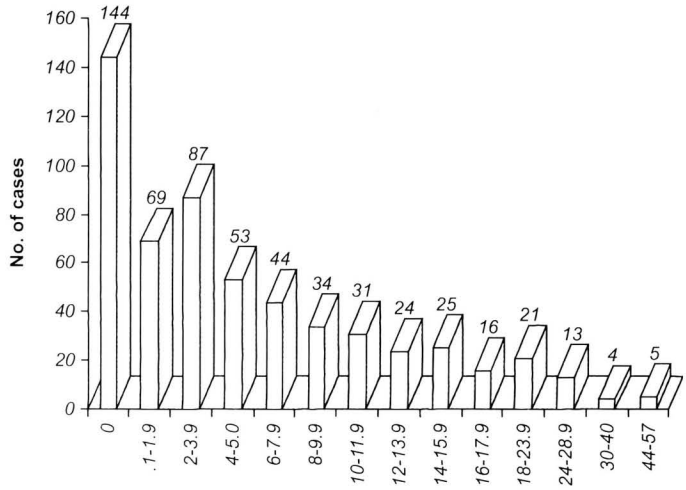

Figure 2. Liver vitamin E values (μg/g) of 570 aborted bovine fetuses from 1983-1994.

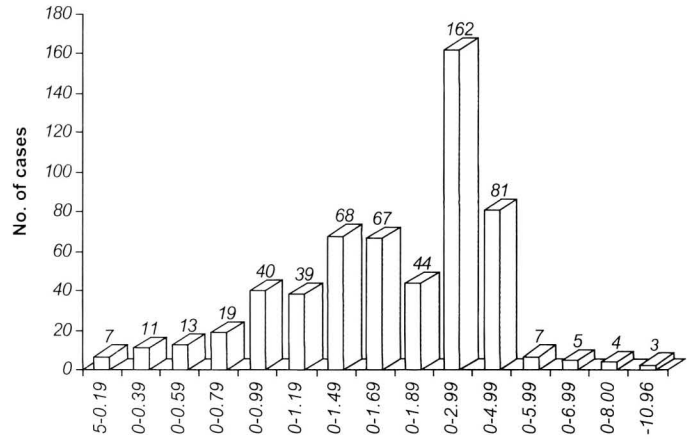

Figure 3. Liver selenium values (μg/g) of 570 aborted bovine fetuses from 1983-1994.

Histologic Examination

Degeneration and necrosis were identified in either cardiocytes or skeletal muscle from the 58 aborted fetuses. The lesions were similar to those of nutritional myopathy, with a segmental distribution ranging from mild to severe myofiber swelling, vacuolation, hyalinization, disintegration and hypercontraction bands in skeletal muscle (Figure 4). Myocardium contained areas of degeneration, necrosis and mineralization (Figure 5). Most fetuses were in the third trimester (Table 1) of pregnancy, which is considered the period of most rapid growth. The results of infectious causes of abortion have recently been published.[58]

Discussion

Nutritional myopathy due to vitamin E and/or Se deficiency occurs most commonly in young, rapidly growing calves and lambs, and is a well recognized entity.[3,17,32,44] Congenital nutritional myopathy associated with vitamin E and/or Se deficiency has been reported in sheep and goats, but not in naturally occurring cases in cattle.[10,13,17,26,37] Purkinje cardiocyte degeneration has been described in calves experimentally fed a low-magnesium milk diet, or a diet deficient in vitamin E and magnesium.[23,45] Preferential degeneration and necrosis of purkinje cardiocytes has also been produced in calves fed diets deficient in both vitamin E and Se.[21,22] In one study, Se deficiency has been associated with cardiac failure and myocardial necrosis in aborted bovine fetuses.[39] In the study reported here, congenital degeneration, necrosis and mineralization of cardiac and skeletal muscle were identified in 58 aborted bovine fetuses, of which liver vitamin E and Se values were measured in 40 cases (Table 1).

Deficiency of vitamin E and/or Se have been incriminated as possible causes of infertility, abortion and re-

Table 1. Bovine aborted fetuses with congenital myopathy and cardiomyopathy with their liver vitamin E and Selenium (Se) values.

Case No.	Vit E μg/g DW*	Se μg/g DW*	Age**	Skeletal lesions	Cardiac lesions
1	0.0	0.3	7 1/2	+	-
2	0.0	0.56	7	+	-
3	0.0	0.63	8	+	+
4	0.0	1.0	8	+	-
5	0.0	1.0	7+	-	
6	0.0	1.16	7	+	-
7	0.0	1.20	7	+	+
8	0.0	1.55	-	+	-
9	0.0	1.60	8	+	+
10	0.0	1.85	7 1/2	+	+
11	0.0	2.20	9	+	+
12	0.0	2.24	-	+	-
13	0.0	2.35	7	+	+
14	0.0	2.39	8	+	-
15	0.0	1.30	7	-	+
16	0.0	1.60	8	+	+
17	0.0	2.02	8	+	-
18	0.0	2.17	9	+	+
19	0.0	2.96	8 1/2	+	+
20	0.21	3.11	7	+	+
21	0.57	0.86	6	+	-
22	1.29	0.58	7	+	-
23	1.36	1.59	7 1/2	+	+
24	1.40	1.80	8	+	-
25	1.47	1.66	7	+	-
26	1.83	2.41	6	-	+
27	1.90	2.08	8 1/2	+	-
28	1.94	2.80	9	+	+
29	2.18	2.40	9	+	+
30	2.20	1.70	9	-	+
31	2.56	1.38	8	+	-
32	2.70	1.70	9	+	-
33	2.87	1.25	7	+	-
34	2.91	1.30	9	+	-
35	3.11	1.80	7	+	+
36	3.46	1.10	8	+	-
37	4.45	0.53	7	+	-
38	4.80	0.97	7	+	-
39	6.65	1.92	9	+	-
40	11.00	3.30	7	+	-

* DW = dry weight
** = gestational age, in months
Normal fetal liver vitamin E concentration 4-8 μg/g, dry weight
Normal fetal liver selenium concentration 1.2-2.0 μg/g, dry weight
Vitamin E deficient 36, Se deficient 9, vitamin E and Se deficient 9
All cases were Holstein except case 31 (Jersey)

tained placenta in several species.[1,2,11,12,15,19,24,42,43,46,48,55,57,58] In our study, liver vitamin E and Se concentrations of 570 aborted fetuses varied from non-detectable to 57 μg/g (DW) and 0.05-10.96 μg/g (DW), respectively (Figures 2 and 3). No other explainable cause of abortion was determined for 190 cases with either low liver vitamin E (n=119) concentration, low Se (n=29) concentration, or deficiency of both nutrients (n=42). For these 190 cases, no abortigenic microorganisms were identified, and there were no inflammatory reactions in the

Figure 4. Histologic section of skeletal muscle from an aborted fetus with vitamin E and selenium deficiency. Vacuolation, disintegration, swelling and hypercontraction bands of myofibers. H&E stain.

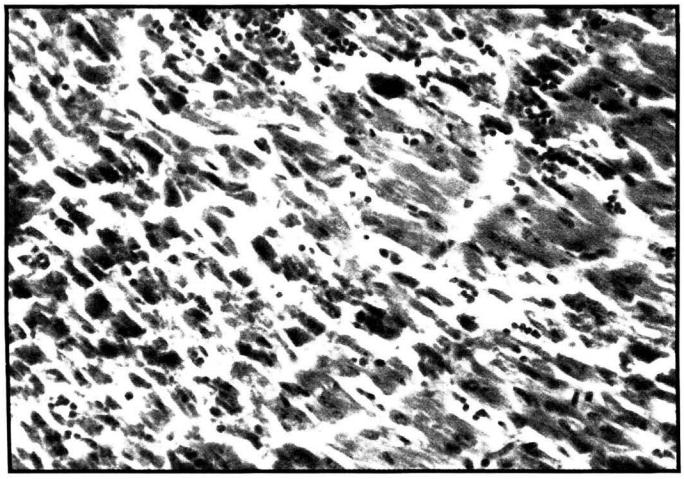

Figure 5. Histologic section of myocardium from an aborted fetus with vitamin E and selenium deficiency. Degeneration and mineralization of myocardial fibers. H&E stain.

tissues examined. However, 40 of these fetuses had evidence of mild to severe myopathy involving cardiac and skeletal muscle (Table 1). The liver vitamin E and Se were not determined in 18 fetuses with degeneration of cardiac and skeletal muscle.

There is little information in the literature regarding transplacental transfer of vitamin E, nor for normal values of this vitamin in fetal tissues. Since the report by Horwitz in 1959, it has been generally accepted that vitamin E does not cross or poorly crosses the placental barrier.[33] In humans, the infant is born with tocopherol deficiency, but low fetal levels are rapidly reversed by breast feeding.[33] Results of this study indicated that vitamin E may cross the placental barrier in the bovine (Figure 2). However, a total of 300 (52.6%) fetuses were considered vitamin E deficient (< 4 μg/g DW; Figure 2). There are no comparative data regarding vitamin E levels in fetal and maternal tissues in farm animals. Limited work in our laboratory has shown that a correlation exists between dam and fetal liver vitamin E concentration. It is believed that the low or non-detectable vitamin E values in these fetuses may reflect a maternal deficiency.

In contrast, more data are available on Se levels in fetal tissues and on placental transfer of this element. Se readily crosses the placenta, at least in beef cattle. When the Se content in the dam is low, the fetus apparently can sequester the element and can attain blood and liver values greater than those of the dam.[24] In this study, 441 (77.4%) fetuses had liver Se concentrations higher than 1.2 μg/g (DW), which most likely reflects adequate supplementation of the dams and possibly the ability of the fetus to sequester Se. However, 129 (22.6%) fetal livers had Se concentration of less than 1.2 μg/g (DW), which most likely indicates deficiency in the dams (Figure 3). The high values of hepatic vitamin E and Se in some of the fetuses (Figures 2, 3) may suggest recent supplementation of the dam, probably associated with an injection in late gestation. This is a routine practice on some dairy farms in our region during the last trimester of pregnancy.

Conclusions

Our data in this study indicated that vitamin E deficiency is more common than Se deficiency in the bovine fetus. Whether fetal vitamin E deficiency is due to inadequate supplementation of the dam's gestational diet or to other maternal and environmental factors is not clear. Myopathy, cardiomyopathy and abortion with low vitamin E and Se in these aborted calves suggests that deficiencies of these nutrients may be involved in the pathogenesis of the abortion. Further studies may help to elucidate the role of these elements in fetal myopathies and abortion.

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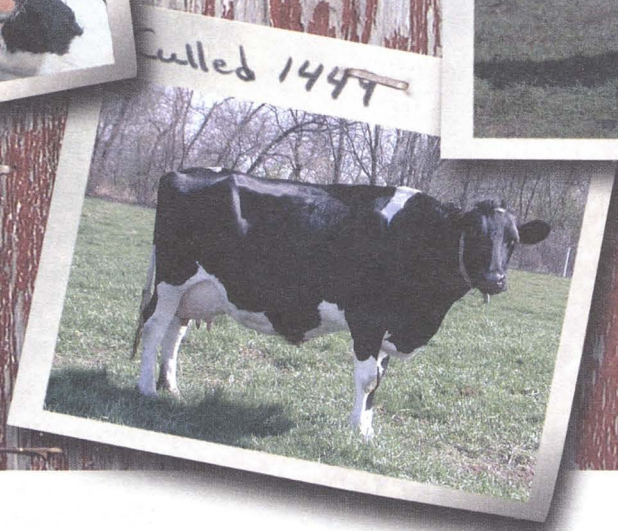

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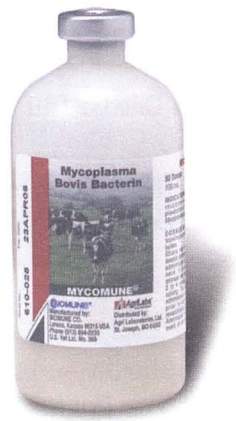

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