Zinc toxicity in dairy heifer calves associated with intra-ruminal bolus administration

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INTRODUCTION

With another facial eczema (FE) season underway, it is important to consider the potential consequences of both inadequate and overzealous preventative measures. Risk of FE varies widely from region to region, season to season and also within regions and seasons. Therefore it is necessary to continually quantify that risk through testing and monitoring, allowing an appropriate level of intervention.

Studies have shown both the frequency and consequences of inadequate FE control measures (Cuttance ***et al.*** 2016) as well as the dangers of overzealous zinc usage leading to toxicity. Zinc toxicity may result from various sources, including zinc salts drenched and in the water supply, incorporated in the feed, zinc boluses, and excess soil zinc (Ackermann ***et al.*** 2012; Briston & Pyke, 2015, Smith 1977). In this case, we report the clinical and pathological features of an outbreak of zinc toxicity associated with administration of intra-ruminal zinc boluses in R1 dairy calves.

CASE HISTORY

The case was initially reported to the attending veterinarian on the 6th April, 2016. The property was located in an area of Hawkes Bay known as a hot spot for facial eczema. It is a dairy grazing unit running 1,200 rising one-year-old dairy heifers annually. All animals are yarded for weighing and animal health treatments on a monthly basis. During the facial eczema season, treatments include the administration of intra-ruminal zinc boluses.

CLINICAL FINDINGS

On the first day of the monthly weigh-in for April, the animals had not performed as expected considering the amount of grass on offer. There was considerable weight loss among all mobs and a high proportion of ill-thrifty animals present. Fifty of the worst animals were drafted off into a mob of their own. The average weight of this mob was 155.5kg, with an average weight loss of 2.85kg/day over a 28-day period (compared with: main line 206kg, gaining 400gms/day). On examination of a race of these heifers, half of them had diarrhoea and pyrexia.

Differential diagnoses included enteric parasitism, BVD infection, bacterial enteritides, trace element deficiencies, and zinc toxicity. The farmer was concerned about facial eczema.

LABORATORY INVESTIGATIONS

Bloods were taken at the initial examination and faecal samples were taken the following day, prior to drenching. Clinically unwell animals were treated empirically for suspected bacterial enteritis using recommended dose rates of Alamycin LA® (Norbrook New Zealand Ltd, Auckland), Metacam® (Boehringer Ingelheim New Zealand, Auckland) and Metabolase Forte® (Ethical Agents New Zealand, Auckland).

Initial laboratory testing results are shown in table 1 (blood samples) and table 2 (faecal samples).

The most notable finding was increased serum zinc concentrations in all heifers tested. The laboratory reference interval for serum zinc in normal cattle is 9-20 µmol/L, whereas those dosed with zinc compounds have serum zinc concentrations of 18-34 µmol/L. 27-92 µmol/L is considered the toxic range, although in cattle administered zinc boluses, serum levels of up to 150 µmol/L have been observed without clinical signs of toxicity.

Campylobacter species were cultured from 6/10 heifers. While normal ruminants may harbour these organisms, opportunistic overgrowth was considered a possible contributor to ill thrift in this case given the clinical signs.

Nematode faecal egg counts were not suggestive of significant worm burdens and there was no evidence of recent exposure to circulating BVD virus. GGT concentrations did not indicate biliary damage due to sporidesmin exposure.

DIAGNOSIS AND MANAGEMENT

In light of the serum zinc results and absence of other significant causes of the clinical signs, zinc toxicity was suspected as the primary cause with possible secondary bacterial enteritis. Intra-ruminal zinc bolus administration was therefore reviewed. It was noted that in February 2016, the heifers had received a larger zinc bolus, 175-250kg, than the previous year, where 130-175kg was used (Time Capsule, Agrifeeds Ltd, Mt Maunganui, NZ). At this time the mobs were averaging 185kg with huge variance in minimums and maximums. Follow-up boluses were administered in subsequent months despite suboptimal weight gain in some, again risking cumulative overdose.

Affected animals were treated through preferential feeding, withholding further zinc treatments, and antibiotic therapy to target enteric bacterial overgrowth. Those animals that had already received zinc boluses in April could only be monitored.

The property was revisited on the 23rd May 2016. While most animals had slowly improved, a small mob of heifers remained in very poor body condition (figure 1). Some of these had developed submandibular

Table 1. Blood test results from ill thrifty R1 heifers 6/4/2016

Animal ID	GGT IU/L	Copper µmol/L	Zinc µmol/L	BVD antibody pooled S/P
1	8	14	110 H	0.08
2	31	7 L	88 H	
3	11	9	44 H	
4	18	11	79 H	
5	3	11	57 H	
6	15	-	60 H	
7	24	8	72 H	
8	11	8	105 H	
Reference Interval	3-47	8-20	12-18.5	

Table 2. Faecal testing results from ill thrifty R1 heifers 7/4/2016

Animal ID	Coccidia oocysts	Strongyle eggs per gram	Campylobacter culture	Yersinia Culture
1	-	-	-	-
2	-	50	+	-
3	+	-	-	-
4	-	50	+	-
5	-	-	+	-
6	+	-	-	-
7	+	50	+	-
8	-	50	+	-
9	-	50	-	-
10	-	-	+	-

Figure 1: Ill thrifty heifers with zinc toxicity

Table 3. Follow-up serum biochemistry results from ill-thrifty heifers 23/5/2016					
Animal ID	Urea mmol/L	Creatinine µmol/L	Zinc µmol/L	Pepsinogen IU/L	GGT IU/L
24	3.5	32 L	49 H	0.4	49 H
106	1.9 L	34 L	46 H	0.4	29
88	2.6 L	33 L	48 H	0.4	22
Reference Interval	2.7-11.9	39-181	12-18.5	0-3	3-47
Animal ID	Bilirubin	GLDH	Total Protein	Albumin	Globulin
24	7	9	48 L	22 L	26
106	9 H	19	49 L	20 L	29
88	5	13	43 L	22 L	21
Reference Interval	0-8	5-35	60-81	27-42	25-47

oedema. Serum samples were taken from three animals for prognostic purposes. The results are collated in table 3.

Serum zinc concentrations had declined but remained within the 'toxic' range despite no further supplementation after the initial investigation in April. Hypoalbuminemia was attributed to protein malabsorption due to pancreatic and enteric damage. Decreased urea and creatinine concentration were attributed to muscle wasting.

GROSS AND MICROSCOPIC PATHOLOGY

The worst affected heifer (#106) was euthanased and post mortem examination was conducted. Nutritional condition was very poor and body fat stores were minimal. The pancreas was firm, fibrous, and nodular (figure 2). There was oedema surrounding the adjacent duodenum (figure 3).

Histopathology of the pancreas revealed diffuse atrophy of exocrine lobules accompanied by broad bands of fibrosis, islet cell prominence, attempted regeneration, and ductular hyperplasia (figure 4). These changes are characteristic of zinc toxicity. In the liver, hepatocyte cords were atrophic, consistent with chronic negative energy balance. Sections of the small intestine showed villous blunting, foci of neutrophilic inflammation, and colonies of bacteria. The intestinal submucosa was oedematous. These findings were interpreted as primary zinc toxicity with secondary bacterial enteritis, presumably associated with an altered intestinal environment.

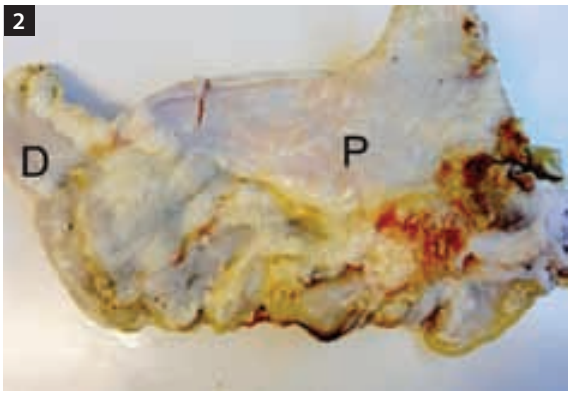

Figure 2: Fixed pancreas (P) and duodenum (D) from heifer with zinc toxicity. The pancreas is white and nodular.

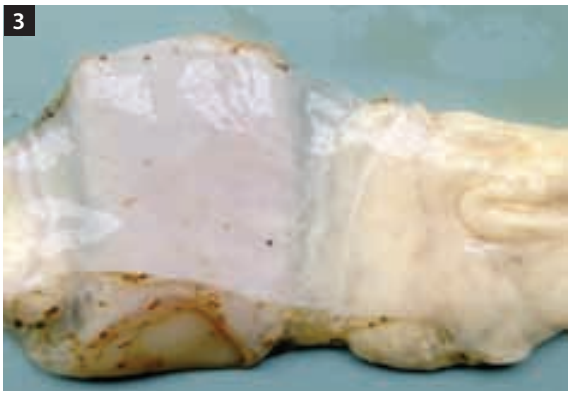

Figure 3: Periduodenal oedema from heifer with zinc toxicity.

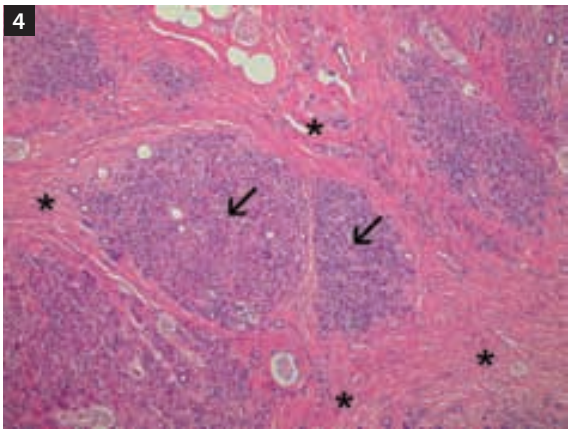

Figure 4: Pancreas from heifer with zinc toxicity. Bands of fibrosis (asterisks) surround and separate residual nests of exocrine cells (arrows). H&E 100x.

By the end of the outbreak, a total of six heifers were euthanased due to suspected chronic pancreatic insufficiency and associated poor prognosis.

DISCUSSION

This case study demonstrates the consequences of overzealous use of zinc in growing cattle. In addition to the loss of six valuable animals, the growth check in less severely affected heifers and ongoing effects on fertility, production, and disease resistance into the future amount to a substantial total cost.

When applying animal health products for prevention or treatment, a common approach is to dose to the heaviest animal in the mob. This applies for internal parasite drenching and antimicrobials where it is important not to under-dose and risk establishment of resistant pathogens. However, this approach is not transferrable to trace elements. Overdosing of zinc, copper and selenium are occasionally associated with acute and chronic toxicity. It is therefore important to: 1) Assess the need for trace element supplementation through animal and feed testing; 2) Accurately weigh animals to be treated; and 3) Calculate dose with care.

In this case, the calves received a zinc bolus in February containing a daily dose of 5.1g zinc oxide. The appropriate bolus size for the lighter calves releases 3.5grams of zinc oxide daily, therefore the calves received an additional 46% zinc per day over the capsule pay-out period. Overall in the first bolus administration the calves would have received an extra 44.8 grams over a 28 day period. The LD50 of zinc salts in cases of acute toxicity has been reported to be ~100 mg/kg (Garland 2012). For a 150kg calf this is 15grams.

After administration of boluses, serum zinc levels rise rapidly and peak at about two weeks after dosing. Levels then decline and at 28 days reduce to below therapeutic levels for high FE challenge. At 35 days, zinc concentrations are still protective, but only for moderate FE levels. Serum zinc levels return to normal at approximately 50 days (Munday et al 2001).

Zinc is primarily absorbed in the duodenum and transported to the liver. From there it is returned to the bloodstream for distribution to liver, pancreas, kidney and spleen, which rapidly accumulate zinc (Garland 2012). Excretion is through the faeces. Toxicity in ruminants may manifest in haemolytic anaemia, lethargy, diarrhoea, and weight loss. Affected animals can have a 'fish-like' odour (Smith 1977). Zinc salts tend to be more toxic than oxides. Pathology reflects sites where zinc is absorbed and accumulated. Gastroenteritis, hepatocellular necrosis, and renal tubular necrosis are described. Pancreatic degeneration and fibrosis is a classic lesion in ruminants (Garland 2012, Smith 1977).

It is suspected that the calves in the present case were overdosed with zinc due to the wrong sized capsule being used. Then, as there was not the expected weight gain it is possible a proportion of the mob were overdosed at subsequent administration at 28 – 30 day intervals. With the additive effect of overdosing per day and continued administration at 28 day intervals, chronic excess zinc exposure would have resulted in necrosis and loss of pancreatic exocrine cells over a prolonged period. This began to be clinically evident in April with high levels of morbidity throughout the mobs. At the end of May, several animals had reached a clinical end stage. The majority of the heifers on farm recovered, although with reduced weight gains.

As a result of this outbreak, several improvements in facial eczema monitoring and control were implemented. Spore counting is conducted with increased frequency to determine the need for zinc treatment and when to start. Calves are dosed according to their individual weights with an appropriate capsule size. Serum zinc concentrations and GGT levels are monitored to detect potentially toxic concentrations or lack of protection leading to sporidesmin-induced biliary damage.

EDITOR'S NOTE: *Camille has communicated with the company supplying the zinc bolus and worked with them during this investigation. They are particularly motivated to ensure that farmers understand they cannot use average mob liveweights for treating animals with Time capsules. They need to have individual weights and dose animals appropriately.*

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