

Efficacy of a combination butaphosphan-cyanocobalamin product and insulin for the treatment of ketosis in lactating dairy cattle

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Introduction

In the early postpartum period, negative energy balance is nearly ubiquitous in dairy cattle. During this period, excessive ketones, generally measured as β -hydroxybutyrate (BHBA), are associated with lower milk production, increased risk of concurrent diseases, and decreased reproductive performance. Insulin has been recommended for the treatment of ketosis because of its anabolic effects. It has been hypothesized that administration of vitamin B12 (cyanocobalamin) may increase gluconeogenesis by increasing the activity of methylmalonyl-CoA mutase, a vitamin B12-dependent enzyme and important component of the Krebs or tricarboxylic acid (TCA) cycle. Recent studies have shown that a combination butaphosphan-cyanocobalamin product (B+C; Catosal®, Bayer Animal Health) is efficacious for the prevention of ketosis when it is administered at calving. However, neither of these medications has been studied for efficacy in the treatment of ketosis in North American dairy cattle under commercial conditions. The objective of this study was to determine the efficacy of a butaphosphan-cyanocobalamin combination product and insulin on ketosis cure rates and BHBA concentrations.

Materials and Methods

From May to September 2011, a double blind randomized clinical trial was performed on 16 commercial dairy herds in Ontario and one in Michigan. Herds were visited once a week and blood samples were collected from eligible cows for determination of blood BHBA concentration using a handheld meter (Precision Xtra® meter, Abbott Laboratories). Animals had two chances to be enrolled (at 3 to 9 or 10 to 16 days-in-milk) and were considered ineligible if they had been enrolled in the study the previous week or had been diagnosed with ketosis or a displaced abomasum prior to testing. Ketosis was defined as a blood BHBA concentration ≥ 1.2 mmol/L and no distinction was made between subclinical and clinical ketosis. All ketotic cows were treated with 300 g of propylene glycol orally for three days. Cows were then randomly assigned to receive one of four additional treatments (200 IU insulin glargine (IG; Lantus®, Sanofi-Aventis) and 25 mL saline solution (placebo 1) subcutane-

ously (SQ); 25 mL B+C and 2 mL saline solution (placebo 2) SQ; 25 mL B+C and 200 IU IG; or both placebos (SQ) in a 2x2 factorial study design. BHBA concentration was determined at seven and 14 days after treatment. Cure was defined as a BHBA concentration < 1.2 mmol/L at seven days post-treatment. Logistic regression was used to determine the effects of treatment on cure, and linear regression was used to examine the effects treatment on BHBA concentration seven days after treatment.

Results

In total, 629 of 1,463 (43%) eligible cows were enrolled in the study; 199 cows were treated with IG and placebo, 115 were treated with B+C and placebo, 108 were treated with IG and B+C, and 207 cows were given both placebos. The disparity in group sizes was caused by the temporary unavailability of B+C in Canada, which resulted in only the 371 cows from Michigan being included in the analyses that evaluated the effects of B+C. All cows were included in the analyses that evaluated the effects of insulin. Blood BHBA concentrations ranged from 1.2 to 7.8 mmol/L. No interaction was detected between IG and B+C. When lactation number and BHBA concentration at enrollment were controlled, there was a tendency for the B+C treatment to increase the odds of cure of ketosis (OR, 1.5; 95% confidence interval, 0.99 to 2.29; $P=0.08$) and decrease the BHBA concentration at seven days after treatment (mean decrease in BHBA concentration, -0.19 mmol/L; $P=0.07$). When herd, lactation number, and BHBA concentration at enrollment were controlled, no association was detected between IG treatment and cure of ketosis (OR, 0.98; $P = 0.93$) or BHBA concentration at seven days after treatment (mean decrease in BHBA concentration, -0.07 mmol/L; $P = 0.91$).

Significance

These results suggest that treatment with B+C may be helpful in the resolution of ketosis; whereas, treatment with IG did not appear to be beneficial for the treatment of ketosis. Further investigation is warranted to determine the impact of treatment with B+C on cow performance.