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Randomized clinical field trial on the effects of butaphosphan-cyanocobalamin and propylene glycol on ketosis resolution and milk production

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ABSTRACT

The purpose of this study was to determine the effects of a butaphosphan-cyanocobalamin combination product (B+C) and 2 durations of propylene glycol treatment (PG; 3 versus 5 d) on ketosis resolution and early lactation milk yield. Cows from 9 freestall herds (8 in Ontario and 1 in Michigan) were tested at weekly intervals between 3 and 16 d in milk. Ketosis was defined as blood β -hydroxybutyrate (BHB) ≥ 1.2 mmol/L. Ketotic cows were randomly assigned to treatment with 25 mL of B+C or 25 mL of saline placebo for 3 d and 3 or 5 d of 300 g of PG orally in a 2×2 factorial arrangement. Outcomes evaluated for all farms included ketosis cure (blood BHB < 1.2 mmol/L at 1 wk after enrollment), maintenance of ketosis cure (blood BHB < 1.2 mmol/L 1 and 2 wk after enrollment), and blood BHB concentrations at 1 and 2 wk after enrollment. Daily milk weights were collected in 3 herds. Poisson regression was used to evaluate cure and maintenance of cure, whereas repeated-measures ANOVA was used to evaluate blood BHB concentrations in the 2 wk after enrollment and average daily milk production in the 30 d after treatment. A total of 594 animals were enrolled in the study with 124 treated with B+C and 5 d of PG, 176 treated with B+C and 3 d of PG, 128 treated with saline and 5 d of PG, and 166 treated with saline and 3 d of PG. Animals with blood BHB > 2.4 mmol/L at the time of enrollment were 1.7 times more likely [95% confidence interval (CI): 1.4 to 2.2] to cure and had a decrease of 0.25 ± 0.11 mmol/L blood BHB at 1 wk after enrollment if treated with 5 d of PG compared with 3 d, though this response was not seen in animals with BHB of 1.2 to 2.4 mmol/L at enrollment. Cows with blood glucose concentrations < 2.2 mmol/L at enrollment produced 3.1 kg/d (95% CI: 1.3 to 5.0) more milk if treated with B+C and 3.4 kg/d (95% CI: 1.7 to

5.1) more milk if treated with 5 d of PG compared with their respective controls. This response was not seen in animals with blood glucose ≥ 2.2 mmol/L at enrollment and there was no interaction between treatments. These results indicate that extended PG treatment is beneficial in decreasing blood BHB concentrations in more severely affected animals. Additionally, both B+C treatment and extended PG treatment improved milk yield in animals with low blood glucose at the time of ketosis diagnosis.

Key words: ketosis, cyanocobalamin, propylene glycol, glucose

INTRODUCTION

Metabolic disease is common in early lactation dairy cattle due to a period of negative energy balance that occurs at the beginning of lactation for nearly every animal (Bauman and Currie, 1980; Baird, 1982; Herdt, 2000). Lactation is given a high priority in metabolic demands, to the point that body stores are heavily utilized to support lactation (Bauman and Currie, 1980). Adaptations occur in many animals that allow changes in physiology and metabolism to support lactation without subsequent disease through a process of homeorhesis (Bauman and Currie, 1980). However, in some animals, these adaptations are inadequate and metabolic disease results, often in the form of hyperketonemia (Bauman and Currie, 1980; Herdt, 2000).

Production of ketone bodies is part of the homeorhetic changes that allow lactation to proceed and support higher levels of production (Herdt, 2000). However, pathologic levels of ketone bodies are associated with increased risk of displaced abomasum, poorer reproductive performance, and decreased milk production (Duffield et al., 2009; Ospina et al., 2010a,b; McArt et al., 2012b). All of these outcomes can lead to decreased animal welfare and economic losses for the producer.

Glucose is required for milk production and is an important part of the endocrine mechanisms that control homeorhesis in early lactation (Herdt, 2000). Blood

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ketones and glucose generally have an inverse relationship, as low blood glucose concentrations stimulate fat breakdown and ketone production (Herd, 2000). However, animals have varying abilities to compensate and homeostatic mechanisms do not function to the same extent in all animals. Thus, some animals with high blood ketones may have normal or high blood glucose (Herd, 2000). This suggests a difference in the mechanism of ketosis development and may play an important role in the effectiveness of ketosis treatment regimens (Herd, 2000; Gordon et al., 2012).

Propylene glycol (PG) was first described for ketosis treatment in 1954 (Johnson, 1954; Maplesden, 1954). When PG enters the rumen, it is either absorbed directly or converted to propionate; PG that is absorbed directly stimulates gluconeogenesis by entering the tricarboxylic acid (TCA) cycle (Nielsen and Ingvarsen, 2004). Propionate produced from metabolism of PG can be used as a precursor for gluconeogenesis and helps stimulate insulin release to decrease fat catabolism (Studer et al., 1993). Although PG has often been studied (Nielsen and Ingvarsen, 2004), many of these studies were small or poorly designed. Recently, a large-scale clinical field trial illustrated the benefits of PG use for treatment of subclinical ketosis (McArt et al., 2011, 2012a). Cows in that study were tested for ketosis 3 times a week and treated with PG until ketosis was resolved, from 2 to 16 d. Although the study showed several benefits of treatment with PG, there were 2 challenges with the study design. Giving an oral drench of PG is labor intensive and the results do not identify a minimum effective duration of treatment. Additionally, animals with BHB ≥ 3.0 mmol/L were removed from the trial, so it is unclear whether more severely affected animals benefit from PG treatment.

Recently, a combination butaphosphan and cyanocobalamin product (B+C, Catosal, Bayer, Shawnee, KS) has been investigated for ketosis treatment (Lohr et al., 2006; Gordon et al., 2012). Cyanocobalamin is a form of vitamin B₁₂, which has been hypothesized to increase gluconeogenesis by increasing the activity of methylmalonyl-CoA mutase, a vitamin B₁₂-dependent enzyme and important component of the TCA cycle (Kennedy et al., 1990). Butaphosphan, an organic phosphorus source, might also stimulate gluconeogenesis by phosphorylating intermediate compounds in the process (Rollin et al., 2010). However, it is unclear whether this form of phosphorus is biologically available to the animal. The use of this combination product has been shown to increase rumination in cows after surgical correction of a left displaced abomasum (Lohr et al., 2006) and to increase ketosis cure and milk production in multiparous cows (Gordon et al., 2012). Data from these studies were collected subjectively (Lohr et al.,

2006) or from a single herd (Gordon et al., 2012), so it is unclear how efficacious B+C would be in various commercial herds.

The objective of this study was to examine the effects of B+C and varying durations of PG treatment for resolution of ketosis and the effects on early lactation milk production. A secondary objective was to examine the association between blood glucose concentration at enrollment and treatment outcomes.

MATERIALS AND METHODS

Study Population

Data were collected from 8 dairy herds in Ontario (farms A through H) and 1 in Michigan (farm Z) from May 14 to August 27, 2012. Herds were purposively selected due to their proximity to study sites and willingness to participate. To be eligible for inclusion, herds were required to be enrolled in monthly milk testing through their local DHI organization or to collect daily milk weights on farm. Enrolled herds were housed in freestall facilities ranging from 100 to 3,200 lactating cows. All herds delivered a TMR to all lactating cows.

Data Collection and Study Design

Herds were visited weekly during the study period. Individual herds were visited on the same day of the week and at the same time of day. At each visit, cows 3 to 16 DIM were tested for ketosis using the Precision Xtra meter (Abbott Laboratories, Abbott Park, IL). Cows were excluded from enrollment if they had been previously diagnosed with ketosis or a DA or had been enrolled in the study the previous week. Ketosis was defined a priori as blood BHB ≥ 1.2 mmol/L. The Precision Xtra meter is a handheld device that measures BHB in whole blood. This meter has previously been validated for use in cattle and has 88% sensitivity and 96% specificity at this cut-point (Iwersen et al., 2009). This testing scheme provided 2 opportunities for enrollment for each animal, once at 3 to 9 DIM and again at 10 to 16 DIM.

Blood was drawn from the coccygeal vessels using a 20-gauge $\times$ 2.54-cm needle and 3-mL syringe. Ketone testing was performed immediately according to manufacturer's instructions. In animals that were classified as ketotic (blood BHB ≥ 1.2 mmol/L), blood glucose concentration was measured using a second Precision Xtra meter. Blood was tested for glucose immediately after the ketone results were displayed (10 s from application of blood to the strip) and were displayed after 5 s. The use of Precision Xtra for glucose determination has also been validated in cattle (sensitivity 76.2%,

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