

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

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## Introduction

Ketosis, generally measured as increased concentrations of beta-hydroxybutyrate (BHBA) in the blood, is common in dairy cattle and caused by a period of negative energy balance that is nearly ubiquitous at the beginning of lactation. The consequences of ketosis include increased risk of other diseases and decreased production and reproductive performance. Propylene glycol (PG) has been recommended for treatment of ketosis because of its role in gluconeogenesis, and has recently been shown to be effective for the treatment of subclinical ketosis in a large-scale clinical field trial. 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 tricarboxylic acid (TCA) cycle. Results of a recent study conducted on 1 herd suggested that a combination of butaphosphan-cyanocobalamin (B+C; Catosal<sup>®</sup>, Bayer Animal Health) was efficacious for the treatment of cows with ketosis. The purpose of this study was to determine the effects of B+C and the duration of PG treatment (3 vs 5 days) on ketosis resolution and early lactation milk yield in dairy cows.

## Materials and Methods

A double-blind randomized clinical trial was performed in 8 herds in Ontario and 1 herd in Michigan from May to August, 2012. Herds were visited weekly and all animals 3 to 16 days in milk (DIM) were tested for ketosis by means of the Precision Xtra<sup>®</sup> meter (Abbott Laboratories). Ketosis was defined as a blood BHBA concentration  $\geq 1.2$  mmol/L. Cows were ineligible for enrollment if they had been diagnosed with ketosis or a displaced abomasum prior to testing, or if they were enrolled the previous week. Ketotic cows were randomly assigned to treatment with 25 mL B+C or 25 mL saline (0.9% NaCl) solution placebo, SC, and 3 or 5 days of 300 g PG orally in a 2 x 2 factorial design. On all farms, BHBA was measured at 7 and 14 days after treatment and blood glucose was measured at the time of enrollment and 7 and 14 days after treatment. Individual-cow

daily milk weights were monitored in 3 herds for 30 days after treatment. Cure was defined as BHBA  $< 1.2$  mmol/L at 7 days post-treatment. Poisson regression was used to evaluate cure and repeated measures ANOVA was used to evaluate blood BHBA concentration during the two weeks after enrollment and milk production for 30 days after treatment.

## Results

Incidence of ketosis during the study was 763 of 1,742 (44%). The blood BHBA concentration of the majority (601/763 [78.8%]) of ketotic cows enrolled in the study ranged from 1.2 to 8.7 mmol/L. One hundred twenty-four cows were treated with B+C and 5 days of PG, 176 cows were treated with B+C and 3 days of PG, 128 cows were treated with saline placebo and 5 days of PG, and 166 cows were treated with the saline solution placebo and 3 days of PG. The disparity in treatment group sizes was caused by labor issues, which required that PG be administered for only 3 days for some of the herds. Cows with a blood BHBA concentration  $> 2.4$  mmol/L at enrollment were 1.7 (95% confidence interval, 1.4 to 2.2) times more likely to cure and had a mean  $\pm$  SD decrease in blood BHBA concentration of  $0.25 \pm 0.11$  mmol/L at 1 week after enrollment if treated with 5 days of PG, compared to treatment with only 3 days of PG; however, this effect of PG administration frequency was not observed for cows with a blood BHBA concentration of 1.2 to 2.4 mmol/L at enrollment. Cows with ketosis and a blood glucose concentration  $< 2.2$  mmol/L at enrollment produced 6.8 lb (3.1 kg)/d (95% confidence interval, 2.9 to 11 lb [1.3 to 5.0 kg]/d) more milk if treated with B+C and 7.5 lb (3.4 kg)/d (95% confidence interval, 3.7 to 11.2 lb [1.7 to 5.1 kg]/d) more milk if treated with 5 days of PG, compared to their respective controls. This increase in milk production was not detected for cows with a glucose concentration within reference limits at enrollment, and there was no interaction between treatments.

## Significance

Findings of this study indicated that extended PG treatment (5 days vs 3 days) was beneficial in decreasing

blood BHBA concentrations in more severely affected cows. Additionally, both B+C and extended PG treatment improved milk yield in cows with a low blood glucose concentration at the time of ketosis diagnosis. Blood glucose concentration at the time ketosis is diagnosed

may be an important predictor of treatment efficacy, and more research is warranted to understand the relationship between blood BHBA and glucose concentrations in ketotic cows.