# Clinical Trial of Early Ketosis Detection and Therapy in Fresh Cows

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## Introduction

Postparturient (type II) ketosis, mostly subclinical in degree, is a common disease associated with decreased milk production, decreased reproductive performance, and increased risk of displaced abomasum (DA) in dairy cattle. Based on the assumption that early treatment of ketosis will prevent the anticipated losses, it is often recommended to perform ketosis screen-and-treat programs in fresh cows. However, secondary prevention trials using cowside tests have yet to be published. Therefore, the extent of losses that may really be prevented by such intervention is unknown. The objective of this study was to evaluate the effect of treating ketosis cases found with a fresh cow screening program.

#### **Materials and Methods**

The impact of treatment was evaluated with a randomized controlled clinical trial. Fresh cows mostly between one and 15 days-in-milk (DIM) from four freestall Holstein herds were screened daily for the presence of urinary ketones using the Ketostix test strip (Bayer Corporation, Elkhart, IN). Cows with a positive urine sample at the small level or greater (>15 mg/dL of acetoacetate) and without a concurrent DA were eligible for enrollment. Upon enrollment, ketotic cows were randomly allocated to one of two groups: treated or controls.

On the day of enrollment (day 1), the treated group received an IV bolus of 500 ml of 50% dextrose, 20 mg of dexamethasone, and 5 mg of vitamin B12, as well as an oral bolus of 500 ml of propylene glycol by drenching gun. On day 2 and day 3, the dose of propylene glycol was repeated. Cows from the treated group could be retreated with more than a single three day course of therapy if still found positive after completion of a previous three day course. Cows from the control group were left untreated. However, for humane reasons, protracted ketosis cases showing deterioration among the control cows could receive a relief three day course of therapy identical to the one administered in the treated group. They were nonetheless analyzed as per randomization (intent-to-treat).

The clinical outcomes for this study were: 1) the occurrence of a DA within 60 DIM; 2) milk yield per day, as reported on DHI at monthly intervals; 3) the interval from calving to pregnancy, to be used in time-to-event analyses; and 4) the interval from calving to culling (death or sale), also to be used in time-to-event analyses. Cows were followed until their next calving or culling.

Occurrence of a DA was modeled by logistic regression. Milk production was analyzed by repeated measures mixed regression. Time-to-pregnancy and time-to-culling were modeled with crude survival curve analysis and Cox proportional hazard models. For all models, adjustment for lactation group, herd, DIM at enrollment, and ketosis level at enrollment were offered.

## Results

Of a total 3,969 cows screened, 561 cows were enrolled in the clinical trial (279 treated and 282 controls). Cows from the treated group averaged 1.35 courses of therapy per cow, whereas cows from the control group received on average 0.15 relief treatments per cow. Treating ketotic cows proactively (treated group) versus treating as a last resort only (control group) had no significant effect on DA occurrence (odds ratio = 0.75, P=0.264), milk production (-2.2 lb or -1.0 kg/day, P=0.109) or time-to-pregnancy (hazard ratio = 0.84, P=0.130). However, it had a negative effect with regard to removal from the herd, with 161 and 127 cows culled from the treated and control groups, respectively. In survival analysis, there was a 40% increase in the risk for culling in treated cows (hazard ratio = 1.4, P=0.005).

### Significance

A standard ketosis therapy failed to prevent (and even increased) the negative impacts of ketosis in fresh cows. This raises questions about the actual role of elevated ketones in causing those apparent effects. A better understanding of the mechanism and cause of ketosis development is necessary to find ways to reduce negative outcomes often associated with this disease.

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