A randomized clinical trial assessing the use of a single injection of dexamethasone combined with oral propylene glycol therapy for the treatment of hyperketonemia

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Introduction

The treatment of hyperketonemia (HK, blood β-hydroxybutyrate (BHBA) > 1.2 mmol/L) with oral propylene glycol has proven benefits. Parenteral administration of glucocorticoids has been suggested as an adjunctive therapy; however it has not been assessed in a randomized controlled trial. The objective of this research was to evaluate the effect on the probability of cure, risk of subsequent disease, and milk production of a 1-time intramuscular injection of dexamethasone as an adjunctive therapy for HK.

Materials and Methods

A randomized controlled trial was conducted from May to August 2014 on 4 dairy farms in New York State. Blood BHBA was tested once weekly between 3 and 16 days in milk (DIM) using the Precision Xtra device. All cows testing positive for HK were randomly assigned to receive a single intramuscular injection of 20 mg dexamethasone (DX) or an equivalent volume of sterile saline placebo (PB). Both groups received 4 days of oral propylene glycol therapy (300g, once per day). Cure was determined by blood BHBA concentration obtained once weekly for the first 2 weeks following enrollment. Multivariable regression models were constructed for the outcomes of: treatment failure (having HK at either follow-up or being clinically ketotic from enrollment to 30 DIM), test day milk production at the first 3 tests, 305ME at third test, and the risk of being diagnosed with post-partum disease (displaced abomasum, metritis, clinical ketosis) from diagnosis of HK to 30 DIM. There was a significant interaction between herd and treatment for both the outcome of HK at 1 week after diagnosis, and for treatment failure, and therefore herd was controlled as a fixed effect for those models. For the other outcomes, herd was controlled as a random effect.

Results

A total of 508 cows were enrolled, 254 in each treatment group. Treatment failure was not different (P=0.21) overall (48% in the DX group and 53% in the PB group), but it depended on the herd and the concentration of BHBA at enrollment. At low BHBA (1.2-1.4 mmol/L) at diagnosis, the odds of treatment failure were 2 to 6 times higher (CI 95%: 1.1-19.7) in the PB groups in 3 herds. In these same herds, as enrollment BHBA concentration increased, the odds of treatment failure no longer differed between treatment groups. In the fourth herd, there was no difference in the odds of persistent HK between treatment groups at low enrollment BHBA, and at high BHBA concentrations (>2.0 mmol/L), receiving dexamethasone actually increased the odds of treatment failure (OR: 2.8, CI95%: 1.3-5.9). Treatment had no impact on the risk of post-partum disease within the first 30 DIM or test-day milk production.

Significance

Although there may be a benefit of adding dexamethasone to treatment of HK with propylene glycol when blood BHBA concentration is between 1.2 and 1.4 mmol/l at diagnosis, the lack of benefit in disease prevention and milk production and the potential detrimental effect at higher enrollment BHBA suggests that dexamethasone may not be a useful addition to HK therapy.