Implications of allopregnanolone in weak calf syndrome

P. Riedel, BS; **J. Dascanio**, VMD, DACT, DABVP; **J. Johnson**, DVM, MS, DACT; **L. Miller,** DVM, DACT, PhD
College of Veterinary Medicine, Lincoln Memorial University, Harrogate, TN 37752

Introduction

Weak calf syndrome (WCS) produces "dummy calves" that are weak and unable to stand or nurse. The causes of WCS are not well understood and often attributed to hypoxic and ischemic injury without confirmation.[2]

Recent research in other species has pointed to an alternative mechanism behind neonatal syndromes comparable to WCS.[3,4,5] This involves the persistence of progesterone metabolites in the neonatal brain resulting in symptoms consistent with WCS. One specific progesterone metabolite, allopregnanolone, may be a significant contributor to WCS pathogenesis, which this study intended to demonstrate.

Materials and Methods

Two healthy neonatal Jersey calves were used for this study. One was given an intravenous allopregnanolone solution and 1 served as a control and was given intravenous saline. Each followed the same protocol of multiple infusions of increasing dosages. The animals were isolated in pens with their dams and observed throughout the protocol. A neurobehavioral (NB) scoring system adapted from Madigan *et al* was used during periodic exams to evaluate the effects of the treatments.[3] A higher NB score correlates with symptoms of WCS.

Results

Within minutes of receiving allopregnanolone, the experimental calf's NB score increased and it showed clinical signs consistent with WCS including obtundation, reduced responsiveness to dam, and inability to suckle. These clinical signs increased linearly with the dosage of allopregnanolone and completely ceased within 24 hours of the last infusion. The control calf showed only transient disinterest in suckling with no other signs of WCS.

Significance

This study demonstrated that exogenous allopregnanolone temporarily creates a neurologic state similar to WCS in the healthy calf. This supports our hypothesis that progesterone metabolites persisting in the fetal brain can be a cause of WCS. The next step would be to analyze blood and cerebrospinal fluid samples from calves with WCS for the presence of allopregnanolone. Further confirmatory research may lead to practical treatments for WCS as has been the case in other species.[1]

References

1. Aleman M, Weich K, Madigan J. Survey of veterinarians using a novel physical compression squeeze procedure in the management of neonatal maladjustment syndrome in foals. *Animals* 2017; 7:12.
2. Bianco A, Moore G, Taylor S. Neonatal encephalopathy in calves presented to a university hospital. *J Vet Int Med* 2017; 31:8.
3. Madigan J, Haggett E, Pickles K, Conley A, Stanley S, Moeller B, et al. Allopregnanolone infusion induced neurobehavioural alterations in a neonatal foal. *Equine Vet J* 2012; 44:4.
4. Naerta Gl, Mauricea T, Tapia-Arancibiaa L, Givalois L. Neuroactive steroids modulate HPA axis activity and cerebral brain-derived neurotrophic factor (BDNF) protein levels in adult male rats. *Psychoneuroendocrinology* 2007; 32:17.
5. Yawno T, Yan E, Hirst J, Walker D. Neuroactive steroids induce changes in fetal sheep behavior during normoxic and asphyxic states. *Stress* 2011; 14:10.