Fetal Consciousness’ Impact on Equine Neonatal Health

John Madigan, DVM, MS, Dipl. ACVIM, ACAW, professor in the Department of Medicine and Epidemiology at the University of California, Davis, School of Veterinary Medicine, presented a lecture entitled “Why Foals Die” at the 2013 American College of Veterinary Internal Medicine Forum, held June 12-15 in Seattle, Wash. The lecture focused on neonatal maladjustment syndrome (NMS), which is characterized by neurological abnormalities and death or serious brain damage in young foals. The condition is major challenge to equine medicine and requires better understanding and treatment options.

NMS cases are rare, occurring in less than 1% of live births. Despite extensive research and efforts to develop treatments, NMS remains incurable in the vast majority of cases. Madigan hypothesized that a possible reason neurosteroids might persist and prompt NMS in some cases is that normal signaling events during the birthing process don’t take place properly. For instance, he said, if a foal passes rapidly through the birth canal or is delivered via cesarean section, normal transition signals that would prompt a reduction in fetal pregnane levels might not take place, leaving the foal with elevated neurosteroids.

Recent Research

These disparities prompted Madigan and colleagues to take a closer look at what else might cause NMS. They found that neonates, especially premature ones, were exhibiting NMS-like behaviors and elevations in neurosteroids. These findings suggested that NMS may not be the result of a single, definable abnormality.

Madigan and colleagues administered a pregnane called allopregnanolone to healthy equine neonates in the experimental setting to produce clinical signs consistent with NMS (e.g., the foals don’t want to nurse, don’t stand, are listless). They used an electroencephalogram to evaluate electrical impulses in the foals’ brains. He said the readings were consistent with slow wave sleep while the foals were standing.

Allopregnanolone is a natural occurring neurosteroid that is released in the brain and acts as a modulator of neurotransmitter activity. It is responsible for the state of sleep that occurs in the transition between the quiet sleep and rapid eye movement states. The foals were given allopregnanolone and showed a consistent reduction in brain waves, suggesting a decrease in activity and the presence of slow wave sleep.

In addition, the foals exhibited two other common signs of NMS: paroxysmal (spasmodic or seizurelike) behaviors and alterations in states of consciousness, altered behavior, and responsiveness to stimuli. These effects were short lasting, and foals returned to normal after administration.

Another theory, he said, is that some neonates revert to fetal state in the uterus, or “in utero” state. This can occur when the mare is in pain or stressed, or when the foal is in distress. In these cases, the foal may show signs of inactivity, listlessness, and decreased responsiveness, consistent with NMS.

Behavioral alterations in states of consciousness may also occur due to alterations in hypothalamic-pituitary-adrenal axis function, which is also associated with NMS. This axis regulates the pregnane secretion so the foal can transition to birth consciousness.

The signal for the foal to “wake up” involves the hypothalamic pituitary adrenal axis, which they believe down regulates the pregnancy. Madigan hypothesized that a possible reason neurosteroids might persist and prompt NMS foals is that normal signaling events during the birthing process don’t take place properly. For instance, he said, the internal thoracic (chest) area in healthy foals to induce recumbency, non standing, then allows him to stand, nurse, and run. Squeeze called squeeze this method might signal to the foal that he is outside the uterus and that it’s time for pregnane production to decrease, allowing him to stand, nurse, and run. Squeeze was used in recent studies on pigs and foals to observe if it could induce NMS-like behaviors.

Potential Therapeutic Options

Based on these findings, the concept of reducing post birth circulating plasma pregnanes would seem to offer a potential new therapeutic option for NMS foals and perhaps other ill foals which appear weak and are not able to stand. In addition, the concept of reducing post birth circulating plasma pregnanes might also help treat chronic pain conditions in humans. This could have a significant impact on neonatal health.

One potential therapeutic option Madigan and his colleagues have evaluated is the use of a technique they developed called “squeeze.” The technique involves squeezing the foal’s chest to induce recumbency, non standing, then allows him to stand, nurse, and run. Squeeze was used in recent studies on pigs and foals to observe if it could induce NMS-like behaviors.

For many years, Madigan said, veterinarians and researchers believed neonatal maladjustment syndrome (or NMS) is a result of hypoxia, brain injury, or trauma. However, recent studies have shown that NMS may be caused by alterations in neurosteroid levels. These steroids are produced in the brain and act as modulators of neurotransmitter activity.

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According to Madigan, there are several implications of these findings. First, it highlights the importance of understanding the role of neurosteroids in the brain and their potential role in the development of NMS. Second, it suggests that identifying the factors that contribute to altered neurosteroid levels in the brain could lead to new strategies for preventing or treating NMS.

Madigan noted that his team’s research has shown that other ill neonatal foals with weakness and lethargy believed to be due to hypoxia, brain injury, or trauma may also have elevated neurosteroids. This suggests that neurosteroids may play a role in a variety of neurological disorders in neonatal foals.

These findings also have implications for human health. Neurosteroids are also implicated in the development of neurological disorders in humans, including autism and schizophrenia. Understanding the role of neurosteroids in the brain of neonatal foals could provide new insights into the mechanisms underlying these disorders in humans.

In conclusion, Madigan said, the findings from his research highlight the importance of understanding the role of neurosteroids in the brain and their potential role in the development of NMS. Identifying the factors that contribute to altered neurosteroid levels in the brain could lead to new strategies for preventing or treating NMS. Understanding the role of neurosteroids in the brain of neonatal foals could also provide new insights into the mechanisms underlying neurological disorders in humans.

He said that while the research is ongoing, preliminary findings suggest that allopregnanolone might be a potential therapeutic option for NMS foals and other ill foals. He noted that future studies will evaluate this more closely.

The research is continuing, and Madigan said that his team is exploring the potential use of other techniques to reduce neurosteroid levels in the brain of neonatal foals. He noted that his team is evaluating the possible use of a technique he and his colleagues developed called “squeeze.” The technique involves squeezing the foal’s chest to induce recumbency, non standing, then allows him to stand, nurse, and run. Squeeze was used in recent studies on pigs and foals to observe if it could induce NMS-like behaviors.

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