Update on the Management of Neonatal Sepsis in Horses

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KEYWORDS

• Severe sepsis • Septic shock • Fluid therapy • Antimicrobials • Vasoactive agents • Antimediator therapy • Glucose control • Corticosteroids

KEY POINTS

- The diagnosis of sepsis, severe sepsis, and septic shock is based on clinical judgment. None of the associated clinical signs or immediately available laboratory findings are specific for sepsis, so management must be initiated before a definitive diagnosis is reached.
- As important as selecting the most appropriate antimicrobial is, both early initiation of treatment and insuring the dose and frequency will allow adequate drug levels in the face of sepsis and shock, which will change many aspects of the antimicrobial's pharmacodynamics.
- Plasma therapy may not only deliver useful immunoglobulins and other immunologically important factors but can also serve other important functions, such as aiding in the repair of the damaged endothelial glycocalyx layer, which is vital in preserving fluid balance and volemia in the neonate.
- Fluid therapy should follow the "Goldilocks approach." Too much fluid is dangerous. Too little fluid is dangerous. A balance is needed.
- Although many approaches have been tried, no antimediator therapy has been successful in mitigating the damage caused by uncontrolled sepsis and, in fact, many therapies which are based on experimental models would seem be rational have actually increased mortality in clinical trials in man.

INTRODUCTION

Development of a bacterial infection is a common cause of morbidity and mortality in neonatal foals. It is not only the most common cause of fatality during this period but also the most important comorbidity of other neonatal diseases, such as prematurity and neonatal encephalopathy, increasing the risk of a more complicated course and a fatal outcome. The concept of sepsis is ancient, being described by both the Egyptians and Hippocrates,[1,2] but it was Schottmueller[3] in 1914 who first established a

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link between the presence of pathogenic microbes in the bloodstream and the development of systemic symptoms and signs. In Schottmueller's words, "Septicemia is a state of microbial invasion from a portal of entry into the blood stream which causes signs of illness." Sepsis, the host's response to infection, is a continuum of clinical syndromes ranging from signs, such as fever and catabolism secondary to a localized, well-controlled infection, to septic shock with its refractory shock and its accompanying multiorgan dysfunction. Sepsis results from the dysregulation of the systemic host response to cascading inflammatory and anti-inflammatory mediators induced by infecting organisms.[4]

During the last 2 decades, as the complexities of the sepsis response have begun to be understood, many ideas have emerged aimed at managing clinical sepsis by mitigating the damage caused by the inflammatory response while simultaneously preserving the ability to purge the initiating microbial invaders as well as resist secondary infections. Working from bench to patient side, many initially promising therapies have often fallen flat, which is a reflection of the complexity of the response with multiple redundant pathways making control of the cascading responses problematic. The evidence of efficacy in the treatment of sepsis comes from large blinded clinical studies in adult humans. There is some evidence from human neonatal studies, but unfortunately, there are no adequately powered clinical studies in septic neonatal foals to lend evidence to any of the approaches to therapy. Therefore, at best, evidence has been "borrowed" from human trials to direct many of the clinical approaches to septic neonatal foals. This approach is dangerous because the host response may differ greatly.

There is some information from sepsis models in foals and horses, but we need to heed the lesions from human medicine that many of the most promising approaches to managing sepsis based on models have actually resulted in increased fatality rates when used in clinical settings.[4,5] Another important lesson to learn from human medicine is the reliance on models that use endotoxin to induce sepsis may result in misplaced confidence in the usefulness of the therapy in clinical situations.[5] Although endotoxin models may help in understanding many aspects of sepsis, more clinically relevant models that involve multiple initiators of sepsis are more likely to yield more valuable therapeutic information.[2,5] The movement to more clinically realistic models of sepsis would be a big step forward in the development of effective management approaches to equine sepsis. Until then, the most reliable methods to manage sepsis in the neonatal foal will remain grounded on the same cornerstones that were established more than 2 decades ago: infection control (antimicrobials, plasma, drainage when possible), cardiovascular support (fluids, inopressors), respiratory support (intranasal oxygen insufflation/ventilation), and nutritional support.[6]

THE SEPTIC NEONATAL FOAL

Many terms have been used to define "sepsis" since Schottmueller first established a link between the clinical signs and infection.[3] The often interchangeable use of terms, such as infection, septicemia, bacteremia, and sepsis syndrome, has led to some confusion. However, using the concept of sepsis as the host response to infection and a hierarchy of terms based on severity, the associated terminology becomes relatively simple (**Box 1**).[4] In 1991, Bone and colleagues[7] coined the concept of systemic inflammatory response syndrome. It is a useful term when describing the pathogens of sepsis but their original definition, based on patient temperature, heart rate, respiratory rate or P_{CO_2}, and white blood cell count, was designed to cast a broad net to include as many patients as possible in early sepsis therapeutic trials with the knowledge that the nonspecific nature of the inclusion criteria would mean enrolling many