BOVA
Your prescription, your way.

1 / 304-318 Kingsway
Caringbah NSW 2229
T: 02 9525 3044 F: 02 9542 7645
scripts@bovacompounding.com.au
www.bovavet.com.au

Antimicrobial selection in the neonatal foal

Ben Sykes BSc BVMS MS Dip ACVIM Dip ECEIM MBA

Introduction

Infectious disease is an important cause of morbidity and mortality in the neonatal foal with approximately 8% of foals affected by some form of infectious complication in the first 30 days of life in one recent study[1]. Early recognition and treatment of infectious complications in the neonatal period is important to maximise outcome. The purposes of this article are to review antimicrobial selection in the neonatal foal and the role of passive transfer of colostral antibodies. The definition of a neonatal foal varies in the literature but for the purposes of this article the focus is on the first 1- 2 weeks of life.

Antimicrobials

Antimicrobials are indicated where infection is documented or where a high clinical index of suspicion is present. However, in line with the profession's obligation of responsible antimicrobial stewardship, the indiscriminate use of antimicrobials is discouraged and there appears to be no benefit of wide spread antimicrobials for prophylaxis, as discussed below.

Blood culture is an important tool in tailoring antimicrobial therapy in individual patients. Its use does not affect initial antimicrobial selection but a positive culture can prove useful in selecting subsequent antimicrobials in patients that are non-responders or that require long duration therapy. Given the costs associated with the collection of blood culture, consideration should be given to the likelihood of a positive culture being obtained. In the author's experience it is most useful in critically ill foals with obvious septicaemia while its utility in foals with mild disease is questionable. Considering this the author's approach is to apply its use to selected cases where it is believed that the likelihood and implications of a positive culture justify the additional expense.

In the absence of culture results to guide antimicrobial selection the choice is empirical and based upon a number of factors with spectrum and penetration the most important primary factors. Spectrum is often discussed in isolation but it is critical that penetration be considered as effective antimicrobial penetration is critical to a successful therapeutic outcome. For many of the disease conditions seen in the neonatal period, such as septicaemia and septic arthritis, all of the commonly used antimicrobials will achieve therapeutic concentrations at the site of infection, however penetration becomes critical for conditions such as osteomyelitis and meningitis where many of the water soluble drugs (penicillin, ceftiofur, gentamicin/amikacin) do not achieve therapeutic concentrations at the site of infection.

Spectrum is a critical determinate of efficacy and in order to logically choose an appropriate antimicrobial(s) an understanding of common pathogen distribution and their sensitivity patterns is needed. A wide range of pathogens have been isolated from neonatal foals with gram-negative organisms the most

BOVA
Your prescription, your way.
1 / 304-318 Kingsway
Caringbah NSW 2229
T: 02 9525 3044 F: 02 9542 7645
scripts@bovacompounding.com.au
www.bovavet.com.au

common. However, gram-positive organisms make up a significant percentage of isolates and it has been suggested that, similar to trends observed in human medicine, that they may be increasing in prevalence[2]. Considering this, broad spectrum antimicrobial therapy is indicated in most cases of neonatal infectious disease.

Fortunately a wide range of broad spectrum antimicrobials are available for use in the foal including ceftiofur (+/- gentamicin/amikacin), penicillin/ampicillin + gentamicin/amikacin combinations, tetracyclines, trimethoprim-sulphur combinations (TMPS) and chloramphenicol. Commonly used dose rates for each antimicrobial are shown in table 1. Regional variations are likely to exist for bacterial sensitivities but the best available evidence for the Australian situation is a 2008 report from Scone, NSW[2]. In that study chloramphenicol was the single most efficacious antimicrobial with 78% of isolates reported as sensitive compared with 72% and 68% of isolates for penicillin + gentamicin and ceftiofur + gentamicin combinations, respectively. If multi-drug resistant organisms were excluded the efficacy of the penicillin + gentamicin and ceftiofur + gentamicin combinations increased to 92% and 96%, respectively[2]. Tetracycline and TMPS combinations were moderately effective with 69% and 68% of isolates sensitive, respectively.

In applying this information to an individual patient the author's approach is to then consider a number of other factors such as ease of administration, cost and availability of the antimicrobial as well as the severity of illness in the patient. The use of oral antimicrobials (chloramphenicol, doxycycline and TMPS) is reasonable in patients with mild disease and a functional gastrointestinal tract, while parental administration is preferred in more severely affected foals and/or those with gastrointestinal disease. Where oral antimicrobials are initiated as front line therapy close observation is important to monitor the patient for deterioration, in which case a switch to systemic administration may be indicated.

Two antimicrobials warrant further specific, discussion; namely gentamicin and chloramphenicol. Of the antimicrobials discussed gentamicin is unique in that it is a concentration dependent antimicrobial. As such, its efficacy is primarily dictated by the peak serum concentration achieved which, being a water soluble antimicrobial, is in turn dictated by the volume of distribution in the patient and the route of administration. Foals have a relatively higher percentage of their bodyweight as water when compared with adults. The implication of this is that when a standard mg/kg dose of gentamicin is administered to a foal the peak serum concentration achieved in foals is less than that achieved in adults, and as such the efficacy of the drug is reduced. To compensate for this greater dilution, a higher mg/kg must be administered to achieve the same peak serum concentration. The author routinely uses 10 – 12 mg/kg IV SID for this purpose, reducing back to 8.8 mg/kg IV SID by two weeks of age. Similarly, gentamicin should not be administered by intra-muscular injection because the peak serum concentration, and thus efficacy, is reduced compared to intravenous administration.

The other antimicrobial that warrants particular mention is chloramphenicol primarily because of human health considerations. Exposure to chloramphenicol in people has been linked with the development of aplastic anaemia and "grey-baby" syndrome. As such it should not be handled by pregnant women and it

BOVA
Your prescription, your way.
1 / 304-318 Kingsway
Caringbah NSW 2229
T: 02 9525 3044 F: 02 9542 7645
scripts@bovacompounding.com.au
www.bovavet.com.au

should not be used in horses destined for human consumption. However, despite the human health concerns chloramphenicol is still widely used in human medicine, particularly in ophthalmic preparations, and it is the author's opinion that its judicious use is justified, particularly where the sensitivity patterns of common isolates supports its use.

Failure of passive transfer

Failure of passive transfer results from inadequate absorption of colostrum, and in particular colostral antibodies, in the first 24 hours of life. An incidence of partial or complete failure of passive transfer (as defined by a serum IGG of < 800 mg/dl) exceeding 30% has been reported in NSW where no specific intervention was employed[3]. The factors that contribute to failure of passive transfer are wide and varied but can be broken down into three broad types;

- Pre-existing neonatal disease: Any disease that limits the foal's capacity to stand and nurse in a timely manner is likely to increase the risk of failure of passive transfer. This includes diseases such as septicaemia, neonatal hypoxia and meconium impaction. Further, some diseases such as septicaemia result in the rapid consumption of immunoglobulins. Particular attention should be paid to this group as early recognition and treatment of both the primary disease and any secondary complications such as sepsis and/or failure of passive transfer are likely to improve outcome.
- Post-partum maternal disease: This includes diseases such a post-partum colic wherein the foal is normal at birth but factors related to the mare prevent it from nursing adequately. In such cases particular attention should be paid to the foal's colostral transfer state and the foal should be closely monitored for secondary disease.
- Poor colostral quality/quantity: In such cases both the mare and foal are normal throughout the peri- parturient period but failure of passive transfer occurs because the quantity and/or quality of colostrum produced by the mare are inadequate. Similar to the situation where post-partum maternal factors influence the ability of the foal to nurse, the foal itself is initially normal but at an increased risk of disease due to its impaired immune system.

The exact level of IGG required for adequate immunity in the neonatal foal has not been well demonstrated. In general the author accepts a cut-off of > 400 mg/dl in foals that are otherwise healthy (such as foals influenced by post-partum maternal disease or poor colostral quantity/quality or otherwise normal foals). In contrast, where the risk of neonatal disease is higher, such as foals with pre-existing disease, or in foals born to mares with pre-partum disease, such as ascending placentitis, a cut off of > 800 mg/dl is preferred.

Prophylactic interventions

Given the implications of neonatal septicaemia it has been suggested that prophylactic antimicrobials may be beneficial. However, a recent study demonstrated that the administration of prophylactic antimicrobials to otherwise healthy foals does not decrease the incidence of infectious disease[1].

BOVA
Your prescription, your way.
1 / 304-318 Kingsway
Caringbah NSW 2229
T: 02 9525 3044 F: 02 9542 7645
scripts@bovacompounding.com.au
www.bovavet.com.au

Further, the routine administration of antimicrobials is likely to increase selection pressure and result in an increased rate of development of multi-drug resistant strains of bacteria, an effect that is already being seen with 32% of isolates in one recent Australian considered to be multi-drug resistant[2]. As such, the routine administration of antimicrobials is not recommended. Instead foals considered at high risk of disease should be monitored closely and particular attention should be paid to their passive transfer status.

Along these lines it has been shown that a proactive approach using targeted colostral supplementation to the management of failure of passive transfer can reduce the incidence to as low as approximately 5% with <1% of foals reported to have an IGG of < 400 mg/dl[4]. These findings support this approach and the author believes that management of the foal in the immediate post-partum period should focus as much as possible on ensuring that the foal is healthy with adequate immunity rather than the use of antimicrobials to provide "protection" from infectious disease.

Conclusions

The management of infectious disease in neonatal foals centres on an understanding of appropriate antimicrobial selection and maximisation of the foal's immunity. A variety of broad spectrum antimicrobials can be used in the foal depending on the severity of disease, likely pathogen distribution and sensitivity, and available antimicrobials. Prophylactic antimicrobial therapy is ineffective and instead management in the immediate post-parturient period should focus on the recognition and treatment of failure of passive transfer and close observation for the development of disease.

x

Table 1 – Dose rates for commonly used antimicrobials in neonatal foals

Antimicrobial	Dose	Comments
Penicillin (Procaine)	22 mg/kg IM BID	Rarely indicated as sole therapy. Combined with gentamicin.
Ceftiofur	5 - 10 mg/kg IV/IM BID	Can be used as sole therapy or in combination with gentamicin.
Gentamicin	10 – 12 mg/kg IV SID	Not used as sole therapy. Use combined with penicillin or ceftiofur.
Chloramphenicol	50 mg/kg PO QID	
Oxytetracycline	5 mg/kg IV BID	
Doxycycline	10 mg/kg PO BID	
Trimethoprim-Sulphur	30 mg/kg PO BID	

BOVA
Your prescription, your way.

1 / 304-318 Kingsway
Caringbah NSW 2229
T: 02 9525 3044 F: 02 9542 7645
scripts@bovacompounding.com.au
www.bovavet.com.au

References

1. Wohlfender, F. D. *et al.* Diseases in neonatal foals. Part 1: The 30 day incidence of disease and the effect of prophylactic antimicrobial drug treatment during the first three days post partum. *Equine Vet. J.* **41,** 179–185 (2009).

2. Russell, C. M., Axon, J. E., Blishen, a & Begg, a P. Blood culture isolates and antimicrobial sensitivities from 427 critically ill neonatal foals. *Aust. Vet. J.* **86,** 266–71 (2008).

3. Tyler-McGowan, C., Hodgson, J. & Hodgson, D. Failure of passive transfer in foals: incidence and outcome on four studs in New South Wales. *Aust. Vet. J.* **75,** 56–59 (1997).

4. Nath, L. C., Anderson, G. A., Savage, C. J. & McKinnon, A. O. Use of stored equine colostrum for the treatment of foals perceived to be at risk for failure of transfer of passive immunity. *J. Am. Vet. Med. Assoc.* **236,** 1085–90 (2010).