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Short communication

Initial antimicrobial treatment of foals with sepsis: Do our choices make a difference?

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ABSTRACT

The study objectives were to provide cumulative antimicrobial susceptibility data at the patient level and to evaluate the effect of initial antimicrobial treatment on survival in foals with sepsis. Foals below 30 days of age with a diagnosis of sepsis, confirmed by isolation of bacteria from normally sterile sites on the day of hospital admission, were included. Susceptibility testing was performed using the broth microdilution procedure. In total, 213 foals and 306 bacterial isolates were included. The likelihood of survival for foals from which all bacteria were susceptible to the initial antimicrobial treatment was 65.4% (n = 106/162; 95% confidence interval (CI) 57.6% to 72.7%) versus 41.7% (n = 10/24; 95% CI 22.1% to 63.4%) if one or more isolates were resistant (relative risk 1.57, 95% CI 0.96 to 3.06). Based on this study, amikacin combined with ampicillin remains an appropriate antimicrobial drug combination for initial treatment of foals with sepsis.

Several studies have reported antimicrobial susceptibility of bacteria isolated from foals with sepsis (Brewer and Koterba, 1990; Marsh and Palmer, 2001; Hollis et al., 2008; Russell et al., 2008; Sanchez et al., 2008; Theelen et al., 2014; Hytychová and Bezdeková, 2015). However, those studies did not consider that sepsis in foals is often polymicrobic, with a reported incidence ranging from 8% to 45% (Brewer and Koterba, 1990; Gayle et al., 1998). In polymicrobic infection, the antimicrobial susceptibility patterns of the bacteria involved often differ. For clinical decision-making, cumulative antimicrobial susceptibility data at foal level is more useful than data at isolate level. The first objective of this study was therefore to report on cumulative antimicrobial susceptibility data at foal level.

Legislation for prescribing antimicrobials is becoming increasingly restrictive, encouraging veterinarians to minimise use of antimicrobials. Therefore, it is important to evaluate the efficacy of antimicrobial treatment. The second objective of this study was to evaluate potential differences in survival between foals initially treated with antimicrobial drugs to which all of the bacteria isolated at hospital admission were susceptible ('correct' initial antimicrobial therapy) and foals treated with antimicrobial drugs to which at least one of the bacteria was resistant ('incorrect' initial antimicrobial therapy). The third objective was to evaluate the effect of type of infection (single organism versus polymicrobic infection) on survival.

All foals below 30 days of age admitted to the University of California, Davis, USA, between 1 January 1990 and 31 December 2015 with a diagnosis of sepsis, confirmed by isolation of bacteria from normally sterile sites on the day of hospital admission, were included. Only foals for which complete susceptibility data were available for all isolated bacteria were included. Necropsy culture results were included if the necropsy was performed on the day of hospitalisation and all bacteria were isolated from more than one normally sterile site, to minimise the likelihood of including contaminated samples.

Bacterial isolation, identification, classification and antimicrobial susceptibility testing were performed as described previously (Theelen et al., 2014). Breakpoints published by the Clinical & Laboratory Standards Institute (CLSI) were used to determine susceptibility, occasionally modified based on equine research (See Appendix: Supplementary Table S1 in the online version at DOI: 10.1016/j.tvjl.2018.11.012) (CLSI, 2015).

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Table 1
Cumulative susceptibility at 'foal level' of bacteria isolated from foals with sepsis at hospital admission (UC Davis, USA) between 1 January 1990 and 31 December 2015.

Antimicrobial drug (combination)	Number of foals	Percentage of foals from which all isolates were susceptible	95% confidence interval
Amikacin	213	63.4%	56.5–69.9
Amikacin + penicillin	210	88.6%	83.5–92.5
Amikacin + ampicillin	213	91.5%	87.0–94.9
Gentamicin	213	62.0%	55.1–68.5
Gentamicin + penicillin	211	82.0%	76.1–86.9
Gentamicin + ampicillin	213	83.6%	77.9–88.3
Ceftiofur	211	86.3%	80.9–90.6
Ceftiofur + amikacin	211	89.6%	84.6–93.4
Ceftizoxime	194	89.7%	84.5–93.6
Chloramphenicol	207	81.6%	75.7–86.7
Enrofloxacin	211	82.9%	77.2–87.8
Imipenem	175	92.6%	87.6–96.0
Trimethoprim/sulfa-methoxazole	213	59.6%	52.7–66.3

Table 2
Survival of foals with sepsis in relation to the choice of initial antimicrobial treatment at UC Davis (USA) between 1 January 1990 and 31 December 2015.

Initial antimicrobial therapy	Total number of foals	Survival (%)	Non-survival (%)	RR[a]	95% CI[b]
'Correct'[c]	162	106 (65.4%)	56 (34.6%)	1.57	0.96–3.06
'Incorrect'[d]	24	10 (41.7%)	14 (58.3%)	1.0	

[a] RR, relative risk.
[b] 95% CI, 95% confidence interval.
[c] All bacteria isolated at hospital admission were susceptible to the initial antimicrobial therapy.
[d] At least one of the bacteria isolated at hospital admission was resistant to the initial antimicrobial therapy.

Table 3
Survival of foals with sepsis in relation to the type of infection at UC Davis (USA) between 1 January 1990 and 31 December 2015.

Type of infection	Total number of foals (%)	Survival (%)	Non-survival (%)	RR[a]	95% CI[b]
All types of infection	213 (100%)	118 (55.4%)	95 (44.6%)		1.10–2.29*
Single organism infection	149 (70.0%)	92 (61.7%)	57 (38.3%)	1.52	
Polymicrobic infection	64 (30.0%)	26 (40.6%)	38 (59.4%)	1.0	

[a] RR, relative risk.
[b] 95% CI, 95% confidence interval.
* $P < 0.05$.

In total, 213 foals and 306 bacterial isolates were included (See Appendix: Supplementary Table S2 in the online version at DOI: 10.1016/j.tvjl.2018.11.012). The percentages of foals from which all bacteria isolated at hospital admission were susceptible to the tested antimicrobial drug or combinations are presented in Table 1. Based on these data, the combination of amikacin and ampicillin appears suitable for empirical treatment in foals with sepsis. Based on the WHO list of critically important antimicrobials,[1] and the results of the current study, there is limited justification for the use of enrofloxacin, ceftizoxime or other third generation cephalosporins as initial antimicrobial therapy without bacteriological culture and susceptibility testing, in the absence of contraindications to use amikacin or ampicillin. Carbapenems such as imipenem should be reserved for use in human patients and should not be used in veterinary species.[2]

To evaluate the effect of initial antimicrobial treatment on outcome, information on initial antimicrobial treatment was required; otherwise foals were excluded from this analysis. Foals that died or were euthanised at hospital admission and did not receive antimicrobial treatment were excluded from this part of the study. Outcome was defined as 'survival' if the foal survived until discharge or 'non-survival' if the foal died or was euthanised during hospitalisation. Commercial software was used for statistical analysis (StatXact Version 11, Cytel Software Corporation). The relative likelihood for survival reported as risk ratio (RR) and 95% confidence intervals (95% CI) are presented.

Initial antimicrobial treatment was known for 186 foals. If all bacteria isolated from a single foal were susceptible to the initial antimicrobial treatment, the likelihood of survival was 65.4% ($n = 106/162$; 95% CI 57.6% to 72.7%), compared to 41.7% ($n = 10/24$; 95% CI 22.1% to 63.4%) if one or more bacteria were resistant (RR 1.57; 95% CI 0.96 to 3.06, $P = 0.054$) (Table 2). A similar result was reported in a study in human patients with sepsis (Harbarth et al., 2003). Interestingly, 34.6% ($n = 56/162$; 95% CI 27.3% to 42.4%) of the foals died despite receiving 'correct' antimicrobial therapy and 41.7% ($n = 10/24$; 95% CI 22.1% to 63.4%) of foals survived despite being treated with 'incorrect' antimicrobial drugs initially, highlighting the influence of other factors on outcome.

All 213 foals were included in the evaluation of the effect of type of infection on outcome. Thirty per cent of foals ($n = 64/213$; 95% CI 24.0% to 36.7%) had polymicrobic infection. Foals with single organism infection had a significantly higher likelihood of survival (61.7%; $n = 92/149$; 95% CI 53.4% to 69.6%) compared with foals with polymicrobic infection (40.6%; $n = 26/64$; 95% CI 28.5% to 53.6%) (RR 1.52; 95% CI 1.10 to 2.29; $P = 0.005$) (Table 3). This finding is in contrast to previous studies in other geographical regions (Hollis et al., 2008; Sanchez et al., 2008).

[1] See: WHO, 2016, WHO List of Critically Important Antimicrobials (CIA) – 5th Revision. http://www.who.int/foodsafety/publications/antimicrobials-fifth/en/ (accessed 14 November 2017).
[2] See: British Small Animal Veterinary Association (BSAVA) Medicine Guide – Antibacterials https://www.bsava.com/Resources/Veterinary-resources/Medicines-Guide/Antibacterials (accessed 21 February 2018).

Potential limitations of this study are that findings could be geographically restricted, cases might have been excluded because essential information was missing, and administration of antimicrobial drugs before hospitalisation could have influenced bacterial culture results. Unfortunately, information on other factors potentially affecting outcome was not consistently available. Finally, some foals may have been euthanised based on economic considerations.

Our results indicate that empirical treatment of foals with antimicrobials to which the infecting bacteria are susceptible has a positive effect on outcome and supports the common practise of initiating antimicrobial treatment prior to culture and susceptibility results being available. Nevertheless, it remains important to collect samples for bacteriological culture from these foals to evaluate the potential efficacy of the chosen therapy. Based on this study, the combination of amikacin and ampicillin remains an appropriate choice for initial treatment of foals with sepsis.

Conflict of interest statement

None of the authors of this paper have a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

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