Fluid therapy and sepsis in ruminants

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Because they are prey animals, ruminant newborns can quickly adjust to their environments, stand and join the herd. Also, these species show robustness, hiding signs of illness as long as possible to prevent being targeted by predators. Whereas the robustness would actually provide calves with better survival chances, in modern farming situations their nature to hide clinical signs often results in a too late disease detection by the producers and poorer prognosis. Therefore, bovine veterinarians are frequently confronted with the critically ill calf. They need to deal with these patients in field situations, without access to advanced measurement devices and a legally limited pharmaceutical options.

Key features of the critically ill patient are severe respiratory, cardiovascular or neurological derangement, often in combination. The different types of shock can be part of the presentation. Especially newborns and calves aged < 3 weeks old are presented in a critically ill state. In newborn calves, metabolic and respiratory acidosis (dystocia and maladaptation to extrauterine live), neonatal respiratory distress syndrome, congenital heart defects, hemorrhage and septicemia are among the most common differential diagnoses. In the first three weeks, enteritis (Enterotoxic Escherichia coli, rotavirus, coronavirus and Cryptosporidium parvum) is the leading disease. As a consequence, animals dehydrate, develop acidosis, ion disturbances, malabsorption and hypoglycemia. If this situation of negative energy balance and dehydration persists, renal failure, a cachectic state and negative effects on innate immunity develop. Very often, calves with neonatal diarrhea, either develop pneumonia at the same time or are more susceptible to pneumonia in later live (Pardon, 2013). Older studies show that of all calves with diarrhea, both critically ill or not, about 30% is septicemic (Fecteau et al., 1997a). Calves are born almost agammaglobulinemic and need to consume colostrum to assure adequate passive transfer of immunity. However, failure of passive transfer, is very common in cattle farming (20-40% of the animals), and one of the main risk factors for septicemia (Lofstedt et al., 1999). In contrast to other species, calves are prone to the development of D-lactic acidosis, due to dysbiosis (Lorenz, 2009). Signs of this condition include severe depression, tachypnea, abnormal posture and an instable gait. A reduced or incomplete palpebral reflex was identified as a reliable clinical indicator for the degree of D-lactic acidosis in calves (Trefz et al., 2012). Therefore, D-lactic acidosis can be life-threatening condition as such, and an important differential diagnosis for a septicemic calf.

This lecture aims at giving practitioners a state of the art on diagnosis and treatment of sepsis in calves. A tone of ‘scepsis about sepsis’ will never be far away, given the current possibilities for food animals in practice. A paper on this talk with full scientific reference is available elsewhere (Pardon et al., 2018).

To successfully treat sepsis, early administration off appropriate antimicrobials is crucial. In veterinary practice the critically important fluoroquinolones and cephalosporin’s are popular
molecules for this indication, because of their bactericidal effects, broad-spectrum activity and relatively low resistance levels. In different European countries legislation has placed the use of critically important antimicrobials under strict terms. In Belgium for example, these molecules can only be used in food animals when (1) the patient is examined by a veterinarian, (2) the disease has a bacterial etiology, (3) after adequate sampling and bacteriological culture in an accredited laboratory, (4) identification of the bacterial strain which likely caused the infection and (5) comparison of the strains susceptibility with at least 7 other not critically important antimicrobials, belonging to at least 5 different antimicrobial classes. The legislation allows the following exceptions in which critically important antimicrobials can be used without previous laboratory confirmation: (1) if no laboratory result is reached or sampling is impossible (in this case the veterinarian can use the molecules based on recent scientific data); (2) if laboratory results fulfilling the first 5 requirements above are available for the same group of animals in the same farm (valid for 6 months in veal calves, and 1 year for other cattle operations) and finally (3) for ‘urgency’ reasons to save the life of a single animal. In the latter case the veterinarian needs to treat the patient him/herself, after a clinical examination and obligatory sampling and culturing. As soon as an antimicrobial susceptibility test result is reached, re-assessment of antimicrobial therapy and de-escalation to a non-critically important antimicrobial is obliged, whenever possible. In Belgium and the Netherlands, formularies to advice veterinarians on their antimicrobial choice are available. Given the different advices currently provided for the different species, it is clear that merging the priority to minimize fluoroquinolone and cephalosporin use with the desire to work evidenced based is particularly difficult for sepsis.

Key information is that approximately 30% of diarrheic calves is septicemic, with no further insights on what proportion has sepsis, severe sepsis or septic shock (Fecteau et al., 1997a). To predict sepsis, largely three published models/scoring systems for calves are available, with reported sensitivity and specificity ranging between 39% and 77%, and 90.6% and 75%, respectively (Fecteau et al., 1997b and Lofstedt et al., 1999). However, evaluation of these models on a new dataset of critically ill calves, showed very poor sensitivity and specificity. Most laboratory parameters can improve the diagnostic accuracy of these models only with some percentages (Lofstedt et al., 1999). As in humans, procalcitonin is the most promising biomarker for sepsis, and recently a cut off of >68 pg/mL was suggested (Sensitivity= 77%; Specificity= 79%) (Bonelli et al., 2018). Cow-side tests or faster laboratory turnaround times are required to make this test available for practice. The world health organization approach for antimicrobial decision making will be applied to the case of sepsis in calves. In contrast to humans, sepsis in calves is predominantly of gram negative origin, with mainly Escherichia coli and to a lesser extend Salmonella spp. (Fecteau et al., 2009). The gastro-intestinal tract and umbilicus are the most likely source of infection in calves, although no hard evidence is available. Recommended samples for etiological diagnosis are sterile taken blood cultures (enriched environment, eg. Bactec systems). A single, large volume sample is recommended. In some cases of outbreaks of septicemic bacteria such as Histophilus somni, Mycoplasma bovis or Salmonella spp. a respiratory or faecal sample might be sufficient. MALDI-TOF MS offers promising technology to reduce the turn-around time between sampling and availability of the antibiogram. For example, etiological bacteria can be detected from blood cultures within 3-6 hours after sampling (Morgenthaler and Kostrzewa, 2015). An antibiogram for bovine pathogens can be available as quickly as within 3 hours after culture, with better accuracy than the disc diffusion antibiogram (Van Driessche et al., 2018). E. coli and Salmonella spp. are both
renowned for their accumulation of resistance genes. In our clinic, *E. coli* isolated from sepsis cases show high levels of resistance to sulfonamides-trimethoprim, oxytetracycline, doxycycline, and amoxicillin, whereas recent *Salmonella spp.* isolates showed little resistance. Fast (< 1h) administration of a bactericidal, broad spectrum antimicrobial remains the cornerstone to survive sepsis in every species. Rapid administration of cristalloids at 30 mL/kg body weight is recommended for humans (Dellinger et al., 2017). A major difference with other species is D-lactic acidosis in calves, which requires intensive treatment with hypertonic bicarbonate solutions. Corticosteroids did not show benefits for survival, not in humans nor calves (Plessers et al., 2012, Aronoff et al., 2012). In contrast to humans, in calves ketoprofen significantly reduced the rise in temperature and respiratory rate in an endotoxin challenge model (Plessers et al., 2016). Prognosis of sepsis in calves is poor with mortality rates ranging between 46.8% and 77.1% in the handful of studies available (Fecteau et al., 1997b, Trefz et al., 2017). In humans, the disastrous effect of the use of an inappropriate antimicrobial (antimicrobial for which the bacteria are resistant) as first intention treatment on survival (~42%) has been clearly documented (Kumar et al., 2009).

In conclusion, a lot needs to be done before bovine veterinarians will have reliable diagnostic tests to identify sepsis patients in the field. The inverse interest of on the one hand working evidence based and maximizing survival chances of the animal and on the other safeguarding products for human medicine, will remain a hot topic in the years to come. The least what practitioners can do is attempting to work as much evidence based as possible, limiting the use of critically important antimicrobials to selected case, underbuilding their decision with a laboratory diagnosis.

References


