CONCENTRATE (PharmaCOkiNetics of ampiCillin/sulbactam in dogs with acutE kidNey injury of infecTious oRigin during the polyuric phase after renAl replacement ThErapy)

Background

Infectious AKI

Acute kidney injury of infectious aetiology in dogs is an uncommon but potentially life-threatening presentation encountered in the south-east of France. Leptospirosis, an infectious disease with zoonotic potential, is considered a leading cause.(1) Timely antimicrobial therapy is key to clearing the infection, but severe disease, such as acute kidney injury can develop regardless. Amongst dogs that respond to treatment such as dialysis, a severe polyuric phase can follow during which urine production can exceed 20 ml/kg/h.(1)

Antimicrobial pharmacokinetics (PK)

The One Health Initiative includes improving antimicrobial use in the veterinary profession.(2) Whether improving dosing protocols or reducing unnecessary use, good antimicrobial stewardship requires accurate pharmacologic data, also known as pharmacokinetics (PK) and pharmacodynamics. Local and even national veterinary programs to improve antimicrobial use has shown to positively contribute to the global One Health Initiative.(3)

Recent investigations have demonstrated altered antimicrobial PK in dogs with renal dysfunction, where both decreased and increased drug excretion has been documented.(4)(5) This could lead to suboptimal dosing and ineffective treatment and increasing selection pressure for resistant organisms.

Antimicrobial use in infectious AKI in dogs

This AKI dog population with suspected or confirmed leptospirosis is regularly hospitalized for oligoanuria and renal replacement therapy.(6) We are currently collecting data to create pharmacokinetic models in this population of dogs during dialysis treatment. For dogs that respond to therapy and progress to a polyuric phase when drug excretion can be very rapid leading to a risk of underdosing, there is similarly a paucity of relevant PK studies that provide data to guide antimicrobial dosing. Further research is needed to aid clinicians in providing optimal antimicrobial dosing against leptospirosis during the polyuric phase.

Gap

Existing animal and human literature shows that profound changes in renal function, including marked polyuria, can alter antimicrobial PK. This in turn can diminish efficacy, and in cases of infectious AKI such as leptospirosis, can have life-threatening consequences.

There are currently no pharmacokinetic models for an aminopenicillin in dogs with post-dialysis polyuric AKI.

Objectives

The aim of this study will be to establish a PK model for ampicillin/sulbactam in dogs with marked polyuria (≥ 4 ml/kg/h) that have been hospitalized for confirmed or suspected infectious AKI.
We hypothesise that clearance of ampicillin/sulbactam in this population of dogs markedly increases and that current dosing regimens result in poor plasma drug concentration time above MIC. This would trigger the need for altered dosing regimens in these dogs to ensure drug efficacy.

References

1. Schuller S, Francey T, Hartmann K, Hugonnard M, Kohn B, Nally JE, et al. European consensus statement on leptospirosis in dogs and cats. J Small Anim Pract [Internet]. 2015 Mar;56(3):159–79. Available from: http://dx.doi.org/10.1111/jsap.12328

2. Robinson TP, Bu DP, Carrique-Mas J, Fèvre EM, Gilbert M, Grace D, et al. Antibiotic resistance is the quintessential One Health issue. Trans R Soc Trop Med Hyg [Internet]. 2016 Jul;110(7):377–80. Available from: http://dx.doi.org/10.1093/trstmh/trw048

3. Lehner C, Hubbuch A, Schmitt K, Schuepbach-Regula G, Willi B, Mevissen M, et al. Effect of antimicrobial stewardship on antimicrobial prescriptions for selected diseases of dogs in Switzerland. J Vet Intern Med [Internet]. 2020 Nov;34(6):2418–31. Available from: http://dx.doi.org/10.1111/jvim.15906

4. Monaghan KN, Labato MA, Papich MG. Ampicillin pharmacokinetics in azotemic and healthy dogs. J Vet Intern Med [Internet]. 2021 Mar;35(2):987–92. Available from: http://dx.doi.org/10.1111/jvim.16026

5. Stewart SD, Allen S. Antibiotic use in critical illness. J Vet Emerg Crit Care [Internet]. 2019 May;29(3):227–38. Available from: http://dx.doi.org/10.1111/vec.12842

6. Barthélemy A, Magnin M, Pouzot-Nevoret C, Bonnet-Garin JM, Hugonnard M, Goy-Thollot I. Hemorrhagic, Hemostatic, and Thromboelastometric Disorders in 35 Dogs with a Clinical Diagnosis of Leptospirosis: A Prospective Study. J Vet Intern Med [Internet]. 2017 Jan;31(1):69–80. Available from: http://dx.doi.org/10.1111/jvim.14626