Abstract: P292

**Evaluation of anti-arrhythmic efficacy of the IK1 inhibitor PA-6 in domestic dogs with chronic atrial fibrillation**

**Authors:**
MAG Van Der Heyden¹, Y Ji¹, V Szatmari², B Van Herwijnen¹, A Bossu¹, MA Vos¹, ¹University Medical Center Utrecht, Division Heart and Lungs, Medical Physiology - Utrecht - Netherlands, ²Utrecht University, Clinical Sciences of Companion Animals - Utrecht - Netherlands,

**Topic(s):**
Basic Science - Cardiac Diseases: Drugs, Drug Targets

**Citation:**
Cardiovascular Research (2018) 114 (Supplement 1), S75

**Funding Acknowledgements:**
Supported by an Advances in Veterinary Research grant (#AVR-15-05) from the dept of Clinical Sciences of Companion Animals, Utrecht University

**Background:** The inward rectifier inhibitor pentamidine analogue 6 (PA-6) is effective in cardioversion of anaesthetised goats with persistent rapid pacing induced atrial fibrillation (AF) and is not pro-arrhythmic in anaesthetised experimental dogs with chronic third-degree AV block. However, efficacy and safety in the clinical setting is unknown.

**Purpose:** To test efficacy and safety of PA-6 in converting AF to sinus rhythm (SR) in awake dogs with naturally occurring AF.

**Methods:** Ten giant and large breed dogs (8 males; 57.7±16.6 kg; 7.4±2.6 year) with persistent or permanent AF (mean duration of AF 5.8±6.5 month (range 1-19 months)) were included. PA-6 was applied i.v. as a bolus of 2.5 mg.kg⁻¹.10min⁻¹ followed by a maintenance infusion of 0.04 mg.kg⁻¹.min⁻¹ for a maximum of 50 minutes under awake conditions. Standard three lead ECG (I, II and III) was recorded during the entire procedure. Visible and audible signs of adverse effects were scored during the entire procedure.

**Results:** PA-6 did not change QRS duration of QTc interval. RR interval was lengthened at the end of the bolus (363±85 vs. 441±96 ms). No cardioversion to SR was observed. Three dogs did not display any adverse effects. Five dogs showed premature ventricular contractions during PA-6 infusion. Respiratory distress and laryngeal stridor, muscle twitch and weakness were the main non-cardiac adverse effects observed in five dogs. Adverse effects resolved spontaneously and follow up was unremarkable.

**Conclusions:** Chronic naturally occurring AF in large and giant breed dogs could not be cardioverted to SR by PA-6. Further clinical testing must first focus on paroxysmal AF under conditions of anesthesia and artificial ventilation.