VASOMERA™, A NOVEL VPAC2-SELECTIVE VASOACTIVE INTESTINAL PEPTIDE AGONIST, ENHANCES CONTRACTILITY AND DECREASES MYOCARDIAL DEMAND IN DOGS WITH BOTH NORMAL HEARTS AND WITH PACING-INDUCED DILATED CARDIOMYOPATHY

Poster Contributions
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Background: The natural vasoactive intestinal peptide (VIP) has been proposed as a therapeutic agent for heart failure via the activation of the G-protein-coupled VPAC1 and VPAC2 receptors; however, VIP’s clinical utility is limited due to its short half-life and VPAC1-mediated side-effects. Vasomera™ is a novel long-acting biopolymer-based selective VPAC2-receptor agonist. Here, the acute load-independent functional effects of Vasomera, when given as a continuous IV infusion to dogs with normal and failing ventricles were evaluated.

Methods: Beagle dogs (n = 7) were instrumented for the determination of systemic/left-ventricular hemodynamic as well as for the evaluation of cardiac-output (via thermo-dilution) and load-independent left-ventricular inotropy/lusitropy via pressure-volume relationships; a subset of animals (n = 4) had heart failure induced via overdrive right-ventricular pacing, as documented via both echocardiography (LVIDd: + 9 ± 3%, EF: -35 ± 2%, P < 0.05) and neurohumoral changes (NT-proBNP: 413 ± 53 to 2091 ± 426 pM/L, P < 0.05). In all cases the acute effects of Vasomera (0.1 µg/kg/min IV) on LV mechano-energetics were evaluated.

Results: Vasomera decreased LV end-systolic pressures and arterial elastance and with negligible changes in heart rate. At 0.1 µg/kg/min (IV), steeper ESPVR (+25 ± 9%, 2.8 ± 0.7 to 3.5 ± 0.9 mmHg/mL*, P < 0.05) and PRSW (+25 ± 5 %, 49 ± 7 to 60 ± 8 mmHg*, P < 0.05) slopes were observed, suggesting positive (load independent) inotropy. Concomitantly, cardiac output increased while the LV pressure-volume area, a correlate of myocardial demand, decreased significantly (PVA: (-20 ± 3%, 4.4 ± 0.9 to 3.5 ± 0.8 mmHg*L, P < 0.05)

Conclusion: Vasomera, a novel VPAC2 agonist, decreased myocardial loading and energetic demand, while improving LV function in a load-independent manner.