METHODS and RESULTS: Four-week-old DBA/2 mice were inoculated with the encephalomyocarditis virus (day 0). We compared the effects of benidipine, 10 mg/kg, versus diltiazem, 60 mg/kg, on survival, myocardial injury, and plasma malondialdehyde (MDA) concentrations. In vivo left ventricular pressure-volume relationships were compared between benidipine-treated and untreated mice. On day 7, 26 of 39 mice (67%) treated with benidipine had survived, versus 17 of 41 mice (42%) treated with diltiazem ($p<0.05$). Benidipine also limited the severity of myocardial lesions, and formation of plasma MDA (10.4±1.3 μmol/L in benidipine-treated vs, 39.1±9.8 μmol/L in control mice, $p<0.05$). On day 14, contractility and compliance were greater, end-diastolic pressure lower (7.30±1.31 vs. 15.15±2.35 mmHg, $p<0.01$) and chamber volume and end-systolic elastance smaller (4.85±0.51 vs. 6.88±0.45 mmHg/μLx100 mg, $p<0.01$) in the benidipine-treated than in untreated mice. Heart rate remained similar in both groups. In addition, benidipine improved left ventricular remodeling and hemodynamic parameters on day 90.

CONCLUSIONS: In this model of dilated cardiomyopathy, benidipine, but not diltiazem, conferred a therapeutic benefit attributable to its antioxidant properties.

Keywords: left ventricular remodeling; dilated cardiomyopathy; viral myocarditis

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P-B-37

Adiponectin Protects Doxorubicin-induced Cardiomyopathy in Mice

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Abstract

Background: Adiponectin has been reported to protect cardiac dysfunction such as ischemia reperfusion injury and hypertrophy. However, there are few reports about its cardioprotective effects in doxorubicin (DOX) -induced cardiomyopathy. We investigated whether adiponectin is effective for DOX-induced cardiomyopathy or not *in vivo* using adiponectin transgenic mice.

Methods and Results: We quantified cardiac pathology in C57BL/6mice (WT mice) and adiponectin transgenic mouse (Tg mice) (K Saito et al: Biochimica et Biophysica Acta 2006) after a single acute administration of DOX (15mg/kg i.p.). Heart rate was similar in both groups (583±47 vs. 588±23bpm, n=5 vs. 5, p=NA) but systolic blood pressure was preserved in Tg mice compare to WT mice (83±3 vs.73±4mmHg, $p<0.005$). Echocardiographic evaluation revealed that cardiac function in Tg mice was significantly improved compare to WT mice (FS=48.5±2.8 vs. 31.2±4.0, $p<0.005$). Tg mice had significantly smaller increased in LV chamber size and smaller decreased in wall thickness than WT mice. We also assessed myocardial pathological changes, and observed that fibrosis and scattered cardiomyocytes were significantly decreased in Tg mice compare to WT mice.

Conclusion: In this study, we observed adiponectin improves cardiac function in DOX-induced cardiomyopathy. Adiponectin could be associated with protection of heart failure in this model.

Keywords: Adiponectin; Doxorubicin; Transgenic mice

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P-B-38

Blockade of Histamine H_2 Receptors Ameliorates the Progression of Canine Heart Failure Independent of Active States of β-Adrenergic Receptors

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Background: Stimulation of histamine H_2 receptors expressed in the heart increases intracellular cAMP levels via Gs protein as well as stimulation of β-adrenergic receptors and worsens the pathophysiology of heart failure. To test if histamine H_2 receptor blockers were effective in addition to blockade of β-adrenergic receptors, we investigated whether famotidine mediates cardioprotection even in the presence of β-adrenergic receptor blockers.

Methods and Results: We induced heart failure by rapid ventricular pacing (230 beats/min) in dogs with receiving no drug (Control group), famotidine (1 mg/kg/daily), carvedilol (0.1 mg/kg/daily) or combination with carvedilol and famotidine. Both cardiac catheterization and echocardiography were performed before and 4 weeks after the onset of pacing.

Immunohistochemical studies showed the appearance of mast cells and histamine in the myocardium 4 weeks after the pacing. In CHF group, left ventricular ejection fraction (LVEF) at 4 weeks decreased compared with the pre-operation (LVEF: 71±2 vs. 27±2 %, $p<0.05$) and increased mean pulmonary wedge pressure (PCWP: 8±1 vs. 19±3 mmHg). Famotidine attenuated decreases in LVEF and increases in PCWP, and the combination with carvedilol and famotidine further attenuated both decreases in LVEF and increases in PCWP compared with the other groups. These beneficial effects of famotidine were consonant with decreases in myocardial cAMP levels.

Conclusions: Blockade of histamine H_2 receptors preserves cardiac systolic function in pacing-induced canine heart failure even in the presence of β-adrenergic receptor blockers.

Keywords: Heart failure; histamine; β-adrenergic receptor blocker

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P-B-39

End-tidal Carbon Dioxide as a Predictor for the Clinical Recovery of Fulminant Myocarditis

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Background: Although percutaneous cardiopulmonary support (PCPS) has been widespread for managing fulminant myocarditis (FM), there are only a few distinct parameters to predict clinical recovery leading to the weaning from the device.

Methods & Results: Thirteen consecutive patients (45±11 yo) with FM who required PCPS together with mechanical ventilation were divided into 2 groups based on their clinical course: non-survivors (non-S; n=5) and survivors (S; n=8). There was no significant difference regarding mixed venous oxygen saturation (SVO_2) (non-S vs. S, 84.3±13.0 vs.80.3±13.4%, NS) and end-tidal carbon dioxide ($ETCO_2$) (non-S vs. S=11.6±10.2 vs.10.8±11.3%, NS) at PCPS introduction between the groups. The patients retained more than 75% of SVO_2 and less than 15% of $ETCO_2$ in the non-S group during the clinical course until death. In the S group, however, the obvious flexion points could be recognized during the recovery phase: E- and C-points together with an abrupt decrease of SVO_2 . The E-point was defined as the clinical period in which $ETCO_2$