Long-Term Treatment With Selective Endothelin ETA Receptor Antagonist Suppressed NADPH Diaphorase Activity and Improved Left Ventricular Diastolic Function in Cardiomyopathy

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Background: Endothelin-1 (ET-1) receptor antagonist is expected to improve prognosis of patients with heart failure, but the effect of ETA and ETB receptor antagonist on cardiac function and structure is still controversial. We assessed the hypothesis that long-term treatment with ETA receptor antagonist could reduce inducible nitric oxide synthase synthesis and improve the cardiac dysfunction in the model of cardiac diastolic dysfunction. Methods: A selective ETA receptor antagonist ABT-627 (ETa; 10 mg/kg/day) or a selective ETB receptor antagonist A-192611 (ETb: 15 mg/kg/day) was given in 22-week-old J2-5/N cardiomyopathic (Kyk) hamsters, representing severe heart failure, for 2 months. ET-1 content and NADPH diaphorase activity in left ventricular (LV) myocardium were studied by electron microscopy. Results: Though ETb showed inotropic and chronotropic effect on cardiac function, degeneration of cardiomyocytes remarkably progressed. ETA efficiently preserved the LV diastolic function and tissue damage, furthermore suppressed the NADPH diaphorase activity representing INOS and ET-1 content in LV. Conclusions: Both ETa and ETb are potent to improve cardiac function. However, only ETA could reduce INOS and ET-1 content, and also preserve the fine structure of LV myocardium in cardiomyopathy.

1039-66 Oscillatory Pattern of Respiratory Gas Exchange During Cardiopulmonary Exercise Test in Chronic Heart Failure: Clinical and Functional Correlates

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Background: Ondop Growth Factor (OGF) is an inhibitory pentapeptide that interacts with its receptor (OGFr) to target cell proliferation and DNA synthesis. Previous studies have shown that chronic upregulation of the OGF/OGFr interaction by nuclear factor (NFk) had a stimulatory effect on myocardiad development. We hypothesized that in vitro exposure to OGF affected neonatal cardiac function.

Methods: Timed-pregnant Sprague-Dawley rats received injections of 30 ng/kg of OGF or 0.3 ml saline twice a day throughout gestation. Offspring were cross-fostered to non-injected, lactating females. Left ventricle (LV) size and function were evaluated by echocardiography in postnatal day (PD) 26, 55 and 110 Nk+ and control rats. Six to eight male and female offspring of each group were studied for LV diastolic dimension, LV thickness, shortening fraction (SF) and heart rate.

Results: PD 26 male and female and PD56 female offspring exposed to OGF had significantly increased LV end diastolic dimension, LV thickness, LV systolic function and heart rate. The Nk+ exposed rats had dilated left ventricles at earlier ages. The Nk+ rats had decreased ventricular systolic function and decreased heart rates at all ages studied. This data suggests that in vivo blockage of OGF activity by Nk+ leads to significant ventricular dilation and impaired systolic function. This information may provide a unique model that will allow for further study of dilated cardiomyopathies.

1039-65 Newborn Lysinexone Exposure Adversely Affects Postnatal Cardiac Development: A Model for Dilated Cardiomyopathy

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Background: Newborn Lysinexone (OxG) is an inhibitory pentapeptide that interacts with its receptor (OGFr) to target cell proliferation and DNA synthesis. Previous studies have shown that chronic upregulation of the OGF/OGFr interaction by nuclear factor (NFk) had a stimulatory effect on myocardiad development. We hypothesized that in vitro exposure to OGF affected neonatal cardiac function.

Methods: Timed-pregnant Sprague-Dawley rats received injections of 30 ng/kg of OGF or 0.3 ml saline twice a day throughout gestation. Offspring were cross-fostered to non-injected, lactating females. Left ventricle (LV) size and function were evaluated by echocardiography in postnatal day (PD) 26, 55 and 110 Nk+ and control rats. Six to eight male and female offspring of each group were studied for LV diastolic dimension, LV thickness, shortening fraction (SF) and heart rate.

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1039-64 Novel Lamin A/C Mutations in Idiopathic Dilated Cardiomyopathy and/or Conduction Disease

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Background: In chronic heart failure (CHF), periodic oscillations in VO2 consumption (Vq). CO2 production (VCO2) and ventilation may appear in the initial phases of cardiovascular exercise test, with controversial clinical significance. AIM: To characterize, in patients with (still) pure CHF, the oscillatory pattern ln monoclonal T-cell populations. Clonal TCR-P PCR-products were directly sequenced.

Methods: DNA extracted from explanted DCM hearts (n=17, 1 female; 49+/-13 years; 152A ABSTRACTS - Cardiac Function and Heart Failure

Results: PD 26 male and female and PD56 female offspring exposed to OGF had significantly increased LV end diastolic dimension, LV thickness, LV systolic function and heart rate. The Nk+ exposed rats had dilated left ventricles at earlier ages. The Nk+ rats had decreased ventricular systolic function and decreased heart rates at all ages studied. This data suggests that in vivo blockage of OGF activity by Nk+ leads to significant ventricular dilation and impaired systolic function. This information may provide a unique model that will allow for further study of dilated cardiomyopathies.

Conclusion: Clonal T-cell composition is exclusively present in DCM, as detected by specific clonal TCR-P PCR-products from the n=9 DCM hearts determined VP-19.01 in n=6 cases (67%), and VP6-3.01 and VP10-3.04 in each of the remaining cases.

Conclusions: Clonal T-cell composition is exclusively present in DCM, as detected by specific clonal TCR-P PCR-products from the n=9 DCM hearts determined VP-19.01 in n=6 cases (67%), and VP6-3.01 and VP10-3.04 in each of the remaining cases.