A Multicenter Study of the Safety and Efficacy of Disopyramide for Treating Symptomatic Obstructive Hypertrophic Cardiomyopathy

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Background: Disopyramide (diso) has been shown to reduce gradient and improve symptoms in patients (pts) with obstructive hypertrophic cardiomyopathy (HCM). It is often administered to medically refractory pts who would otherwise need septal myectomy or other interventions. However, the clinical course of HCM pts treated with diso has never been investigated in a large cohort. Methods: 141 pts with HCM were treated with diso at 4 treatment centers from 1990 to 1999. Resting echo gradient and NYHA class were compared before diso and at follow-up on medication. Results: 141 pts (mean age 46.6) were treated with diso for a mean of 3.9 years with a mean highest dose of 428 ± 180 mg/day. Most recent gradient on diso was 45 ± 34 mm Hg, significantly lower than baseline gradient 78 ± 35 mm Hg, a 42% reduction, p<0.001. 74% of pts had < 15 mm Hg reduction in gradient, and 42% had > 40% reduction. NYHA class improved on drug, 16/65/23/0 to 36/47/6/0 for classes I, II, III, IV respectively, p<0.01. Also, the percentage of patients in NYHA class III and IV decreased after diso from 27% to 16%, p=0.05. There were 4 HCM-related sudden cardiac deaths that occurred on diso, occurring mean 34 months after baseline assessment of diso. Annual rate of sudden cardiac death was 0.88% and annual rate of all-cause cardiac death was 1.29%. There were 93 pts (88%) who were still on diso at follow-up. The majority of pts could be managed without myectomy or other intervention; but, while taking diso 32% ultimately required intervention for relief of obstruction. Conclusions: Patients with HCM treated with disopyramide showed a significant and persistent decrease in outflow gradient of 42% and improvement in limiting symptoms. No excess sudden cardiac death occurred. A therapeutic trial of disopyramide should be considered before proceeding to major intervention in obstructive HCM.

Molecular Mechanism of Ventricular Remodeling

Monday, March 31, 2003, 9:15 a.m. - 10:30 a.m.
Mc Cormick Place, Room S405

Early Postinfarction Ventricular Restraint Prevents Adverse Remodeling and Preserves Borderzone Contractile Function

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Background: Postinfarction ventricular remodeling is the major cause of CHF. Early infarct expansion (ischemia) initiates adverse remodeling and progressive contractile dysfunction in normally-perfused borderzone (BZ) myocardium. Early LV restraint may prevent this maladaptive phenomenon. Methods: An infarction of 20% of the LV mass known to cause CHF and LV dilatation in normally-perfused borderzone myocardium was performed in 42 rats. Rats were randomized to either control or diso (0.5 mg/kg/dose) over 8 weeks. LV remodeling, diastolic function, regional contractility and perfusion were assessed by echocardiography, sonomicrometry and microsphere injections, respectively, over 8 weeks. Results: The control group experienced progressive LV dilatation, expansion of the anemic segment and progressive borderzone contractile dysfunction. Infarction expansion, LV dilatation and borderzone contractile dysfunction were prevented or significantly reduced in the animals, having early postinfarction LV wrapping. Myocardial perfusion was unchanged in the uninjured regions in all animals. There was no evidence of wrap-induced diastolic dysfunction. Conclusion: Early postinfarction ventricular restraint to prevent infarct expansion prevents adverse remodeling and preserves contractile function in non-infarcted myocardium.

Wild mTNF mTNF-M sTNF stTNF-M
Type End-Diastolic Volume (μL) 39±6 42±4 36±3 61±4* 49±4*†
Ejection Fraction (%) 66±1 66±2 73±1 68±2 71±1
Emax (Maximal Chamber Elasticity, 5.3±0.8 5.1±1 11.3±1.4 5.3±1.0 10.4±2.2)
mL/min(g/l)
LV Mass/Tibia (mg/mm) 5.8±0.3 8.2±0.4 8.3±0.4 8.6±0.5 7.8±0.5
3* 3* 9:45 a.m.

Testosterone Aggravates Cardiac Performance and Remodeling in Mice After Myocardial Infarction

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The cardioprotective effects of estrogen have been widely studied. However, little is known about the effects of testosterone (T) on chronic remodeling and prognosis after MI. We found that female mice given supplemental T had significantly higher mortality (due to cardiac rupture) than those treated with placebo (P) during the first week after MI regardless of ovariectomy, whereas ovariectomy significantly reduced mortality in males. We hypothesized that testosterone may aggravate chronic cardiac remodeling and dysfunction, whereas estrogen may be cardioprotective after MI. 4-week-old males and females underwent either castration (cas), or sham castration (s-cas), and ovariectomy (ovx) or sham ovariectomy (s-ovx), respectively. S-cas females were treated with either