1134-156
Effects of Antidepressant Medication on Mortality in Patients With Congestive Heart Failure


Major Depressive Disorder (MDD) is a common entity in patients with cardiovascular (CAD) disease. Studies have previously demonstrated that MDD is present in 20%-45% of CAD patients. Rates of depressive disorders following myocardial infarction (MI) are especially high, with a depressive episode in 50% of patients immediately following MI, and more than 70% one year after MI. Congestive heart failure (CHF) due to ischemia occurs in many of these patients. Despite numerous studies in this population, few have focused on the prevalence of depression and its prognostic effect in patients with CHF. Recently Jiang et al. published results demonstrating that overall mortality in patients with co-morbid MI and depression was increased at 3 months and 1 year compared with patients with CHF who were not depressed. MDD with CHF was found to be an independent risk factor for increased mortality. In the current work we have confirmed these findings, with increased mortality in patients with CHF and co-morbid depression by Beck Depression Inventory (BDI≥10) in 226 of 674 patients with ejection fraction less than or equal to 55%. Patients who were not depressed at baseline but had CHF had a mortality rate of 12.12%. Those patients at baseline on antidepressant medication, and in all likelihood responsive to medication, had a mortality rate of 14.14%. While patients who at baseline were depressed and treated with medication, suffered increased mortality over controls at 22.55%. In CHF patients with major depression whose depressive symptoms did not respond to medication had an even higher rate of mortality at 38.60% (p-value<0.5). This data suggests that patients with co-morbid CHF and depression and who remain non-responders despite medication have higher rates of mortality over those without depression. Furthermore, patients responsive to medication. This data supports the notion that the effect of adequately treating depression in patients with CHF may reduce mortality, and if the CHF/depressed patient remains non-responsive to medication, mortality may be significantly higher than that depressed-responsive/CHF or non-depressed patients with CHF.

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Endothelin Antagonism With Bosentan, a Dual Receptor Blocker, Normalizes Dysregulated Transforming Growth Factor Beta Signaling Pathways in Rats With Chronic Heart Failure

Ingeborg Schothaler-Zoppoth, Mary O. Gray, John R. Teacher, San Francisco VA Medical Center, San Francisco, California, UCSF, San Francisco, California, California.

Background: We have previously shown that dysregulation of the TGF beta signaling pathway plays a critical role in adverse ventricular remodeling in CHF. Endothelin (ET) also plays a central role in ventricular remodeling and its many actions are mediated by TGF beta. Therefore, we hypothesized that the beneficial effects of ET antagonism with bosentan on ventricular remodeling may be mediated by improvements in the TGF beta signaling pathway.

Methods: Adult male Sprague-Dawley rats (270-300g) underwent coronary artery ligation (CAL) or sham operation (Sham group) followed by conscious echoangiography on day 5-7 after surgery, CAL rats with ejection fraction 35% in all groups.

Results: Baseline (BL) body weight showed no differences between the treatment groups. In myocytes from CHF rats, bosentan tended to increase inhibitory Smad6 by 51% (p=0.13), with no effect on the positive effectors, Smad3 or Smad4. In fibroblasts from CHF rats, bosentan decreased Smad4 and SAFB (Smad anchor for receptor activator) by normalizing the overexpression of Smad7 (p<0.008). The improvements in fibroblast Smad7 concentrations directly correlated with attenuation of ventricular dilation by bosentan, as measured by LV volume at 20 mmHg distending pressure (p<0.001; r=0.69).

Conclusion: These data confirm our earlier findings of TGF beta signaling pathway dysregulation in CHF and demonstrate that chronic ET blockade with bosentan results in normalization of these pathways. Inhibition of the TGF beta pathway was directly correlated to the beneficial effects of bosentan on ventricular remodeling. These findings suggest that the TGF beta pathway may mediate the adverse effects of endothelin in CHF and that this pathway may be an important therapeutic target in CHF.

1134-158
Long-Term Cervidil Treatment in Idiopathic Dilated Cardiomyopathy: Biological Effects Beyond Pharmacological Activity

Brenata De Maria, Antoniole Gavazzi, Gianfranco Negra, Oberdon Parodi, Carlo Camarda, Danilo Neglia, Mauro Giachetti, Marcella Lusini, Luigi Lavecchia, CNR Clinical Physiology Institute, Section of Milan, Milan, Italy, Cardiovascular Dept Ospedali Riuniti, Bergamo, Italy.

Background. Despite the established effects of cervidil on morbidity and mortality in heart failure (HF), the mechanisms of its clinical efficacy are still poorly understood. We conducted a multicenter, double-blind, randomized controlled trial in HF patients with idiopathic dilated cardiomyopathy to assess the effects of cervidil (C) on submaximal exercise tolerance during long-term pharmacological treatment and after withdrawal. Methods and Results. 99 patients with HF due to documented idiopathic dilated cardiomyopathy and an ejection fraction ≤35% underwent a 2-week open-label challenge with C; 64 of them (mean age 54±10 years, 64% males) were randomized to chronic treatment with C (n=45) or placebo (P), (n=39) on top of ACE-inhibitors and form the intention-to-treat sample. C was titrated up to 25 mg bid (mean final dose 23.1±4.8 bid) or placebo (P) in patients with CHF who were not depressed. MDD with CHF was found to be an independent risk factor for increased mortality. In the current work we have confirmed these findings, with increased mortality in patients with CHF and co-morbid depression by Beck Depression Inventory (BDI≥10) in 226 of 674 patients with ejection fraction less than or equal to 55%. Patients who were not depressed at baseline but had CHF had a mortality rate of 12.12%. Those patients at baseline on antidepressant medication, and in all likelihood responsive to medication, had a mortality rate of 14.14%. While patients who at baseline were depressed and treated with medication, suffered increased mortality over controls at 22.55%. In CHF patients with major depression whose depressive symptoms did not respond to medication had an even higher rate of mortality at 38.60% (p-value<0.5). This data suggests that patients with co-morbid CHF and depression and who remain non-responders despite medication have higher rates of mortality over those without depression. Furthermore, patients responsive to medication. This data supports the notion that the effect of adequately treating depression in patients with CHF may reduce mortality, and if the CHF/depressed patient remains non-responsive to medication, mortality may be significantly higher than that depressed-responsive/CHF or non-depressed patients with CHF.

Conclusion: In cardiac amyloid, systolic and diastolic myocardial dysfunction show any difference between the ‘no-CRF” and controls. Similarly, peak SRI-E in the “no-CHF” showed a significantly lower value than in the controls at the mid-ventricle but not the base, whereas TDI-E did not show any difference between the ‘no-CRF” and controls.

Results: Using TDI, differences in systolic function were only apparent between the CHF and their the other 2 groups, but TDI could not distinguish the controls from “no-CRF”. In contrast, peak SRI-E showed a significantly lower value than in the controls at the mid-ventricle but not the base, whereas TDI-E did not show any difference between the “no-CRF” and controls.

Conclusion: In cardiac amyloid, systolic and diastolic myocardial dysfunction show any difference between the ‘no-CRF” and controls.