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The cellular and physiologic effects of beta blockers in heart failure.

Sabbah HN.

Department of Medicine, Henry Ford Heart and Vascular Institute, Henry Ford Health System, Detroit, Michigan, USA.

Enhanced and sustained cardiac adrenergic drive occurs in heart failure (HF) and contributes, in part, to the progression of left ventricular (LV) dysfunction and remodeling that are characteristic of this disease state. Enhanced sympathetic drive in HF can lead to downregulation and desensitization of cardiac beta-adrenergic receptors with a consequent impairment of myocardial reserve and exercise tolerance. This sympathoadrenergic maladaptation can also lead to cellular abnormalities in the failing heart, manifested by defects in calcium handling of the sarcoplasmic reticulum, by defects in myocardial energetics, and by ongoing loss of cardiomyocytes through necrosis or apoptosis. Chronic treatment with beta blockers in patients with HF and in animals with experimentally induced HF has been shown to reverse, prevent, or, at the least, arrest many, if not all, of these adverse processes. Beta blockers improve function of the failing LV, prevent or reverse progressive LV dilation, chamber sphericity, and hypertrophy, and consequently have positive impact on cardiac remodeling. Beta blockers also reduce heart rate and LV wall stress, leading to reduced myocardial oxygen consumption, a clear benefit to the failing heart. Beta blockers can also improve the intrinsic contractile function of cardiomyocytes and have also been shown to improve myocardial energetics in HF, possibly through desirable changes in substrate utilization. Recent studies from our laboratories have also shown that beta blockers can attenuate cardiomyocyte apoptosis in HF. These benefits provide strong reinforcement to the clinical findings that beta blockers are highly beneficial for the management of patients with chronic HF and, when properly used, afford unequivocal reductions in mortality and morbidity in this patient population. At present, there is general agreement that increased cardiac sympathetic drive occurs in HF and may potentially be an important contributor to the progression of LV dysfunction and chamber remodeling that is characteristic of this disease state. Experimental studies in animal models of HF as well as clinical studies in patients with HF have suggested that chronic therapy with beta blockade is effective in preventing the progression of LV dysfunction and remodeling, the latter evidenced by reversal and/or prevention of progressive LV dilation and chamber sphericity. Results of recent multicenter clinical trials support these findings and have made it abundantly clear that long-term therapy with beta blockade inhibits clinical progression and has a major impact on mortality and morbidity in patients with HF that is at least as favorable, if not better, than that observed with angiotensin-converting enzyme (ACE) inhibitors. Beta blockers improve mortality and morbidity in HF and also improve LV ejection fraction (EF), a beneficial feature that, until recently, has only been attributed to positive inotropic agents.

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