Chemoreflex dysfunction in heart failure: Why it should not be ignored

Enhanced arterial chemoreflex function is strongly related to cardiorespiratory disorders and disease progression in heart failure (HF). The mechanisms underlying chemoreflex sensitization during HF are not fully understood. We have utilized preclinical animal models of HF to describe a key role of both carotid body and central chemoreceptor function on autonomic and cardio-respiratory dysfunction in both HFrEF (cardiac pacing in rabbits and myocardial infarct in rats) and HFP EF (arteriovenous fistula in rats). Despite the etiology of HF, HFrEF and HFP EF animals exhibit similar cardio-respiratory abnormalities of periodic breathing, sympathovagal imbalance, and arrhythmias. In HFrEF animals, carotid body chemoreflex sensitivity is enhanced, but central chemoreflex sensitivity is minimally impacted, whereas in HFP EF animals, the opposite scenario is true. In HFrEF, carotid body ablation restores normal breathing patterns and autonomic balance, reduces arrhythmias and increases survival. The enhanced neural activity from the carotid body in HFrEF and its impact on sympathetic hyperactivity and breathing instability are related to a chronic reduction in cardiac output that down regulates a flow sensitive transcription factor KLF2 in the carotid body. In HFP EF, carotid body function is not markedly altered, consistent with normal blood flow and KLF2 expression in the carotid body, but central chemoreflex sensitivity to changes in PaCO2 is markedly enhanced and correlates with the sympathetic hyperactivity and breathing instability observed in that condition. These studies suggest that the differential influences of HFrEF and HFP EF on carotid body and central chemoreceptor function are related to differences in systemic hemodynamics and blood flow. Nevertheless, elevated chemoreflex activity, whether from the carotid body or central chemoreceptors, contributes a major role to the sympathetic hyperactivity and breathing instability seen in HF. Clinical evaluation of chemoreflex sensitivity in HF patients can provide important information about the etiology of autonomic/respiratory dysfunction and disease progression in these patients and may guide more targeted therapeutic strategies.

Biography

Harold D Schultz research interests are preclinical translational studies aimed to improve baro and chemoreflexes control of autonomic, respiratory, renal and cardiac function, using a variety of approaches such as gene manipulation, novel pharmacological interventions, exercise/diet, and surgical interventions (e.g. cardiac, carotid body, renal denervations).

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