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The impact of ranolazine on left ventricular ejection fraction, autonomic measures, and outcomes in patients with chronic heart failure

Background: Ranolazine (RAN) reduces the late sodium current (INa) in congestive heart failure (CHF), reducing myocardial calcium overload, thereby potentially improving left ventricular (LV) function. RAN also blocks neuronal sodium channel 1.7 (Nav 1.7), potentially altering parasympathetic and sympathetic (P & S) activity.

Objective: The objective of the study is to report RAN's effect upon LV ejection fraction (LVEF), P & S function, and major adverse cardiac events (MACE) in CHF.

Methods: New York Heart Association (NYHA) class 2-4 CHF patients were given open-label RAN, 1000 mg p.o. b.i.d. (RANCHF, 41 systolic, 13 diastolic) added to guideline-driven therapy, or no adjuvant therapy (NORANCHF, 43 systolic, 12 diastolic). Echocardiographic LVEF was measured at baseline, confirmed by a nuclear multi-gated acquisition (MUGA) study, and reassessed yearly. P & S measures (ANX 3.0, ANSAR, Inc., Philadelphia, PA) were obtained every 6 mo. (mean follow-up 22.8 months), and MACE (cardiac deaths, CHF hospitalizations, ventricular tachycardia [VT]/ventricular fibrillation [VF] therapies) were recorded.

Results: Systolic RANCHF patients' LVEF increased from 0.30 to 0.36 (p=0.001); diastolic RANCHF patients' LVEF increased from 0.43 to 0.52 (p=0.002). NORANCHF patients' LVEF remained unchanged. In RANCHF patients, P & S measures demonstrated improved sympathovagal balance (SB=S/P). SB worsened in NORANCHF subjects. MACE were qualitatively reduced in RANCHF vs. NORANCHF patients: deaths 5.6% vs. 12.7%; CHF admissions 22.2% vs. 27.3%; and VT/VF events 11.1% vs. 23.6%. Of the independent predictors for MACE, SB performed slightly better than LVEF: when SB was ≤2.5 or LVEF was ≥0.32, 80% of subjects were MACE-free; when SB was >2.5, 59% of patients suffered MACE, vs. 50% of patients when LVEF was <0.32.

Conclusion: RAN improves LVEF and autonomic function in CHF patients. RAN qualitatively reduced MACE, and SB performs slightly better than LVEF for prognostication.

Biography

Gary L Murray received a Phi Beta Kappa Bachelor's degree from Rhodes College, Memphis, TN, USA, receiving the Belk Bible Award for the most outstanding Bible student. After graduating from the Tulane University School of Medicine, New Orleans, LA, USA, his Postdoctoral training was at the University of Tennessee Center of Health Care Sciences, Memphis, TN, USA. He became Co-Director of the Cardiac Catheterization as well as Nuclear Cardiology laboratories at Baptist Hospital, Memphis, TN, USA. He then became Chief of Medicine, Nellis AFB, North Las Vegas, NV, USA. Since, he has been in private practice in Memphis, yet he has managed to publish several articles and co-created the Shad-Murray first pass RNA exercise test for coronary disease that was employed at many centers in the USA and Europe. He participated in clinical trials of the first elective coronary stent, as well as the first coronary atherectomy and laser devices. His ANS studies have been cited in the new textbook on clinical autonomic disorders by Colombo. He has spoken in several countries worldwide. He currently is Director of Research at the Heart and Vascular Institute, Germantown, TN, USA.

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