INTRODUCTION

- Heart failure (HF) currently affects an estimated 6.5 million adults in the United States, of which approximately 50% have HF with preserved ejection fraction (HFpEF).
- Despite normal or near normal left ventricular ejection fraction, HFpEF is associated with increased morbidity and mortality.
- The complex pathophysiology of HFpEF remains incompletely understood.
- Inflammation and left ventricular (LV) fibrosis play an important role in the development of HFpEF.
- We have previously shown that low level transcutaneous vagus nerve stimulation (LLTS) is antiarrhythmic and anti-inflammatory.

PURPOSE

- The goal of this study was to determine the effect of chronic intermittent LLTS on cardiac fibrosis, diastolic dysfunction, and left ventricular (LV) gene expression in a rat model of HFpEF.

METHODS

- Dahl salt-sensitive (DSS) rats of either sex were randomized into high salt (HS, 8% NaCl) or low salt (LS) diet (0.3% NaCl) at 7 weeks of age.
- After 6 weeks of LS or HS diets, HS rats were randomized into 4 groups: HS rats, HS sham LLTS, HS active LLTS plus Methyllycaconitine (MLA) (n=36), a specific blocker of α7-nicotinic acetylcholine receptor (a7nAChR), which mediates the anti-inflammatory effects of LLTS.
- Stimulation was delivered for 30 min daily (20Hz, 3mA) for 4 weeks.
- We have previously shown that low level transcutaneous vagus nerve stimulation (LLTS) is antiarrhythmic and anti-inflammatory.

RESULTS

- **Figure 1. Study protocol.**
- **Figure 2. End point comparison of SBP measurements.** The active stimulation group showed significant attenuation of BP elevation compared to HS active plus MLA and HS sham groups.
- **Figure 3. End point comparison of echocardiographic parameters.** Left panel: Circumferential strain. Right panel: e’. Active stimulation resulted in a significant amelioration of echocardiographic parameters compared to sham and this effect was attenuated in the presence of MLA.
- **Figure 4. End point comparison of fibrosis measurements.** The active stimulation group showed significant decrease in fibrosis compared to sham and this effect was attenuated in the presence of MLA.
- **Figure 5. Effect of LLTS on myocardial gene expression – Ingenuity Pathway Analysis (IPA).** LLTS significantly changed the expression of genes involved in mitochondrial dysfunction, siruin signaling pathway and oxidative phosphorylation in comparison to HS sham.

CONCLUSIONS

- Autonomic modulation with LLTS attenuates the unfavorable changes in echocardiographic parameters and LV fibrosis induced by HS diet through its anti-inflammatory effects.
- The data support our hypothesis that inhibiting the anti-inflammatory effect of LLTS attenuates the antifibrotic effect.
- These results provide the basis for the examining the role of LLTS in patients with HFpEF.
- Further studies are required to examine the molecular mechanism of this difference.

REFERENCES


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