Effects of Low-Level Tragus Stimulation on Inflammation in Acute Decompensated Heart Failure

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Introduction

Acute decompensated heart failure (ADHF) is associated with increased systemic inflammation secondary to renin-angiotensin and sympathetic system over-activation

Hypothesis

Low-level tragus stimulation (LLTS) is a novel, non-invasive method of autonomic modulation and may reduce systemic inflammation associated with ADHF

Methods

- In this proof-of-concept study, we enrolled 19 patients with acute heart failure with reduced ejection fraction (HFrEF) admitted for management of ADHF in a double-blind randomized controlled fashion
- Patients received LLTS with a transcutaneous stimulator (20 Hz frequency, pulse width of 200 μs) or sham stimulation (ear lobule), 8 hours daily (4 hours AM and 4 hours PM) during the course of admission
- Inflammatory markers including C-Reactive protein (CRP), Tumor necrosis factor-alpha (TNF-α), Interleukin-6 (IL-6), IL-10, soluble intercellular adhesion molecule-1 (sICAM-1), and soluble vascular cell adhesion molecule-1 (sVCAM-1), along with markers of oxidative stress including serum hydrogen peroxide (H2O2), Superoxide free radicals, and mitochondrial Reactive Oxygen Species (ROS) were measured at baseline and upon discharge using standard laboratory assays

Summary of Biomarker Changes

Biomarker	Experimental Group			Control Group			p-Value
	Median (Baseline)	Median (Discharge)	% Change (Discharge-Baseline)	Median (Baseline)	Median (Discharge)	% Change (Discharge-Baseline)	
CRP (mg/L)	93	39.29	-12.69	62.93	48.74	6.74	0.514
IL-10 (pg/ml)	4.32	4.04	-11.84	7.92	7.92	-26.32	0.63
IL-6 (pg/ml)	7.42	0.89	-78.48	27.54	30.36	-8.63	0.013
TNF-a (pg/ml)	18.14	14.42	-10.91	18.54	20.33	4.78	0.165
sICAM1 (ng/ml)	515.86	429.25	-2.82	307.13	341.66	2.29	0.683
sVCAM1 (ng/ml)	1500.85	1304.01	-3.46	1046.46	1174.59	19.38	0.369

Table 1: Summary of Biomarker Changes According to the Treatment group

Our proof-of-concept study demonstrates that 8 hours of LLTS in patients with ADHF led to improvement in inflammatory markers and had favorable effects on oxidative stress

Results

- A total of 8 patients received LLTS while 11 patients received sham stimulation. Mean age was 70 years in the LLTS group, and 56 years in the control group. Fifty percent of patients in LLTS group were male, whereas 91% of patients were male in the control group
- Serum levels of IL-6 were significantly reduced in active group, with a median change (discharge - baseline) of -78% in the active group as compared to -8% in the control (p=0.013)
- Pro inflammatory markers such as CRP, TNF-α, sICAM-1, and sVCAM-1 were also decreased in experimental group compared to control but did not achieve statistical significance
- Decrease in IL-10 (anti-inflammatory cytokine) was also attenuated by LLTS in experimental group compared to control (Table 1)
- Reactive Oxygen Species demonstrated a statistically significant reduction in the LLTS group as compared to control. Patients in LLTS group demonstrated a significant decrease in serum H2O2 and Superoxide free radicals as compared to the control group

Disclosures

The Authors do not have relevant conflicts of interest to disclose