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Project: *Effects of hypercapnia on heart rate and symptoms in Postural Orthostatic Tachycardia Syndrome (POTS) and long-COVID*



Background

Postural Orthostatic Tachycardia Syndrome (POTS) and Long-COVID are under-recognized and often misdiagnosed conditions associated with autonomic dysfunction [8]. POTS is defined as an excessive and sustained increase in heart rate (HR) >30 bpm within 10 minutes of standing (orthostasis) without a decrease in blood pressure (BP) [1]. Notably, there are numerous reports of COVID patients who suffer from ongoing symptoms after the resolution of the acute illness, termed “Long-COVID”. Long-COVID closely resembles POTS. Patients living with POTS and Long-COVID experience frequent, chronic (>3-6 months) and debilitating symptoms in the upright position that are only relieved by lying down. Symptoms include excessive HR, chest pains, shortness of breath, blurred vision, and mental clouding [2,6].

Patients living with POTS and Long-COVID have significantly reduced quality-of-life that is equivalent to that of heart failure [2]. Patients are limited in their day-to-day functioning at work, school, and home, leading to detrimental effects on patients’ physical, mental, and emotional well-being. Unfortunately, therapeutic options for patients with POTS and Long-COVID are limited and do not work for all. Therefore, it is imperative to investigate and expand management options for patients to help improve their overall quality-of-life.

A novel solution to counter the excessive HR and symptoms in patients with POTS and Long-COVID is to increase the amount of inspired CO₂ (hypercapnia). The effects of hypercapnia on HR and orthostatic tolerance have been tested in a limited number of studies. The reported net

effect shows improved orthostatic tolerance [3-5]. However, whether hypercapnia can effectively lower HR and reduce symptoms in patients with POTS and Long-COVID is unknown.

In addition, many patients report breathlessness, and upon standing, can experience mild hyperventilation. As a result, patients blow off more CO₂ resulting in low CO₂ (hypocapnia) [3]. Hyperventilation significantly exacerbates HR and symptoms. It is unclear, however, whether it is the increase in ventilation (i.e., increase in tidal volume) or the hypocapnia that makes HR and symptoms worse.

Objectives: We aim to 1) determine if hypercapnia can effectively reduce standing HR and symptoms in patients with POTS and Long-COVID, and 2) determine if hypocapnia during hyperventilation exacerbates symptoms.