



RESEARCH ARTICLE

POST-COVID SYNDROME: A NEW CONCEPT OF REHABILITATION

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ABSTRACT

Pandemic COVID-19 beat every human body system leading to multi-organ disorders impacting medical, health care, socioeconomic and overall quality of life in every country. After recovery from acute infection, a significant number of the population develop persistent signs and symptoms lasting more than three months or more termed a post-COVID syndrome (PCS), persisted post-COVID syndrome (PPCS), and long COVID. A rehabilitation program of multidisciplinary specialties was established to control and treat PCS. Physical exercise training exerts immunomodulatory effects that can enhance recovery, improve quality of life, provide immune protection, modulates inflammation, and stimulates nitric oxide synthesis pathways against PCS. Electrotherapy can prevent muscle atrophy, improve muscle strength, and function, and maintain blood flow in PCS. We must remember factors in PCS rehabilitation are quality of life, activities of daily living, pain, sleep quality, nutritional status, mood, and necessity of returning to work. Electrotherapy in form of high tone power therapy which has a special characteristic of amplitude and frequency able to control post-COVID symptoms and improve quality of life. In this context, we will briefly discuss a new concept of rehabilitation in post-covid syndrome.

INTRODUCTION

Long-term effects of COVID-19 lead to persistent symptoms and an increase in the prevalence of chronic illness (1–3). Post-COVID syndrome (PCS) involves persistent physical, medical, and cognitive problems as symptoms persist for more than three months after the first COVID-19 infection (4). According to experts, COVID-19 infection should affect almost 80% of the world's population, so all these patients to a greater or lesser extent will need rehabilitation for selected manifestations of PCS (5). Rehabilitation of patients after COVID-19 will focus on improving persistent symptoms of dyspnea, fatigue, sleep disturbances, and limiting functional capacity, with the gradual increase in the intensity of the rehabilitation program, the ultimate goal being to improve physical condition and quality of life (6). Common symptoms of PCS include generalized fatigue, poor sleep, and other symptoms related to multi-organ disorders (7). The pathogenesis of PCS arises from chronic low-level inflammation and activation of cell-mediated immunity with an increase in inflammatory mediators (8).

Furthermore, immunosuppression and increase in the level of pro-inflammatory cytokines, and overexpression of interleukin 6 (IL-6) are associated with persistent inflammation and fatigue. Further, immune dysregulation and mitochondrial dysfunction are common causes of fatigue after viral (9). Post-COVID syndrome requires long-term multidisciplinary rehabilitation of several specialties as stated by The British Society of Rehabilitation Medicine (BSRM) (10). There are existing rehabilitation pathways that assess and manage the rehabilitation needs of patients with long-term conditions, pulmonary, neurological, musculoskeletal, psychological, physical, cognitive, and cardiac rehabilitation requires several specialties, time-consuming, and inflated costs so we thinking to introduce a new concept in rehabilitation to save time, low cost, comprehensive, and non-invasive (11). Electrotherapy informs of high tone power therapy is a new quantum leap in which the frequency and the amplitude are simultaneously modulated, delivering high energy into the human cells able to increase mitochondrial activities and promote tissue metabolism. The fluctuation of the cell membrane potential by HTT broad-spectrum frequency leads to tissue structure oscillating, scattering the mediators of inflammation, nutrients, and waste substances to normalize cell activities and revitalize the body (12,13) so that high tone may affect PCS symptoms.

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Although there has been research in the area of post covid, there are no studies have been done to investigate the effect of HTT on chronic fatigue, dyspnea, functional capacity, and sleep disturbances in patients with post covid syndrome. **So, we will decide to make this study to investigate the hypothesis of HTT efficacy in PCS patients.**

DISCUSSION

Application of HTT in form of a whole-body vitalization program on PCS could be a feasible, effective noninvasive modality that leads to improvement in submaximal exercise capacity, fatigue, dyspnea score, and quality of sleep of PCS patients according to initial results of this study. The total whole program was six sessions / three sessions per week. Possible mechanisms of this improvement are the application of HTT leads to increases in mitochondria in number and size, acceleration of the diffusion rate (14), produces a resonance effect to promote metabolism, and scattering of the mediators of inflammation, and nutrients (12). The amplitude and frequency of HTT are simultaneously modulated in which the applied frequencies range continuously from 4.096 to 32.768 Hz. Different frequencies vibrate structures of different sizes with HTT (15). The mechanisms of action of HTT release endogenous analgesic and improve microcirculation by enhancing of bioavailability of nitric oxide (16). Sleep loss induces a systemic low-grade inflammation characterized by the release of several molecules, such as cytokines, chemokines, and acute-phase proteins; all of them can promote changes in cellular components of the blood-brain barrier (BBB), particularly on brain endothelial cells (17). Previous studies Moez *et al.* (16), Nowakowska *et al.* (18), concluded that High tone power therapy showed an increase in dynamics of the blood flow in peripheral microcirculation, increased tissue perfusion, and improved cells and functional capacity. A. Klassen *et al.* (19), conducted a study on uremic peripheral neuropathy in end-stage renal disease patients, they concluded that high tone power therapy improved pain, discomfort, sleep disturbance, and quality of life. Rose *et al.* (20), reported that HTT improved metabolic control in patients with type 2 diabetes, and reduced the production of proinflammatory cytokines (cytokines, chemokines, adipokines, and acute phase proteins). The cytokines, tumor necrosis factor (TNF)- α , tumor growth factor (TGF) β , interleukin (IL)-6, IL-10, the chemokine RANTES, and the adipokine adiponectin are reduced after the end of treatment with possible long-term effects. HTT is the percutaneous electrical stimulation of skeletal muscles using frequencies higher than 40 Hz to produce a muscle contraction. HTT leads to muscle contraction of large motor units first with synchronous depolarization and higher firing rates of their motoneurons, resulting in stronger muscle contraction than a voluntary contraction, but also faster exhaustion and anaerobic metabolism of muscle (12). This "reverse-size" recruitment of motor units results in reduced shear forces between muscle fibers preventing discomfort or pain (20). The cytokine storm associated with COVID-19 infection results in an increased secretion of pro-inflammatory cytokines and chemokines such as IL-6, TNF- α , macrophage inflammatory protein 1-alpha as well as C-reactive protein and ferritin. Cytokines and chemokines can bind to specific receptors on the cerebral microvascular endothelium leading to a BBB breakdown, neuroinflammation, and encephalitis (17). Acute and chronic sleep loss is associated with an increased level of proinflammatory mediators, such as tumor necrosis

factor- α (TNF- α), interleukin-1 (IL-1 α), IL-6, IL-17A, and C reactive protein (CRP) as well as with an increased level of immune-derived inflammatory mediators, such as cyclooxygenase-2 (COX-2), nitric oxide synthase (NOS), endothelin-1 (ET-1), vascular endothelial growth factor (VEGF), and insulin-like growth factor-1 (IGF-1). These changes may increase BBB permeability to low molecular-weight tracer—sodium fluorescein (10 kDa) and the decreased mRNA levels of the tight junction proteins claudin-5, zonula occludens-2, and occludin was observed in all regions of the brain. That in turn, decreases nitric oxide and enhances endothelin, amyloid- deposition, and cerebral amyloid angiopathy (17). Dysfunction in mitochondrial respiration and metabolic changes have been found in chronic fatigue syndrome. The earliest evidence of mitochondrial dysfunction in CFS was structural changes seen in the skeletal muscle cell mitochondria (21). Dyspnea in PCS does occur because of the altered metabolic situation in skeletal muscles, vascular disturbances, and endothelial dysfunction. Mitochondrial and vascular dysfunctions in skeletal muscles can be explained by dysfunctional β_2 -adrenergic receptor (β_2 AdR) signaling. Moreover, microcirculation could be disturbed by two mechanisms in PCS: (1) microthrombi may seriously affect microcirculation. (2) Significant changes in lymphocyte stiffness, monocyte, and neutrophil sizes and deformability, and decreased erythrocyte deformability. Mitochondrial dysfunction could arise from either mitochondrial calcium overload, or mitochondrial calcium deficiency, leading to functional damage, hypometabolism, and muscular fatigue. (22). Reichstein *et al.* (23), proved that possible explanations for the improvements among diabetic neuropathy patients who receive HTT are an increase in ATP production, improve mitochondrial function, and activation of anti-oxidative stress, which support this study. Possible improvement in PCS can be achieved by application of HTT as increased distance walked by 6 min walk test, subsequently, functional capacity improved, quality of life, quality of sleep, dyspnea, fatigue because of improving mitochondrial function, oxygenation, an increase of ATP production, increases mitochondria in number and size, acceleration of the diffusion rate, promote metabolism, scattering the mediators of inflammation, improve microcirculation by enhancement of bioavailability of nitric oxide, improved cells, and functional capacity, reduced production of proinflammatory cytokines (cytokines, chemokines, adipokines, and acute phase proteins).

CONCLUSION

Application of high tone power therapy for two weeks is safe, able to eliminate symptoms, and has low costs. Further study in multi-centers is needed to investigate the underlying physiological effects of these improvements.

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ABBREVIATIONS

Post-COVID syndrome (PCS), Persistent post-COVID syndrome (PPCS), High tone power therapy (HTT), and blood-brain barrier (BBB).

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