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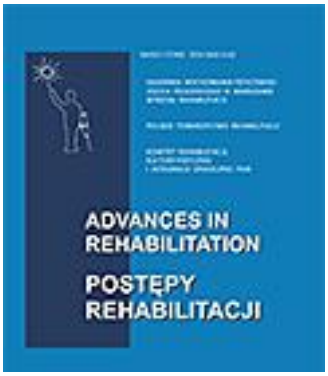

Original article

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Effect of Laser Acupuncture on Immunomodulation and Dyspnea in Post-COVID-19 Patients

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Abstract

Introduction: The post-COVID-19 syndrome is characterized by post-viral chronic fatigue syndrome as well as multi-organ complications. Its usual clinical symptoms are exhaustion, dyspnea, and chest pain. This study examines the effect of laser acupuncture (LA), which implies laser application on acupuncture points, on boosting immunity and reducing the inflammatory symptoms in post-COVID syndrome patients.
Material and methods: A total of 80 patients of both sexes with post-COVID symptoms were enrolled and randomly divided into the LA group (n = 40), which received LA three times/week for 12 weeks, and a placebo group (n = 40) which received sham LA. The following measures were taken for both groups before and after the study: Total lymphocyte count (TLC), Interleukin 6 (IL-6), dyspnea using the modified Medical Research Counseling Dyspnea Scale (mMRC), and fatigue using the Chalder Fatigue Scale (CFQ-11).
Results: LA group showed a significant elevation in TLC ($p < 0.001$) as well as a significant reduction in IL-6 levels, dyspnea, and fatigue scale ($p < 0.001$). On the other hand, the placebo group demonstrated a significant increase in TLC ($p < 0.05$)
Conclusions: The use of lasers at particular acupuncture points related to lung and immunity showed promising results in dealing with the typical main symptoms post-COVID, including chronic fatigue and dyspnea.

Keywords: complementary medicine, exhaustion, cytokines, COVID-19

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Introduction

The COVID-19 pandemic had a substantial and widespread effect all over the world. COVID-19 infections can cause a wide variety of symptoms and complications, including but not limited to asymptomatic infections, respiratory disease, multi-organ failure, and, ultimately, death. It was initially defined as a disease entity in the spring of 2020 when COVID-19 patients continued to experience symptoms for many weeks following their acute infection [1]. Common long-term effects of COVID-19 include fatigue, breathlessness, exercise intolerance, loss of taste and smell, and general discomfort. Approximately 80% of COVID-19 patients experienced at least one of these symptoms, with fatigue and dyspnea being among the five main post-COVID-19 symptoms [2]. Persistent inflammation drives most post-COVID symptoms, even without viral proteins and its maintained by immunological processes, such as generating several cytokines, including IL-1b, IL-6, and TNF [3].

Lymphocytes are essential immune system constituents, responsible for generating antibodies, directly destroying the tumor and virus-infected cells, and controlling immune system reactions [4]. Previous studies reported a decrease in lymphocyte count in patients who recovered from COVID-19 compared to healthy individuals [5,6]. IL-6 could suppress lymphopoiesis by directly affecting STAT-3 activation and hematopoietic stem cells [7]. Fundamentally, lymphocyte count was restored after IL-6 therapy [8].

Acupuncture is one of the traditional therapies that has been used many years before to treat respiratory conditions and alleviate common symptoms, including sleeplessness, fatigue, and dyspnea [9,10]. Additionally, acupuncture has a remarkable ability to control inflammation [11]. Recently, acupuncture practitioners have become familiar with laser acupuncture (LA) which involves using laser irradiation to stimulate acupuncture points. LA is preferred over traditional acupuncture with needles because it does not cause pain, is less invasive, and is associated with fewer side effects [12].

COVID-19 pandemic has affected millions of people worldwide, with many experiencing persistent symptoms like dyspnea and fatigue even after recovering. These symptoms can significantly impact the daily living activities and quality of life of affected individuals. Also, patients may experience immune dysregulation which can manifest as an imbalance of cytokines or reduced immune cells. Laser acupuncture is a non-invasive therapy that has shown promise in other conditions for stimulating immune function and reducing inflammation. As a result, the present study aimed to evaluate the potential benefits of LA on immunomodulation and dyspnea in post-COVID patients.

Materials and methods

Participants

This study followed the Declaration of Helsinki and the Ethics Committee of the Faculty of Physical Therapy, Cairo University, giving its permission to the study protocol (Approval number: P.T.REC/012/003582), and was recorded in clinicaltrials.gov with NCT05271500 number. The study took place between March 15, 2022, and July 2022. Each participant gave their informed consent before being enrolled in the study. A total of 80 patients were enrolled considering the following criteria: patients of both genders, 30–40 years of age (the prime working years of age that post covid symptoms could hinder their ability to work and improve the society), class I obesity (BMI 30-34.9) (as post covid symptoms are moderate and easily controlled), and confirmed COVID-19 by RT-PCR with post-COVID symptoms including cough, fatigue, and dyspnea. Those with Critical COVID-19 were excluded, those with LA contraindications (pregnancy, cancer, blood clotting diseases, or anti-coagulant medications use), uncontrolled diabetes, or an infection around the acupuncture point.

Procedure

Participants from an outpatient internal medicine clinic in El Sahel teaching hospital were invited. Two weeks after they had recovered from covid, all patients underwent fatigue and dyspnea assessment. The initial detection of inflammatory cytokine (IL6), as well as total lymphocytes occurred two weeks after recovery and was repeated after 12 weeks of therapy. Subsequently, the enrolled patients were randomly subdivided into two equal groups: the LA group included forty patients who were on LA, while the control group similarly had forty patients but received sham LA at which laser was off and no light was transmitted (Fig.1).

Intervention

Laser Acupuncture

Gallium-aluminium-arsenide (GaAlAs, infrared laser) (Chattanooga Group, Vista, California, USA) diode device with a continuous wave. An invisible wavelength of 850 nm was used for LA, with 0.07 cm^2 spot area and 100 mV power output. Each acupuncture point (LU1, LI4, LI11 and ST36) in the study group received a dose of 4 joules/cm^2 for 45 s in continuous mode (total dose=32 joules per session for eight points) [13].

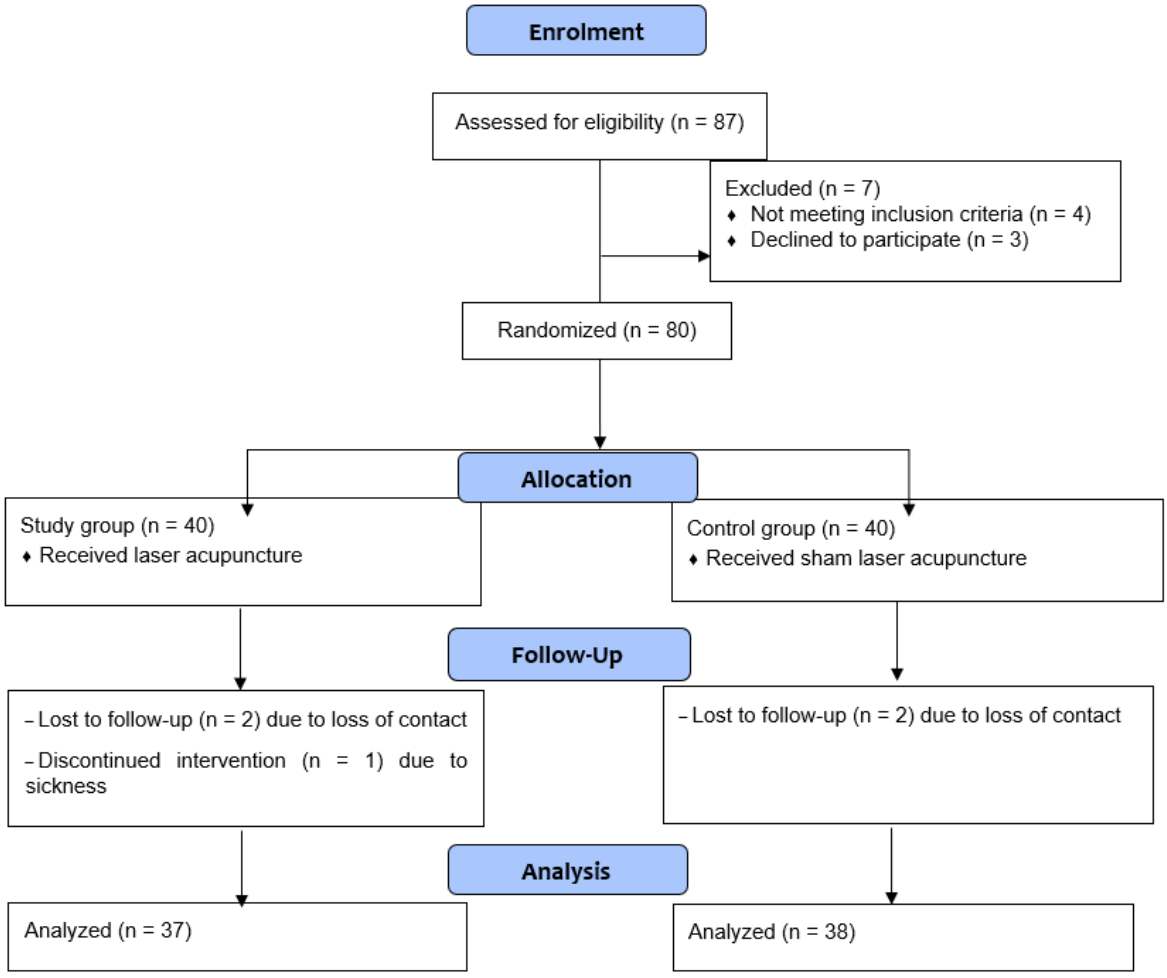

Fig.1. Flow chart of study design.

Outcome measurements

Primary outcomes

Biochemical measures

Blood samples were taken from each enrolled patient using sterile disposable syringes and an aseptic, standardized, painless vein puncture procedure. Samples were collected in glass containers containing EDTA anti-coagulants and labeled with the patient's name and serial number. The automated hematological analyzer (Sysmex KX-21N), which employs the electrical impedance concept, was used to measure the total lymphocyte count (TLC). Following the protocols, the human enzyme-linked immunosorbent assay (ELISA) kit was used to analyze plasma IL-6 levels (Invitrogen, ThermoFisher Scientific, Canada).

Dyspnea

Herein, mMRC dyspnea scale was used to assess breathlessness, with the scale consisting of five grades that indicate varying levels of dyspnea severity. The scale ranges from mild breathlessness after activity (grade 0) to severe shortness of breath that limits leaving the house or performing daily tasks (grade 4)[14].

Secondary outcomes

Fatigue assessment

Utilizing the Chalder Fatigue Scale (CFQ-11), fatigue presence and severity in participants were assessed. The scale comprises 11 items; each score on a Likert scale ranges from 0–3, and 0–33 is considered the total score, with higher scores representing more significant fatigue. The participants were responsible for their own scale administration, which only required a few minutes to accomplish [15].

Statistical analysis

An unpaired t-test was used to compare age and BMI between the groups. The Shapiro-Wilk test was applied to check the normal distribution of the data while using the Levene test to define the homogeneity between the groups. Using a mixed MANOVA, the effect of treatment on TLC and IL6 was investigated. Post-hoc tests using the Bonferroni correction were used for subsequent multiple comparisons. The comparison of dyspnea and CFQ-11 between groups was carried out using the Mann-Whitney test and between pre and post-treatment using the Wilcoxon signed ranks test. We had previously determined that a p-value of less than 0.05 would serve as the cutoff for determining whether or not the results were statistically significant. The statistical analysis was performed using the SPSS version 25 statistical package for windows (IBM SPSS, Chicago, IL, USA)

Results

Subject characteristics

Table 1 shows no significant differences in subject characteristics (age and BMI) between the LA group and the placebo group ($p > 0.05$).

Tab. 1. Comparison of subject characteristics between LA and Placebo groups

	LA Group	Placebo Group	MD	t- value	p-value
	Mean ±SD	Mean ±SD			
Age (years)	36.13 ± 2.78	35.86 ± 3.09	0.27	0.39	0.69
BMI (kg/m²)	32.36 ± 1.18	32.14 ± 1.09	0.12	0.862	0.391
Weight(kg)	90.19 ±6.82	90.11 ±6.84	0.08	0.053	0.958
Height(m)	1.67±0.07	1.67±0.07	0.00	-0.295	0.769

MD− mean difference, p-value− the probability value, SD− standard deviation

Treatment effect on TLC and IL6

Mixed MANOVA indicated a significant interaction effect of treatment and time ($F = 188.19$, $p = 0.001$). Treatment ($F = 6.86$, $p = 0.002$) and time ($F = 268.86$, $p = 0.001$) showed a significant main effect.

The TLC was significantly higher in the LA group ($p < 0.001$) and in the placebo group ($p < 0.05$) post-treatment than pre-treatment. The percentage of increase in TLC of LA and placebo groups was 21 and 1.79%, respectively. IL6 in the LA group decreased significantly by 22.42% after treatment than pre-treatment ($p > 0.001$), while IL6 in the placebo group did not show a significant change ($p > 0.05$). In the LA group, TLC increased significantly, and IL6 decreased significantly in comparison to the placebo group after treatment ($p < 0.01$) (Tab. 2).

Treatment effect on dyspnea and CFQ-11

In the LA group, dyspnea and CFQ-11 were significantly reduced after treatment than pre-treatment ($p > 0.001$). In contrast, the dyspnea scale of the placebo group improved significantly ($p < 0.001$) with no significant changes in CFQ-11 ($p > 0.05$). In the LA group, dyspnea and CFQ-11 decreased significantly than in the placebo group post-treatment ($p < 0.01$) (Tab. 3).

Tab. 2. Mean pre and post-treatment TLC and IL6 of LA and placebo groups

	Pre-treatment	Post-treatment			
	Mean ±SD	Mean ±SD	MD	% of change	p-value
TLC (cells/uL)					

LA Group A	1516 ± 143.95	1834.43 ± 127.56	-318.43	21	0.001
Placebo Group	1554.45 ± 136.57	1582.27 ± 142.78	-27.82	1.79	0.02
MD	-38.45	252.16			
	p = 0.24	***p = 0.001***			
IL6 (pg/ml)					
LA Group A	64.51 ± 20.24	50.05 ± 18.25	14.46	22.42	0.001
Placebo Group	66.11 ± 23.11	64.75 ± 22.98	1.36	2.06	0.12
MD	-1.6	-14.7			
	p = 0.75	***p = 0.003***			

MD− mean difference, p-value− the probability value, SD− standard deviation

Tab. 3. Median values of dyspnea and chalder fatigue scale pre and post-treatment of LA and placebo groups

	Pre-treatment	**Post-treatment**		
	Median (IQR)	**Median (IQR)**	**Z- value**	**p-value**
Dyspnea scale				
LA Group	2 (2-1)	1 (1-0)	-4.54	0.001
Placebo Group	2 (2-1)	1 (2-1)	-3.3	0.001
U- value	640	451		
	p = 0.59	***p = 0.007***		
Chalder fatigue scale				
Group A	5 (6-4)	3 (4-3)	-5.31	0.001
Group B	5 (6-4)	5 (5-4)	-1.63	0.1
U- value	581	123.5		
	p = 0.24	***p = 0.001***		

MD− mean difference, p-value− the probability value, SD− standard deviation

Discussion

In this study, the effects of LA on the immunological parameters as well as dyspnea in post-COVID-19 syndrome, were investigated. Several theories, including hyper-inflammatory states, oxidative stress, and cytokine storm, have been proposed to help explain the pathophysiology of the post-COVID syndrome [16]. Previous studies have shown that IL-6 levels tend to be increased in post-COVID patients [17,18]. Other research study reported that IL-6 contributes to the inflammation that underlies fatigue and sleep disturbances [19]

Our study revealed a significant reduction in IL6 levels and fatigability in the LA group while remaining unchanged in the placebo group. Several studies verified the positive benefits of LA on IL6 as in an earlier study which found that patients with rheumatoid arthritis who

received LA for a period of four weeks experienced a reduction in their levels of the inflammatory marker IL6. [20]. Additionally, patients with repeated injuries experienced a reduction in IL6 after stimulation of the ST-36 and PC-6 acupuncture points [21]. Patients with COVID-19 responded well to acupuncture as a preventive measure and treatment as shown in a study that, cytokine storm is reduced by enhancing vagus-cholinergic anti-inflammatory pathways through (LI4) or (ST36) sites [22]. Alterations in IL6 level are frequently utilized to induce a reduction in fatigability. This is because IL6 is implicated in the development of fatigue and is produced during both acute and chronic inflammatory responses [23].

Contrasting our findings, Petti et al. [24] reported that there were no significant changes in IL-6 after a single acupuncture treatment. It is challenging to evaluate the results of this study because the effects of a single acupuncture session are unlikely to accurately anticipate the significant effects of the acupuncture course.

A significant negative connection was found between IL-6 and TLC, demonstrating the ability of the inflammatory environment to decrease innate and adaptive immune cells [25]. It was found that IL-6 inhibited lymphopoiesis in clinically significant cases of inflammation [26]. As reduced number of lymphocytes could be a significant contributing factor linked to disease severity and higher mortality rates [27], therefore, increasing lymphocyte count can be crucial in combating the negative effects of inflammation on the immune system and can potentially aid in the prevention and treatment of various diseases and infections [28].

Our findings revealed that the LA group showed a more significant increase in TLC compared to the placebo group. This agrees with a previous study that reported that three weeks of acupuncture promote a significant elevation in T-cell proliferation rates [29]. Regarding the impact of acupuncture on immune system performance, the Zusanli (ST36) point may be a unique acupuncture site that modulates immunological activity. This immune modulation and acupuncture analgesia-producing systems may also have a neurological connection [30].

According to our study results, Participants in the laser acupuncture group reported a greater reduction in dyspnea compared to those in the placebo group. In this regard, a previous research study investigated whether combining traditional acupuncture with COPD therapy could improve exercise-induced dyspnea, the acupuncture group had significantly better results on the Borg scale than the control after ten weeks [31]. Similarly, an earlier study compared pharmacological medicines and LA effects on asthma and found that 83% of the patients in the group receiving LA treatment had a detectable improvement in dyspnea and functional and immunological parameters [32]. When acupuncture was included in the post-COVID syndrome rehabilitation regimen, dyspnea was reduced during activity, while energy was increased [33].

Vagus nerve activation and reduced acetylcholine release in the lung, which has bronchodilatory and anti-inflammatory effects, are the proposed mechanisms of acupuncture effects in dyspnea [34].

On the contrary, a previous research study showed that acupuncture treatments for a week did not reduce cancer-related dyspnea compared to a placebo. Although the authors recommended personalizing acupuncture point prescriptions to each patient, our study has shown positive results for the lung when employing the same points [35].

Ultimately, we suggest that LA may be a safe and effective treatment option for managing post-COVID-19 symptoms, particularly for patients who may not tolerate or benefit from traditional pharmacological interventions. This has important implications for improving patients' quality of life after COVID-19 and reducing the risk of adverse effects associated with conventional treatments.

This study is limited by the number of participants per group. Additionally, as the study only evaluates the short-term effects of LA for post-COVID syndrome, its long-term benefits remain unclear. Longer-term studies would provide valuable information on the sustained effects of LA treatment over time. Also, Future research could explore the potential benefits of auricular laser acupuncture as a novel technique for reducing stress, regulating sleep and improving immune function. Other acupuncture points targeting microcirculation modulation could also address COVID-19's impact on vascular health and brain function, including long-term problems like brain fog.

Conclusions

We concluded that patients with COVID-19 have exhibited improvement in immunity, dyspnea, and fatigue after using LA. Its ability to stimulate the immune system and reduce inflammation may be the basis for its potential therapeutic effects. A comprehensive approach to patient care could include the use of LA as an adjunct treatment for the post-COVID syndrome.

Conflict of interest

The authors have no conflict of interest to declare.

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