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The effect of laser acupuncture on immunomodulation and dyspnea in post-COVID-19 patients

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Abstract

Introduction: Post-COVID-19 syndrome is characterized by post-viral chronic fatigue syndrome and multi-organ complications. The typical clinical symptoms are exhaustion, dyspnea, and chest pain. This study examines the effect of laser acupuncture (LA), involving the use of laser treatment on acupuncture points, on boosting immunity and reducing the inflammatory symptoms in patients with post-COVID syndrome.

Material and methods: A total of 80 patients of both sexes with post-COVID symptoms were enrolled. They were 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: The LA group showed a significant elevation in TLC ($p < 0.001$) as well as a significant reduction in IL-6 levels, dyspnea, and fatigue ($p < 0.001$). 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 ameliorating the typical main symptoms post-COVID, including chronic fatigue and dyspnea.

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

Introduction

The COVID-19 pandemic had a substantial effect all over the world. COVID-19 infections can cause a wide variety of symptoms and complications, ranging from asymptomatic infections, through respiratory disease and multi-organ failure, with sometimes fatal results. 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 most common post-COVID-19 symptoms [2]. Most of these symptoms are driven by persistent inflammation, even without viral proteins, which is maintained by immunological processes, such the production of various cytokines including IL-1b, IL-6, and TNF [3].

Lymphocytes are essential constituents of the immune system, responsible for generating antibodies, directly destroying the tumor and virus-infected cells, and controlling immune system reactions [4]. Previous studies have 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 cell content [7]. However, lymphocyte count was restored after IL-6 therapy [8].

Acupuncture is a traditional therapy that has been used many years 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].

The COVID-19 pandemic has affected millions of people worldwide, with many experiencing persistent symptoms, including dyspnea and fatigue, even after recovery. 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. The aim of the present study was to evaluate the potential benefits of LA on immunomodulation and dyspnea in post-COVID patients.

Materials and methods

Participants

This study was in line with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Faculty of Physical Therapy, Cairo University (Approval number: P.T.REC/012/003582), and was recorded in clinicaltrials.gov as NCT05271500. The study took place between March 15, 2022, and July 2022. Each participant gave their informed consent before being enrolled.

A total of 80 patients of both sexes were enrolled. The following inclusion criteria were used: 30–40 years of age, 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. The age group was selected as being the prime productive years, during which post-COVID symptoms could hinder the ability to work and contribute to society. The exclusion criteria comprised critical COVID-19, LA contraindications (pregnancy, cancer, blood clotting diseases, or anticoagulant medication 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 to take part. Two weeks after they had recovered from COVID, all patients underwent fatigue and dyspnea assessment. An initial measurement of inflammatory cytokine levels (IL6), and total lymphocyte count was also performed two weeks after recovery, i.e. before the start of the study, and was repeated after 12 weeks of therapy. The enrolled patients were randomly subdivided into two equal groups: the LA group, including forty patients who received LA, and a control group, including forty patients who received sham LA i.e. the laser was off and no light was transmitted (Fig. 1).

Intervention

Laser Acupuncture

The LA was performed using a 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].

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 name and a 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, a human ELISA kit was used to analyze plasma IL-6 levels (Invitrogen, ThermoFisher Scientific, Canada).

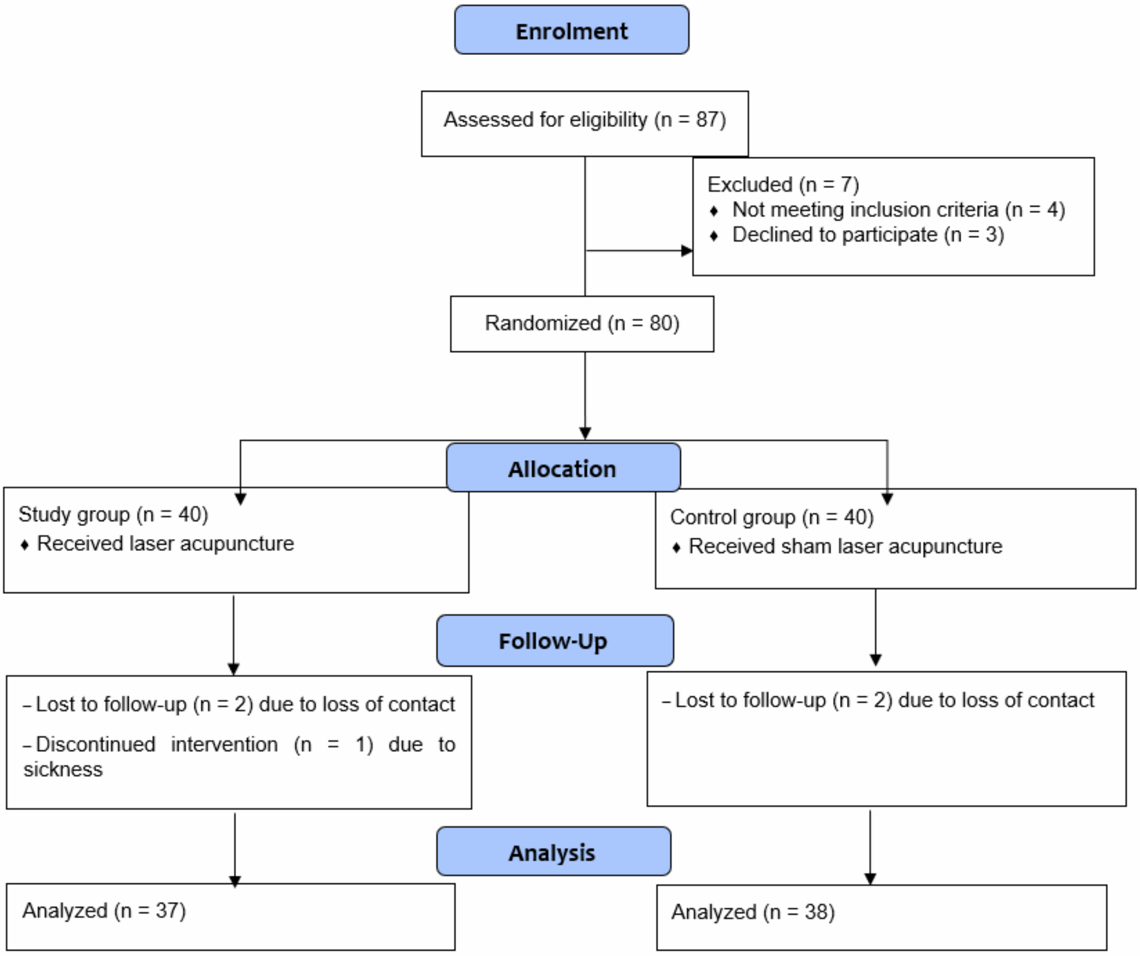

Fig. 1. Flow chart of study design

Dyspnea

The 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

The presence and severity of fatigue in participants were assessed using the Chalder Fatigue Scale (CFQ-11). 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 Levene's test was used to confirm homogeneity between the groups. Using a mixed MANOVA, the effect of treatment on TLC and IL6 was investigated. *Post hoc* tests using Bonferroni's 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. A p-value of less than 0.05 was assumed 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

No significant differences in subject characteristics (age and BMI) were found between the LA group and the placebo group at baseline ($p > 0.05$; Tab. 1).

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

BMI – body mass index, LA – laser acupuncture, MD − mean difference, SD − standard deviation.

Treatment effect on TLC and IL6

The 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 ($F = 268.86$, $p = 0.001$) also showed a significant main effect.

Post-treatment TLC was significantly higher in the LA group ($p < 0.001$) and in the placebo group ($p < 0.05$) compared to pre-treatment. The percentage increase in TLC was 21% in the LA group and 1.79% in the placebo. IL6 decreased significantly, i.e. by 22.42%, after treatment in the LA group compared to pre-treatment ($p > 0.001$), while no significant change was observed in the placebo group ($p > 0.05$). After treatment, TLC increased significantly, and IL6 decreased significantly, in the LA group compared to the placebo group ($p < 0.01$) (Tab. 2).

Treatment effect on dyspnea and CFQ-11

In the LA group, dyspnea and CFQ-11 were significantly reduced after treatment compared to 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 compared to the placebo group post-treatment ($p < 0.01$) (Tab. 3).

Tab. 2. Mean pre- and post-treatment TLC and IL6 values in the 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			

LA – laser acupuncture, MD − mean difference, SD − standard deviation.

Tab. 3. Median pre and post-treatment dyspnea and Chalder fatigue scale values in the 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		

LA – laser acupuncture, MD − mean difference, SD − standard deviation.

Discussion

Several theories, including hyper-inflammatory states, oxidative stress, and cytokine storm, have been proposed to help explain the pathophysiology of post-COVID syndrome [16]. Previous studies have shown that IL-6 levels tend to be increased in post-COVID patients [17,18]. It has also been reported that IL-6 contributes to the inflammation that underlies fatigue and sleep disturbances [19]. Therefore, the present study investigated the effects of laser acupuncture (LA) on various immunological parameters and dyspnea in post-COVID-19 syndrome.

Our study revealed a significant reduction in IL6 levels and fatigability in the LA group, but no such changes in the placebo group. Several studies have verified the positive benefits of LA on the inflammatory marker IL6. In an earlier study, that patients with rheumatoid arthritis who received LA for a period of four weeks experienced a reduction in their IL6 levels [20]. Additionally, patients with repeated injuries experienced a reduction in IL6 after stimulation of the ST-36 and PC-6 acupuncture points [21]. Other patients with COVID-19 responded well to acupuncture as a preventive measure and treatment, more specifically, the cytokine storm was found to be reduced by enhancing vagus-cholinergic anti-inflammatory pathways through acupuncture sites (LI4) and (ST36) [22]. IL6 has been implicated in the development of fatigue, being produced during both acute and chronic inflammatory responses [23], and changes in IL6 level are frequently used to reduce fatigability.

In contrast, Petti et al. [24] report no significant changes in IL-6 after a single acupuncture treatment. However, the effects of a single acupuncture session are unlikely to accurately reflect those of the acupuncture course as a whole.

A significant negative correlation was found between IL-6 and TLC level, demonstrating the ability of the inflammatory environment to decrease innate and adaptive immune cells [25]. IL-6 was previously found to inhibit lymphopoiesis in clinically-significant cases of inflammation [26]. As reduced lymphocyte counts could be a significant contributing factor linked to disease severity and higher mortality rates [27], 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 indicate that the LA group showed a more significant increase in TLC compared to the placebo group. This agrees with a previous study which 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. Such immune modulation and acupuncture analgesia-producing systems may also have a neurological connection [30].

In the present study, the participants in the laser acupuncture group reported a greater reduction in dyspnea compared to those in the placebo group. Similarly, in a previous study investigating 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 comparing pharmacological medicines and LA on treating asthma found that 83% of the patients in the group receiving LA treatment had a detectable improvement in dyspnea and functional and immunological parameters [32]. Elsewhere, when acupuncture was included in the post-COVID syndrome rehabilitation regimen, dyspnea was reduced during activity, while increased energy was reported while performing physical activity [33]. It has been proposed that acupuncture may exert its influence on dyspnea by vagus nerve activation and reduced acetylcholine release in the lung, which has bronchodilatory and anti-inflammatory effects [34].

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

Ultimately, we propose 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 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 the impact of COVID-19 on vascular health and brain function, including long-term problems like brain fog.

Conclusions

We conclude that patients with COVID-19 exhibited improvements in immunity, dyspnea, and fatigue after using LA. It may exert its potential therapeutic effects by stimulating the immune system and reducing inflammation. A comprehensive approach to patient care could include the use of LA as an adjunct treatment for post-COVID syndrome.

Conflict of interest

The authors have no conflict of interest to declare.

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References

1. Greenhalgh T, Knight M, A'Court C, Buxton M, Husain L. Management of post-acute covid-19 in primary care. BMJ. 2020; 370: m3026.
2. Jacobs LG, Gourna Paleoudis E, Lesky-Di Bari D, et al. Persistence of symptoms and quality of life at 35 days after hospitalization for COVID-19 infection. PLoS One. 2020; 15(12): e0243882.
3. Holms RD. Long COVID (PASC) Is Maintained by a Self-Sustaining Pro-Inflammatory TLR4/RAGE-Loop of S100A8/A9 > TLR4/RAGE Signalling, Inducing Chronic Expression of IL-1b, IL-6 and TNFa: Anti-Inflammatory Ezrin Peptides as Potential Therapy. Immuno. 2022; 2(3): 512–33.
4. Larosa DF, Orange JS. 1. Lymphocytes. J Allergy Clin Immunol. 2008; 121(2 Suppl): S364-S412.
5. Hasichaolu, Zhang X, Li X, Li X, Li D. Circulating Cytokines and Lymphocyte Subsets in Patients Who Have Recovered from COVID-19. Biomed Res Int. 2020; 2020: 7570981.
6. Varghese J, Sandmann S, Ochs K, et al. Persistent symptoms and lab abnormalities in patients who recovered from COVID-19. Sci Rep. 2021; 11(1): 12775.
7. Jenkins BJ, Roberts AW, Greenhill CJ, et al. Pathologic consequences of STAT3 hyperactivation by IL-6 and IL-11 during hematopoiesis and lymphopoiesis. Blood. 2007; 109(6): 2380–8.
8. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, et al. Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure. Cell Host Microbe. 2020; 27(6): 992–1000.e3.
9. Suzuki M, Yokoyama Y, Yamazaki H. Research into acupuncture for respiratory disease in Japan: a systematic review. Acupunct Med. 2009; 27(2): 54–60.
10. von Trott P, Oei SL, Ramsenthaler C. Acupuncture for Breathlessness in Advanced Diseases: A Systematic Review and Meta-analysis. J Pain Symptom Manage. 2020; 59(2): 327–338.e3.
11. Oh JE, Kim SN. Anti-Inflammatory Effects of Acupuncture at ST36 Point: A Literature Review in Animal Studies. Front Immunol. 2022; 12: 813748.

12. Chon TY, Mallory MJ, Yang J, Bublitz SE, Do A, Dorsher PT. Laser Acupuncture: A Concise Review. Med Acupunct. 2019; 31(3): 164−8.
13. Li N, Guo Y, Gong Y, et al. The Anti-Inflammatory Actions and Mechanisms of Acupuncture from Acupoint to Target Organs via Neuro-Immune Regulation. J Inflamm Res. 2021;14: 7191−224.
14. Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. Chest. 1988; 93(3): 580−6.
15. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. J Psychosom Res. 1993; 37(2): 147−53.
16. Rizvi AA, Kathuria A, Al Mahmeed W, et al. Post-COVID syndrome, inflammation, and diabetes. J Diabetes Complications. 2022; 36(11): 108336.
17. Sonnweber T, Sahanic S, Pizzini A, et al. Cardiopulmonary recovery after COVID-19: an observational prospective multicentre trial. Eur Respir J. 2021; 57(4): 2003481.
18. Fortini A, Torrigiani A, Sbaragli S, et al. COVID-19: persistence of symptoms and lung alterations after 3-6 months from hospital discharge. Infection. 2021; 49(5): 1007−15.
19. Kappelmann N, Dantzer R, Khandaker GM. Interleukin-6 as potential mediator of long-term neuropsychiatric symptoms of COVID-19. Psychoneuroendocrinology. 2021; 131: 105295.
20. Attia AM, Ibrahim FA, Abd El-Latif NA, et al. Therapeutic antioxidant and anti-inflammatory effects of laser acupuncture on patients with rheumatoid arthritis. Lasers Surg Med. 2016; 48(5): 490−7.
21. Liu CT, Hsieh TM, Shih FY, et al. The effects of electroacupuncture and laser acupuncture therapy for patients with major trauma: A study protocol. Medicine (Baltimore). 2021; 100(52): e28367
22. Jin GY, Jin L, Zheng J, He B. Advantages of anti-inflammatory acupuncture in treating sepsis of coronavirus disease 2019. World J Tradit Chinese Med. 2020; 6(2): 188–95.
23. Grygiel-Górniak B, Puszczewicz M. Fatigue and interleukin-6 – a multi-faceted relationship. Reumatologia. 2015; 53(4): 207−12.
24. Petti FB, Liguori A, Ippoliti F. Study on cytokines IL-2, IL-6, IL-10 in patients of chronic allergic rhinitis treated with acupuncture. J Tradit Chin Med. 2002; 22(2): 104−11.
25. Liu Y, Tan W, Chen H, et al. Dynamic changes in lymphocyte subsets and parallel cytokine levels in patients with severe and critical COVID-19. BMC Infect Dis. 2021; 21(1): 79.
26. Maeda K, Baba Y, Nagai Y, et al. IL-6 blocks a discrete early step in lymphopoiesis. Blood. 2005; 106(3): 879−85.
27. Zhang HJ, Qi GQ, Gu X, et al. Lymphocyte blood levels that remain low can predict the death of patients with COVID-19. Medicine (Baltimore). 2021; 100(28): e26503.
28. Pan WX, Fan AY, Chen S, Alemi SF. Acupuncture modulates immunity in sepsis: Toward a science-based protocol. Auton Neurosci. 2021; 232:102793.
29. Mori H, Kuge H, Tanaka TH, Taniwaki E, Hanyu K, Morisawa T. Effects of acupuncture treatment on natural killer cell activity, pulse rate, and pain reduction for older adults: an uncontrolled, observational study. J Integr Med. 2013; 11(2): 101−5.
30. Yamaguchi N, Takahashi T, Sakuma M, et al. Acupuncture regulates leukocyte subpopulations in human peripheral blood. Evid Based Complement Alternat Med. 2007; 4(4): 447−53.
31. Suzuki M, Namura K, Ohno Y, et al. The effect of acupuncture in the treatment of chronic obstructive pulmonary disease. J Altern Complement Med. 2008; 14(9): 1097−105.
32. Ailioaie C, Ailioaie L. Treatment of bronchial asthma with low-level laser in attack-free period at children. Laser Florence ’99: A Wind Laser Med World. 2000; 4166: 303–8.
33. Trager RJ, Brewka EC, Kaiser CM, Patterson AJ, Dusek JA. Acupuncture in Multidisciplinary Treatment for Post-COVID-19 Syndrome. Med Acupunct. 2022; 34(3): 177−83.
34. Geng WY, Liu ZB, Song NN, et al. Effects of electroacupuncture at Zusanli (ST36) on inflammatory cytokines in a rat model of smoke-induced chronic obstructive pulmonary disease. J Integr Med. 2013; 11(3): 213−9.
35. Javdan B, Cassileth B. Acupuncture Research at Memorial Sloan Kettering Cancer Center. J Acupunct Meridian Stud. 2015; 8(3): 115−21.