

Low-level laser therapy in chronic obstructive lung disease

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Context Chronic obstructive lung disease (COPD) is a common preventable and treatable disease. Low-level laser therapy (LLLТ) appears to be a promising modality in COPD management.

Aims The aim was to study the short-term effects of LLLТ on clinical and cardiac status in patients with stable COPD.

Materials and methods This was a controlled randomized study. Patients with impaired left ventricular ejection fraction less than 50%, those with atrial fibrillation (AF), those with pulmonary hypertension not owing to COPD, and those with any contraindication to exercise test or LLLТ were excluded. A total of 30 patients with stable COPD were divided into laser and control groups (15 patients each). Medical treatment was optimized in both groups with the addition of LLLТ in the laser group.

The following were assessed before and after LLLТ: Modified Medical Research Council (mMRC) scale, 6 min walk test, tricuspid annular plane systolic excursion, and lateral tricuspid annulus tissue Doppler velocities. The LLLТ has wavelength of 905 nm, output of 5–20 mW, and frequency of 500 Hz. Laser probe was placed on intercostal space both anteriorly and posteriorly on chest wall and arm with standardized laser acupuncture points of application with a frequency of five sessions/week for 2 successive weeks.

Statistical analysis Statistical package for the social sciences Software program, version 21 (SPSS). Data were summarized using range, mean, SD, and median for quantitative variables and frequency and percentage for qualitative ones. Comparison between groups was performed using independent sample *t*-test (if parametric) or Mann–Whitney test (if nonparametric) for quantitative variables and χ^2 -test or Fisher's exact test for qualitative ones. Paired quantitative measures were evaluated using

paired *t*-test (if parametric) or Wilcoxon test (if nonparametric). *P* values less than 0.05 were considered statistically significant, and less than 0.01 were considered highly significant.

Results Patients in LLLТ group had higher pulmonary artery systolic pressure, lower early (E') and higher late (A') lateral tricuspid annular velocities by Tissue Doppler echocardiography (TDE) versus control. Overall, 100% of laser patients showed improvement in mMRC scale by at least one grade versus 46% in control. In laser group, 6 min walk test was 24.4±10.4 before versus 52.9±14.7 m at the end of the study (*P*=0.001). In control, it was 32.4±14.9 versus 40.1±19.2, (*P*=0.003). No echocardiographic changes were noticed before versus after the study.

Conclusion Significant clinical improvement of 6 min walk test and mMRC scale grading after LLLТ therapy was observed. No detrimental effects of LLLТ on left ventricle or right ventricle functions or pulmonary artery systolic pressure were seen.

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Keywords: acupuncture, chronic obstructive lung disease, laser, right ventricle, tissue Doppler imaging

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Introduction

Chronic obstructive pulmonary disease (COPD) is considered one of the important public health problems which runs a progressive course [1–3]. Several mechanisms are sought to be the cause of structural and functional changes in COPD (e.g, chronic inflammation, oxidative stress, and imbalance between proteases and antiproteases) [4]. Pharmacologic therapies and pulmonary rehabilitation can improve clinical condition. However, neither disease progression nor the decline in lung function stops [5,6].

Low level laser therapy (LLLТ, also known as photobiomodulation) works by applying direct light energy to body cells, with no rapid or significant temperature rise of the tissues [7]. It has a wide range of effects at the molecular, cellular, and tissue

levels. The most accepted theory is that these lights which are mainly visible red and near infrared are absorbed particularly within the electron transport chain in the mitochondria [8,9]. When cells get stressed, like in chronic diseases, the mitochondria produce nitric oxide (NO) which competitively displaces oxygen thus reducing adenosine triphosphate (ATP) production. Low-level laser therapy of the correct wavelength and density, dissociates NO allowing oxygen back in, so ATP is restored and oxidative stress reduced [8,9].

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Studies on its effect in respiratory diseases have shown improvement in gas exchange and pulmonary functions [10–12]. However, it is still not a routine practice according to latest COPD guidelines.

We aimed in this study to detect the clinical and echocardiographic effect of LLLT in patients with stable COPD. To our knowledge, none of previous studies evaluated the effect of LLLT on pulmonary pressure and right ventricular function by echocardiography.

Materials and methods

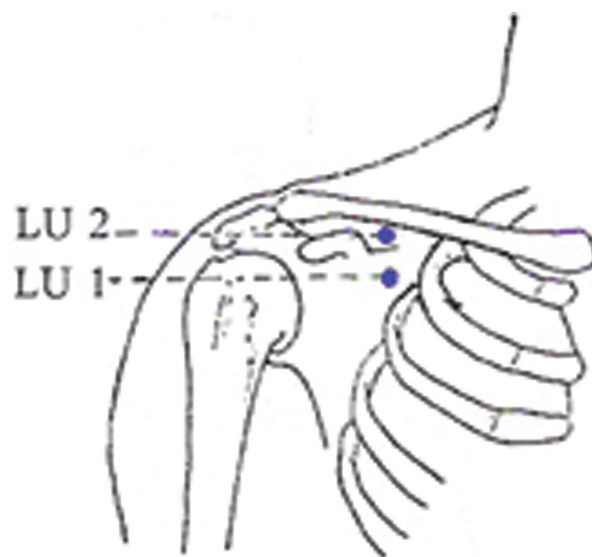
The study was an open-labeled controlled, single center, randomized study. A total of 30 patients with stable COPD were enrolled in the study. The patients were randomized to laser group (first 15 patients, optimum medical treatment+LLLT) and control group (optimum medical treatment alone). The optimization of medical treatment started 2 weeks before enrollment. It followed the Global Initiative for Obstructive Lung Disease guidelines and continued all through the study period. Patients with left ventricular ejection fraction (LVEF) less than 50%, those with atrial fibrillation, those with proven or suspected other causes of pulmonary hypertension, those with history of COPD exacerbation 2 months before the study or, those with any contraindication to exercise test [13] or LLLT were excluded from the study [14,15]. There are no absolute contraindications for LLLT; however, in patients with pacemakers, pregnant, patients with cancer if there is any doubt of a recurrence of metastases, and patients with labile epilepsy, it should be avoided or given with caution. It is also better to avoid applications of LLLT over the thyroid gland, ovaries, and testicles [15,16].

The study protocol was approved by the ethical committee. The study was conducted in the Critical Care Unit, Cairo University.

After enrollment and optimization of medical therapy for at least two weeks, all patients were subjected to the following at the beginning of the study and two weeks later:

- (1) Modified Medical Research Council (mMRC) Dyspnea scale [16]. The scale measures a person's limitation based on a scale of 0–4 and uses the final value to determine how much disability is caused by shortness of breath.
- (2) Six-minute walk test (6MWT) in meters using electrical treadmill (Schiller Quinton 4000; Schiller AG, Baar, Switzerland).
- (3) Echocardiographic examination was performed using Philips I.E 33 machine (Philips Ultrasound, Bothell, WA, USA), transthoracic cardiac probe × 5-1 with tissue Doppler capability. The following parameters were assessed: LVEF% by m-mode, diastolic mitral flow grading, right ventricular end diastolic diameter in apical four chambers view, tricuspid annular plane systolic excursion, pulmonary artery systolic pressure (PASP) [peak tricuspid flow velocity+RA pressure (fixed value of 5 mmHg)], and peak systolic and diastolic tissue Doppler velocities of the lateral tricuspid annulus.
- (4) Laser acupuncture therapy. The first 15 patients were subjected to LLLT using Phyaction CL (Phyaction, Bilzen, Belgium) with the following characteristics: wavelength 905 nm, output 5–20 mw, frequency 500 Hz). Laser probe was placed on acupuncture points which are thought to improve lung performance. They are located on both anterior and posterior chest walls and on both arms as follows:
 - (a) Anterior chest wall (LU1-LU2-CV17) (Figs. 1 and 2).
 - (b) Posterior chest wall (UB13-UB17) (Fig. 3).
 - (c) Arm (LU5-LU7) (Fig. 4).
 Both patients and therapists were wearing protective goggles as a protective strategy. The LLLT was applied five times weekly for 2 successive weeks.
- (5) mMRC scale, 6MWT, and echocardiography were repeated at the end of the study period for all patients (Fig. 5).

Figure 1



Lung points (LU1, LU2) on anterior chest wall. Image courtesy of Mahler D., Medical Acupuncture. Feb 2016, 28(1): 28–32.

Results

The study is a randomized controlled study on 30 patients with stable COPD with optimized medical therapy and LLLT in laser group.

- (1) Baseline clinical data.
- (2) Baseline echocardiographic measurements.
- (3) Clinical data at the end of the study.
- (4) Echocardiographic measurements at the end of the study.

Baseline clinical data

No significant difference between laser group and control regarding age, sex, mMRC dyspnea scale, or 6MWT was observed (Table 1).

Baseline echocardiographic measurements

Patients in the control group showed higher LVEF than control, but both were within normal ranges. Laser group had higher PASP, as well as higher A' velocities and lower E' of the lateral tricuspid annulus compared with control.

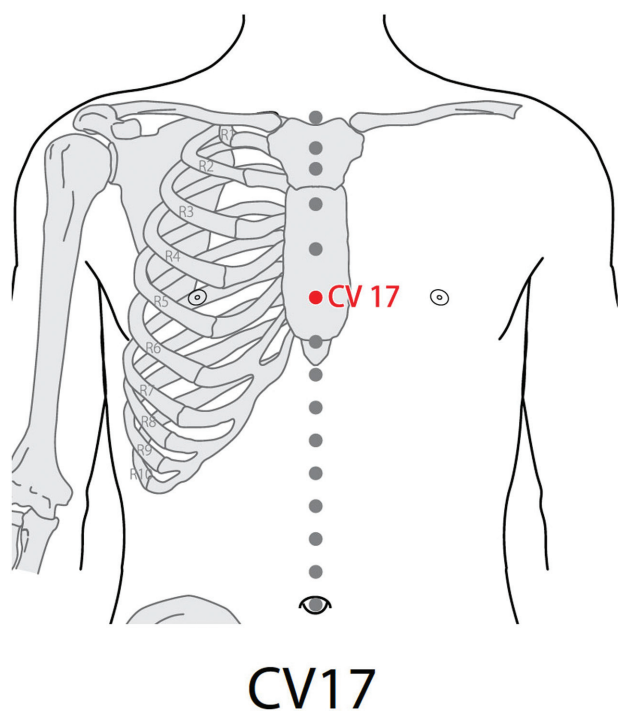
None of the other echocardiographic parameters showed any statistical difference between the two groups (Table 2).

Clinical data at the end of the study

Marked increase in the 6MWT in the laser group was observed compared with control (Fig. 4).

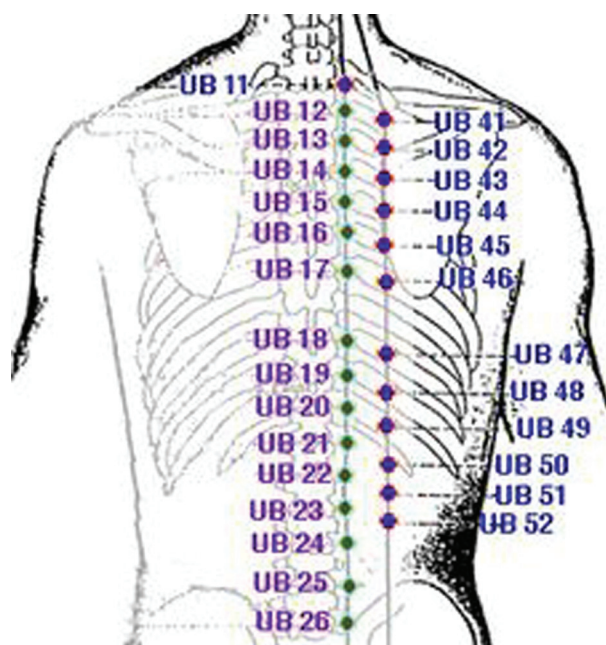
In laser group, the 6MWT was 24.4 ± 10.4 , and then it reached 52.9 ± 14.7 m at the end of the study, whereas in

Figure 2



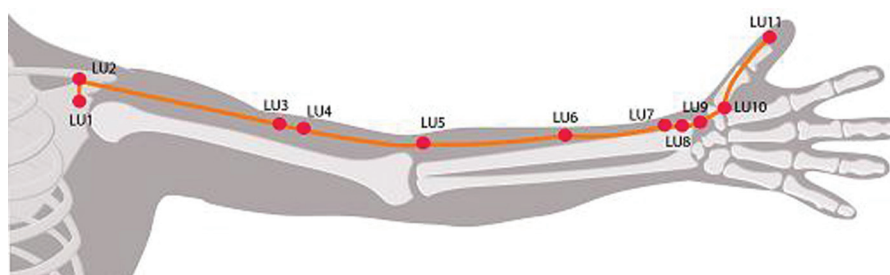
Meridian point, conception vessel 17. Image courtesy of miridiatech.com.

Figure 3



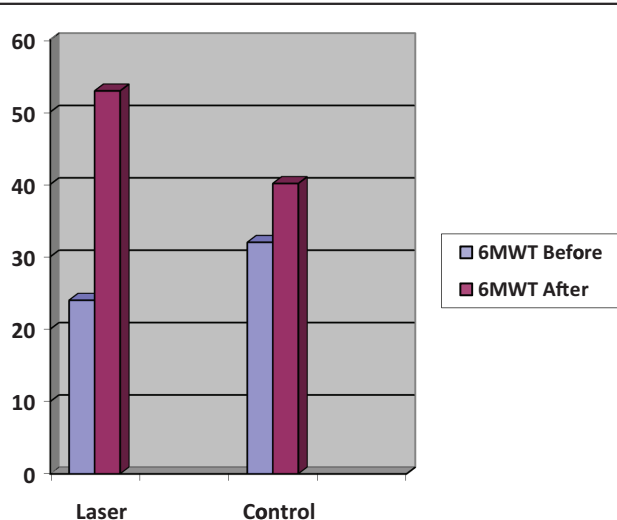
Urinary bladder meridians. Image courtesy of all-about-acupuncture.com.

Figure 4



Lung meridians. Image courtesy of all-about-acupuncture.com.

Figure 5



Six-minute walk test before and at the end of the study.

Table 1 Baseline clinical data in both groups

	Laser group [n (%)]	Control group [n (%)]	P value
Sex (males)	14 (93.3)	14 (93.3)	1.0
Smoking	13 (86.7)	11 (73.3)	0.7
mMRC scale			
Grade 0	0	0	1.0
Grade I	0	0	
Grade II	3 (20)	3 (20)	
Grade III	10 (67)	10 (67)	
Grade IV	2 (13)	2 (13)	
6MWT in meters (mean±SD)	24±10.39	32±17.93	0.3

6MWT, 6 min walk test; mMRC, Modified Medical Research Council.

Table 2 Baseline echocardiographic measurement in the study group

	Laser group	Control group	P value
LVEF%	69.17±5.74	65.41±4.23	0.04
LV diastolic function grading [n (%)]			
Normal	6 (40)	5 (33)	
Grade I	9 (60)	10 (67)	
RVEDD (cm)	2.19±0.63	2.49±0.59	0.09
TAPSE (cm)	2.00±0.38	1.88±0.3	0.3
PASP (mmHg)	42.07±12.3	30.67±14	0.009
TD of RV free wall			
S (cm/s)	12.55±2.55	11.76±2.23	0.3
E' (cm/s)	11.52±3.7	14.75±3.83	0.03
A' (cm/s)	15.54±4.07	9.80±2.6	<0.001

LV, left ventricle; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; RV, right ventricle; RVEDD, right ventricular end diastolic diameter; TAPSE, tricuspid annular plane systolic excursion; TD, tissue Doppler. Bold values mean significant.

the control group, it was 32.4±14.9 and then reached 40.1±19.2 m at the end of the study (Table 3).

Table 3 Clinical data at the end of the study

	Laser group [n (%)]	Control group [n (%)]	P value
mMRC scale			
Grade 0	0	0	
Grade I	3 (20)	1 (6.7)	
Grade II	10 (67)	4 (26.6)	
Grade III	2 (13)	7 (46.7)	
Grade IV	0	3 (20)	
6MWT (mean±SD)	52.93±14.69	40.13±19.22	0.08

6MWT, 6 min walk test; mMRC, Modified Medical Research Council.

Table 4 Echocardiographic parameters at the end of the study

	Laser group	Control group	P value
LVEF%	69.93±3.99	68.91±5.23	0.6
RVEDD (cm)	2.25±0.52	2.42±0.55	0.3
TAPSE (cm)	1.96±0.32	1.88±0.36	0.4
PASP (mmHg)	42.67±12.53	29.27±12.27	0.001
TD of RV free wall			
S (cm/s)	12.61±2.16	11.97±1.31	0.5
E' (cm/s)	10.87±2.78	15.87±3.41	<0.001
A' (cm/s)	14.62±3.58	9.83±1.83	<0.001

LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; RV, right ventricle; RVEDD, right ventricular end diastolic diameter; TAPSE, tricuspid annular plane systolic excursion; TD, tissue Doppler. Bold values mean significant.

An improvement in the mMRC scale grade was observed more in the laser group than control, as 100% of laser patients showed improvement in mMRC scale by at least one grade versus 46% in the control (Table 3).

Echocardiographic measurements at the end of the study

Laser group had higher PASP and A' velocities and lower E' compared with control.

No significant difference was observed between laser group and control regarding other echocardiographic measurements (Table 4).

Discussion

COPD is a common preventable and treatable disease with marked disability in its severe form.

Several treatment strategies are aiming to improve clinical outcome and decrease the incidence of hospital re-admission. LLLT as a noninvasive method for improving COPD symptoms appears promising.

On the mentioned basis, our study was done at the Critical Care Unit, Faculty of Medicine, Cairo University, for

clinical and echocardiographic evaluation of the effect of LLLT on patients with stable COPD. The clinical condition was assessed by 6MWT and mMRC scale. The echocardiographic examination included the evaluation of left ventricle (LV) and right ventricle (RV) systolic and diastolic functions.

There was a clinical improvement in 6MWT on both groups before and after the study, which could be explained by the sustained effect of optimization of medical treatment.

Regarding mMRC scale grading, our results showed more improvement in the laser group compared with control. All patients who underwent LLLT showed improvement in mMRC scale by at least one grade versus 46% in the control.

Suzuki *et al.* [12] tried to determine whether a combination of laser acupuncture treatment and conservative treatment for COPD improves dyspnea on exercise. They divided 30 patients into two groups, one received acupuncture one time per week for 10 weeks and the other received conventional medical treatment. Their results showed the acupuncture group had significant improvement in Borg scale and 6MWT compared to the other group. The laser frequency in the previous study differed from the protocol we used. However, until now, there is no standardized protocol for LLLT, but most studies used 10 sessions protocol with different frequencies.

In a study on patients with asthma, Milojević *et al.* [10] treated 50 patients with laser acupuncture for 10 days, comparing changes with those of a control group of the same number of patients, differing only in that laser acupuncture was not given. A significant improvement of all estimated lung function parameters was observed 30 min after laser treatment.

Mohammed *et al.* [11] studied 31 patients with different respiratory illnesses (COPD, asthma, bronchiectasis, and interstitial lung disease) and showed improvement in 6MWT as well as forced expiratory volume in 1 s in laser group more than control group. LLL was given in the same protocol as our study.

Similarly, Ailioaie *et al.* [17] conducted their study on 98 children (10–18 years) with moderate or severe asthma during an asthma free period. They divided them into three groups, a group received laser acupuncture and laser scanning twice daily for 10 days per month, the other group received an inhaled

β 2 agonist twice daily and the last group received oral theophylline retard two times per day. This protocol continued for 3 months. Favorable clinical, functional and immunological criteria were observed in 83% of the patients in group 1, 70% in group 2 and 53% in group 3. There were no reported side-effects in laser group.

In spite of the higher PASP in laser group, significant clinical improvement of 6MWT and mMRC scale grading was recorded in laser group more than the control group. This could be explained by the mechanism of action of LLL therapy.

The suggested mechanism of LLLT actions includes absorption of photons by the mitochondria and this will stimulate production of more ATP with low levels of reactive oxygen species (ROS). ROS are known to cause two actions according to their levels: at low level, they enhance cellular proliferation, and in high levels, they prevent proliferation and kill cells. Another mechanism for LLLT includes the production of nitric oxide which is released from its binding sites in the respiratory cycle and elsewhere producing its beneficial effects. Future development in the understanding of LLLT mechanisms is needed. This might lead to more acceptance of LLLT in mainstream medicine and may lead also to the use of LLLT for serious cardiovascular and neurological diseases [18].

In our study, laser therapy did not result in any deleterious effect on either LV or RV systolic or diastolic functions.

No harm has been documented for LLLT since its use in clinical trials and research. No long-term side effects were reported for this form of therapy. This gives security and safety for its use now and in the future [19]. Other than averting your eyes from the laser's red or infrared light, the FDA has found no other red flags or adverse side effects from using LLLT.

Conclusion

Significant clinical improvement of 6 min walk test and mMRC scale grading after LLLT therapy was observed. No detrimental effects of LLLT were seen on LV or RV functions or PASP.

Study limitations and recommendations

Limited number of the study group. Pulmonary function tests were not performed to all patients during the inclusion thus limiting one of milestones

needed for COPD diagnosis. Another limitation is the short follow up duration.

We recommend applying this study on mechanically ventilated patients and studying its effect on lung mechanics. We also recommend a larger number of patients and prolonged follow-up period to determine if the effect of laser was sustained or not.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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