EFFECT OF LOW-LEVEL LASER THERAPY ON CHOLESTEROL AND TRIGLYCERIDE SERUM LEVELS IN ICU PATIENTS: A CONTROLLED, RANDOMIZED STUDY

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Introduction:
High cholesterol serum levels increases risk of coronary artery disease. To reduce this risk, statins, which is not devoid of side effects in ICU patients, have been prescribed to inhibit the enzyme responsible for cholesterol synthesis. It was proposed that Low-level laser therapy (LLLT) may reduce cholesterol and triglyceride serum levels. This randomized, controlled study investigates the influence of LLLT on the noninvasive reduction of cholesterol and triglyceride serum levels in ICU.

Materials and Methods:
Twenty ICU patients, 10 in each group, were enrolled in the study. The study group used ilipo LLLT device with 4 laser pads strapped around patient abdomen emitting 650-660 nm (red) laser light. The control group received sham laser. The laser therapy sessions were done for 55 minutes, twice weekly for two successive weeks with 3 days between sessions. Blood samples were drawn prior to the laser administration. A standard lipid panel was studied before the procedure to establish a baseline and at the end of the second procedure week. The serum triglyceride and total cholesterol and low and high density lipoproteins levels before and after the LLLT were compared.

Results:
The total cholesterol and serum triglycerides levels in the study group revealed a statistically significant mean change of −15.43 and −13.7 respectively between study baseline and endpoint ($P < 0.05$).

Conclusion:
The potential application of the noninvasive chemical-free LLLT for cholesterol and triglyceride reduction tended to show favorable results in ICU patients

Keywords: *Laser, low level; cholesterol, lipoproteins; triglycerides*

Introduction:

An obvious relationship exists between increased serum cholesterol levels and coronary heart disease events and the mortality rates attributed to it.[1] Moreover, elevated cholesterol levels have been associated with different co-morbidities including stroke, atherosclerosis and myocardial infarction.[1]

Mostly all of the cholesterol within our bodies arises via biosynthesis. Therefore, physicians aim to reduce cholesterol level in blood by prescribing statins, to decrease the liver and tissue synthesis of cholesterol with resultant decrease in its bioavailability for the synthesis of very low-density lipoproteins which ultimately become low-density lipoproteins. [2-7] Effectiveness of statins in lowering cholesterol concentrations and reducing coronary heart disease risks as well other co-morbidities associated with hypercholesterolemia was revealed in many studies.[7-10] However, side effects have been attributed to statins with The American Heart Association unveiling several types of muscle disorders associated with statins: myalgia, mysoitis, and rhabdomyolysis with concomitant creatine kinase elevation and these were proved in several studies.[11]

It has been revealed that Low-level laser therapy (LLLT) alters gene expression, [12] involved in the biosynthetic cholesterologenesis process.

This randomized, controlled study was performed to assess the effectiveness of low level laser therapy in the reduction of cholesterol and triglyceride serum levels non-invasively and without any chemicals or medications.

Material and Methods:

Twenty ICU patients, divided into two equal groups, were enrolled in this study. The study protocol was approved by the local hospital ethical committee. Written consents were taken from all patients or their next of kin whenever applicable. Randomization was done using a computer generated randomization block. The study members taking the patient samples and performing the analysis were blinded to the patient group allocation. Studied patients were 18 - 75 years old. Patients' main diagnostics included cerebrovascular stroke, aortic aneurysm, and fracture base of skull as well as chronic obstructive airway disease. Patients were excluded if body mass index of 30 kg/m2 or greater; have any wound or external trauma to the areas to be treated with the laser; pregnant, breast-feeding, was receiving or received any cholesterol or triglycerides lowering therapy within the last 2months before the study, if were administered any lipid formulation or propofol or if ICU stay was less than 2 weeks.

Study group (n=10) received cold low level laser treatment while control group (n=10) received sham laser. The device used was ilipo low level laser machine (Chromogenex, South Wales, United Kingdom) (Figure 1) emitting laser wavelength 650-660nm (red laser light) and delivering total energy output of 1.3 W through 38 laser diodes. Four laser pads were securely strapped around the patient abdomen at level of the umbilicus with patient in recumbent position for 55 minutes twice a week for two weeks with three days in between sessions. Patient abdomen was covered with a blanket before laser is on to avoid patient and ICU personnel eye exposure to laser beam. Sham laser was performed using the same device but after covering its pads skin sensors with white plasters rendering laser pads non-functioning as these would not activate laser triggering except when in direct contact with patient skin.

Figure 1: The ilipo Low Level Laser Device

Study Design:

Blood samples were drawn prior to the laser treatment phase to obtain a standard lipid profile at baseline. Lipid profiles were attained at 2 different time intervals: pre-procedure and at the end of the second week. The laser administration phase of the study began immediately following the pre-procedure blood sample drawn. The study protocol lasted 2 successive weeks, with each patient receiving 4 total procedure administrations with the laser pads throughout 2 weeks (2 procedures per week, each one 3 days apart). The ilipo laser device was activated for 55 minutes each session. The purpose of this randomized, controlled study was to investigate the influence of

low level cold laser on serum triglyceride, total cholesterol and low density and high density lipoproteins levels in ICU patients after completion of the 2-week protocol.

A power analysis indicated that a minimum sample size of 20 patients randomly assigned to the treatment groups would provide 80% power for detecting a significant difference between the groups. The sample size calculations were performed using the nQuery Advisor software package (version 4.0; Statistical Solutions, Boston, MA).

Statistical Analysis:

Results were expressed as means +/- SD. Daily comparisons between study and control groups as regards parametric data were analyzed using unpaired Student t-test. For all statistical comparisons, a P value of <0.05 was considered significant. All statistical analysis was performed using Excel and SPSS 16 package.

Results:

There was no statistical difference between groups with respect to anthropometric and demographic data (Table 1). There were 6 ventilated patients in the study group versus 4 patients who needed ventilation at any time throughout the ICU stay in the control group with no statistical significance between groups as well. No significant changes were either revealed between studied groups as concerns lipid profile at baseline of the study.

Table 1: Demographic data

	Age(years)		Sex		Weight(Kg)		Height(cm)		APACHE II	
Group	**mean(SD)**	**Range**	**M**	**F**	**mean(SD)**	**Range**	**mean(SD)**	**Range**	**mean(SD)**	**Range**
Study (n = 10)	47(15)	23-65	5	5	71(12)	56-107	168(6)	150- 179	18(2)	16-22
Control (n = 10)	52(14)	25-71	6	4	68(18)	60-104	164(7)	160-182	18(2)	17-22

80% of the patients who demonstrated an overall reduction in total cholesterol serum levels when comparing pre-procedure and post-procedure Levels were in the study group, though care must be considered due to the small sample size. Table 2 reveals total cholesterol levels at baseline and at the end of the study.

Table 2: Mean and Standard Deviation of Total Cholesterol at Baseline and at the End of Study

Group	**Preprocedure Total Cholesterol Level (mg/dL)**		**Postprocedure Total Cholesterol Level (mg/dL)**		**Change in Total Cholesterol Levels (mg/dL)**		**P value**
	Mean	SD	Mean	SD	Mean	range	
Study (n = 10)	198.22	35.34	182.79	32.35	-15.43	−2.0 to -31.0	< 0.01
Control (n = 10)	195.34	22.13	193.55	42.25	-1.79	+3.0 to -10	>0.05

Low density lipoproteins measurements, on comparing its mean change from baseline to study endpoint in the study group, revealed a reduction of −8.15 points, (P < 0.05; Table 3).

Table 3: Mean and Standard Deviation of Low Density Lipoprotein (LDL) at Baseline and at the End of Study

Group	**Preprocedure LDL Level (mg/dL)**		**Postprocedure LDL Level (mg/dL)**		**Change in LDL Levels (mg/dL)**		**P value**
	Mean	SD	Mean	SD	Mean	Range	
Study (n = 10)	105.68	35.41	97.53	28.54	−8.15	−1.0 to −30.0	<0.05
Control (n = 10)	123.21	33.21	121.30	22.55	-1.91	+1.0 to -12	>0.05

70% of the patients who demonstrated an overall reduction in low density lipoprotein levels when comparing pre-procedure and post-procedure levels were in the study group.

The high density lipoproteins levels in the study group revealed a statistically insignificant mean change of −0.92 between study baseline and endpoint (P > 0.05; Table 4). 75% of the patients who demonstrated an overall reduction in high density lipoprotein levels when comparing pre-procedure and post-procedure levels were in the control group.

Table 4: Mean and Standard Deviation of High Density Lipoprotein (HDL) at Baseline and at the End of Study

Group	Preprocedure HDL Level (mg/dL)		Postprocedure HDL Level (mg/dL)		Change in HDL Levels (mg/dL)		P value
	Mean	SD	Mean	SD	Mean	Range	
Study (n = 10)	67.13	14.12	66.21	13.43	−0.92	+0.1 to −3.0	> 0.05
Control (n = 10)	64.43	17.21	60.55	12.45	-3.88	-2.0 to -8.0	< 0.05

In the study group patients, a favorable improvement was obvious when comparing the baseline ratio of LDL to HDL levels with the study endpoint ratio, with LDL levels decreasing by −8.15 points and HDL numbers reducing by just −0.92 points; however, the improvement in the LDL to HDL ratio did not reach statistical significance (P > 0.05).

The serum triglyceride levels in the study group revealed a statistically significant mean change of −13.7 between study baseline and endpoint (P <0.05; Table 5). 85% of the patients who demonstrated an overall reduction in serum triglyceride levels when comparing pre-procedure and post-procedure levels were in the study group. In the study group, none of the patients demonstrated an unsafe increase in triglyceride levels exceeding 150 mg/dL.

Table 5: Mean and Standard Deviation of Serum Triglyceride Level at Baseline and at the End of Study

Group	Preprocedure Serum Triglyceride Level (mg/dL)		Postprocedure Serum Triglyceride Level (mg/dL)		Change in Serum Triglyceride Levels (mg/dL)		P value
	Mean	SD	Mean	SD	Mean	Range	
Study (n = 10)	83.39	25.97	69.69	26.88	−13.7	−3.0 to -21.0	< 0.05
Control (n = 10)	88.52	23.23	87.33	25.34	-1.19	+1.0 to -13.0	> 0.05

Discussion:

This randomized, controlled study revealed that LLLT 2 times per week for 2 weeks can reduce cholesterol and triglyceride levels and more importantly, reduce LDL levels while preserving HDL levels.

Studies demonstrated that following low level laser irradiation, the mitochondrial membrane potential and proton gradient increases, resulting in mitochondrial optical properties changes with resultant increase in ADP-ATP exchange rate .[13] It is also postulated that low level laser therapy increases the electron transfer rate from cytochrome C to dioxygen by cytochrome C oxidase. [14, 15] Subsequently, a gradual shift toward a more oxidized state has been proved; more importantly, the activation of redox-sensitive transcription factors with ultimate gene expression.[16, 17, 18]

It has been noted that terminal enzymes photoactivation may be the primary response inducing cholesterologenesis suppression. It has also been shown that the initial physical and/or chemical changes of cytochrolme C oxidase alter

the intracellular redox state. [19] The latter is proposed to regulate cellular signaling pathways which control gene expression.[16.20]

Significant reduction in cholesterol and triglyceride levels following the administration of laser therapy with identifiable parameters regarding wavelength, intensity, and frequency was revealed in this study. Even though a statistically significant majority revealed a total cholesterol and triglyceride levels reduction, some patients did not reveal a reduction. This could be attributed to the procedure itself, variability in cholesterol levels, or perhaps mandating crucial alteration in patients' dietary habits.

Finally, this study provides a fruitful perspective concerning the potential application of this therapeutic noninvasive, chemical-free and medicine-free modality in ICU patients and enhancing further studies to accurately elaborate its therapeutic applicability and utility.

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