

Low Level Laser Nose Cavity

Irradiation Therapy Treatment on Hyperlipidemia

Clinical Research Report

Topic:

With common test methods in laboratory, conduct nose cavity low level laser (650nm/5mW) irradiation and compare with effects of common medicine therapy.

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1. Background

1.1 Mechanism of Low Level Laser Irradiation Therapy

In 1984, former Soviet scholar firstly apply Low Level Laser Irradiation (LLLI) in clinical to cure occlusive angionosis, and afterwards there are reports about good therapeutic effects of LLLI cure cerebral vascular disease, cardiac disease, bronchial asthma and ophthalmologic disease. In 1990, Low Level Laser Therapy was introduced into China and promoted speedily in nearly all departments. Therein, LLLI therapy is mostly applied in cerebral and cardiac diseases and obvious effects obtained.

Basic and clinical research indicate that LLLI therapy can improve hemorrheological properties, improve blood circulation, especially micro-circulation; regulate immune status; detoxification; clear oxygen free radicals and over-oxide, reduce blood & plasma viscosity and blood fat, restrain thrombus; research has proved that it can obviously enhance activity of red cell membrane Na^+-K^+ -ATP enzyme, increase SOD level in red cell, clear free radicals and anti-decrepit, also improve blood vessel convulsion and micro-circulation; enhance deformability of red cell.

Presently, LLLI clinical range of indications covers vascular system, immune system and neutral system. Therein, it has a great significance for treatment of ischemic cardiac and cerebral vascular disease, malignant tumor pain relief and C, infectious and immune disease, tumor, diabetes, senile dementia. In addition, it has obvious therapeutic effect for ischemic cardiac and

cerebral vascular disease. Therefore, LLLI therapy become direct cure methods from auxiliary physical therapy, and begin application in internal medicine field.

LLLI therapy has been applied in clinical use for 20 years on million cases, and there is no any side effect reports up to now.

In recent year, with development of semiconductor laser technology research, LLLI therapy has developed into semiconductor laser nose cavity irradiation therapy from optical fiber intra-vascular irradiation therapy. And it is called “ Most Promising Green Therapy in 21Century” by World Medical Circle for its feature of non-cut, non-pain, no medicine side effect and convenience for individual use.

1.2 Hyperlipidemia and clinical significance

In recent year, cardiac vascular disease has always be regarded as first or second death reason in the world medical circle. Therein, coronary heart disease incidence and death rate in some area is of increasing tendency. Proof indicate that many dangerous factors play an important role in coronary heart disease attack, such as high cholesterol, hypertension, smoke and diabetes etc. In addition, low high density lipoprotein is also an important dangerous factor. In above factors, high cholesterol is specially serious, and its clinical significance has been proved repeatedly, that is, with its long- term enhancing, incidence of coronary heart disease is obviously increasing. But long-term control cholesterol in normal level can prevent atherosclerosis, lower cholesterol can induce atherosclerosis and prevent coronary cardiac disease. In recent year, with deep acknowledge of triglyceride factor in atherosclerosis, now it has been listed as a dangerous factor for coronary heart disease. Therefore, intensified prevention and treatment of hyperlipidemia plays an important role in prevention and treatment of atherosclerosis.

Now in treatment program of hyperlipidemia, reasonable diet and life is significant to prevention and treatment of hyperlipidemia, blood fat can be lowered through life mode alteration in most patients. In addition, some newly developed medicine for fat adjustment as TATING can partly control hyperlipidemia which diet treatment can't not. Great achievement was obtained in some large-scale clinical tests with TATING medicine to prevent coronary heart disease I and II grade, and proved that TATING medicine can adjust blood fat and reduce incidence and death rate of coronary effectively, decrease demand of coronary artery cavity shaping and main artery coronary transplantation, lower incidence of brain stroke, and wholly reduce incidence of death rate. Common side effect of this kind medicine is stomach or intestines upset and weak muscle.

1.3 Feasible Analysis of Low Level Laser Nose Cavity Irradiation for Treatment of Hyperlipidemia

Now it is thought that hyperlipidemia is a metabolism disturbance disease which causes nervous, hard breath and four limb paralysis etc, also induce cerebral vascular diseases such as coronary heart disease and cerebral vascular accident. Through laser effects to blood, it can activate enzymes in blood, which can decompose over-fat in blood, thus reducing blood fat. In addition, it can break off some molecular bond in glucose of blood, thus glucose alcohol decomposition produce ATP energy, and red cell obtain enough energy, its deformability increase; meanwhile, aggregation of red cell and platelet decrease which lead to improvement of blood viscosity and hemorreological properties.

This research adopts Low Level Laser Nose Cavity Irradiation because epidermis in nose

cavity is very thin, and rich blood vessels in membrane, as well as slow blood flow speed. Low Level Laser Nose Cavity Irradiation through a nose cavity head, irradiate large area with high penetration of 650nm laser, therefore laser fully contact blood.

2. Objective

Observe therapeutic effects of Low Level Laser (650nm/5mW) Irradiation on nose cavity in treatment of hyperlipidemia.

3. Conductor

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4. Medicine and Test Instrument

- 1) Medicine for blood fat adjustment: TATING (Shu Jiang Zhi), 20mg/pc.
- 2) Low Level Laser Cure Instrument: Made by Guilin Kangxing Medical Instrument Co., Ltd. Model: GX-2000A.
- 3) Laboratory test instrument: Conductor hospital undertakes all work concerning blood sample, model of “ Charm 2000 Automatic blood bio-chemistry instrument”.

Test Standard:

Laboratory test Standard is according to common standard in conductor hospital and add some marginal comparison as well as quality control measurement of test result stability.

5. Receptor

30 patients with original hyperlipidemia that comply with tested condition.

6. Receptor Condition

6.1 Selected Condition

Clinic or Hospitalized patients was selected if it is diagnosed of hyperlipidemia. Refer to “Suggestion on Abnormal Blood Fat Prevention” by China Cerebral Vascular Magazine Edition Commission. The person with normal diet is diagnosed as hyperlipidemia if one of following circumstance found in him:

- 1) Serum total cholesterol (TC) ≥ 5.72 mmol/L (220 mg / dL)
- 2) Serum triglyceride (TG) ≥ 1.70 mmol/L (150mg / dL)
- 3) Low density lipoprotein cholesterol (LDL-C) ≥ 3.64 mmol/L (140mg / dL)
- 4) High density lipoprotein cholesterol (HDL-C) ≤ 0.91 mmol/L (35mg / dL)

6.2 Elimination Standard

- 1) Women with age of 18 below or 70 up, and during pregnancy or breast-feed period.

- 2) The patients with acute cardiac infarction, serious trauma or unstable disease after operation.
- 3) Hyperlipidemia and high cholesterol caused by Kidney synthetics, thyroid gland function decrease, acute or chronic liver, gall bladder disease and diabetes.
- 4) Hyperlipidemia caused by medicine (β -receptor resistant, kidney upper gland cortex hormone and some medical contraception).
- 5) Patients who is taking heparin, thyroid gland hormone medicine and other medicine which affect blood fat metabolism.
- 6) Serious original disease of gall bladder, kidney and blood hemopoietic system combination, mental patients.
- 7)The one who don't follow stipulation of this treatment and test or data literature lack may influent therapeutic effects

7 Ethics and Receptor Knowing Agreement

Conductor hospital submitted this research application report to Ethics Commission of local medical department and was approved.

Each receptor has signed "Receptor Knowing Agreement"

8. Research Design

Divide 30 receptors into two group: medicine group and laser group;

Medicine Group: on the basis of low-fat diet control, take TATING medicine. This test take ShuJiangZhi as treatment medicine. Dose: 1 time/day, 20mg/time, continuous 20 days and take every night.

Laser Group (Low Level Laser Nose Cavity Irradiation Group): On the basis of low-fat diet control, irradiate nose cavity with laser. Dose: wavelength of 650nm, power of 5mW, irradiate nose cavity once a day (45mins) with 7 days a course, and go on second course with an interval of 5 days (Totally 12 days).

Therapeutic Effects Evaluation: On every setting time, test blood of each group, record result data and receptor feeling etc according to case report table, conduct therapeutic effects evaluation. Evaluation time and test items is as Work Flow Chart in detail.

After this test, according to all tests and observed data record, conduct therapeutic effects comparison analysis in groups (medicine group and laser group) respectively, then conduct the one between medicine and laser groups.

Safety Evaluation: Evaluate safety of treatment. If any harmful matter occurs in receptor, necessary medical deal should be conducted; if any receptor is uncomfortable or unwilling to continue this test, he is permitted to withdraw it.

After this test, according to all tested data record, conduct safety comparison analysis on treatment group (medicine group and laser group) during treatment.

9. Work Flow Chart

Detail as "Work Flow Chart"

10. Test Methods

1) Receptor Selected:

In patients, to those diagnosed of original hyperlipidemia and completely meet requirement of this test, the doctor conductor told him the test objective and plan, and get his agreement to join this test, explain Knowing Agreement to him and make he signed voluntarily “Receptor Knowing Agreement”.

2) Random Grouping:

Before test, make 30 sealed envelopes according to random code. Rip envelopes whose No. is as receptor attending turn No., and according to the treatment arrangement in the envelope relevantly, distribute receptors into medicine group and laser group. From Table 1, we may know that at the beginning, several basic cardiac and cerebral vascular diseases dangerous factor and liver function index (ALT and AST) is similarly distributed in two groups, but due to sample quantity, in laser group, serum TC and TG is lower and HDL-C is higher.

Table 1 Basic Comparison of Two Group

	Laser Group	Medicine Group	P Value
TC (mmol/L)	6.2±0.9	7.1±1.8	0.175
TG (mmol/L)	2.5±1.4	3.0±1.4	0.362
HDL-C (mmol/L)	1.5±0.5	1.2±0.3	0.142
Male (%)	45.5	55.6	0.653
Age (Years old)	57.8±9.8	55.0±7.2	0.482
Smoke (%)	9.1	0	0.353
Drink (%)	18.2	0	0.178
Menopause Female (%)	45.5	33.3	0.582
Family Disease History (%)	18.2	11.1	0.660
Systolic Pressure(mmHg)	131.2±23.5	131.3±12.1	0.988
	Laser Group	Medicine Group	P Value
BMI (kg/m ²)	24.5±3.1	25.7±1.8	0.314
WHR	0.88±0.07	0.91±0.08	0.386
ALT (U/L)	22.4±11.2	27.9±10.7	0.277
AST (U/L)	23.9±6.7	26.1±6.2	0.458

BMI: weight index (Weight/Height²); WHR: waist and buttocks ratio; AST: Tiandong Ammonia acid transaminase ALT: Ammonia acid transaminase

3) Treatment Arrangement

Each receptor is arranged to a medicine or laser treatment. According to “Receptor Manual”, doctor explain treat arrangement requirement in detail, including:

- ① How to control diet at low-fat level during test course (explain low-fat diet and recommend control methods);
- ② For medicine group, told how to take medicine; for laser group, tell how to properly use GX-2000A instrument, and test time arrangement.
- ③ As a receptor, how to record and report his own therapeutic effects, feeling or any adverse event.

- ④ Require every receptor follow cure arrangement, so as to complete this test favorably.

4) Operation

- ① On first morning, examine during 7:30~9:30 without breakfast.
- ② On 13th morning, conduct blood biochemistry examination during 7:30~9:30.
- ③ On 20th date, take breakfast after blood biochemistry examination in morning.
- ④ It is commonly arrange 5~6 persons for laser group and medicine group respectively in 1 day.

5) Test Evaluation

Make Time Table of treat and test for each receptor. On each examination time point, prepare and complete laboratory examination for relative receptor; fill case report table in time and simultaneously conduct respective therapeutic effect and test evaluation of safety.

6) Laboratory Examination

Blood Fat Examination: Total cholesterol(TC), Triglyceride(TG), High Density Lipoprotein (HDL-C), Low Density Lipoprotein(LDL-C);

Other index: Tradition blood index(RBC, Hb, WBC, PLT), Kidney function (Urea Nitrogen BNU, sCr,) and transaminase (ALT, AST)

11. Therapeutic Effects Evaluation

1) Single Evaluation:

After each treatment time, complete relative record and therapeutic estimation:

- ① Receptor's feeling: If there is any nervous, hard breath, breast ach, dizzy, headache etc.
- ② Laboratory test: Estimate according to test result in laboratory.

General estimation: conduct estimation according to data in Case Report.

2) General Evaluation

After whole process of clinical research, conduct general evaluation according to data in Case Report Table.

Refer to normal value range of blood fat test result recommended by State Health Ministry in 2004:

TC (Total cholesterol) 2.1~5.7 mmol/dL

TG (Triglyceride) 0.56~2.26 mmol/dL

HDL-C (High density lipoprotein-- cholesterol) 1.16~2.0 mmol/dL

LDL-C (Low density lipoprotein cholesterol) 2.5~3.4 mmol/dL

Select 11 patients for analysis, basic level and blood fat level before and after irradiation is as Table 2, blood fat level has been approved significantly after 2 course of laser irradiation.

Table 2 Change of Blood Fat Level before and after Laser Irradiation

	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)
Basic level	6.22±0.90	2.52±1.28	1.45±0.50
13 th day	6.15±0.89	2.70±1.32	1.22±0.41

20 th day	5.83±0.86	2.05±1.12	1.27±0.36
<i>P</i> Value*	0.031	0.448	0.209

*Comparison of blood fat level on the 20th day after treatment

Analyze difference between groups and the result indicate that after adjustment of age, gender, hyperlipimedi family history, menopause female proportion, systolic pressure, diastolic pressure, if taken medicine for pressure reduction, blood fat level are improved in both laser group and medicine group, but more significantly in medicine group, On 20th date, TC,HDL-C improvement rate is significantly different from laser group. It indicate alteration of blood fat level before and after treatment.

Table 3 Comparison of Blood Fat Improvement before and after Treatment

	Laser Group	Medicine Group	<i>P</i> Values
TC (%) *			
13 th Day	0.8±6.5	-21.0±7.4	0.000
20 th Day	-5.8±8.5	-23.7±6.8	0.011
TG (%) *			
13 th Day	25.4±65.9	-11.9±35.3	0.401
20 th Day	-8.8±39.9	-16.0±26.6	0.651
HDL-C (%) *			
第 13 天	-12.3±23.5	2.4±12.7	0.350
第 20 天	-7.2±29.7	5.4±13.4	0.013

*Blood fat reduction rate after treatment compared with basic level

12.Satey Evaluation

In the whole process of this research, observe and record any adverse event and Serious adverse event.

•**Adverse Event:** Any adverse medical event that happened after Receptors received medicine or laser treatment, but has not certain relationship with the treatment.

•**Serious Adverse Event:** In the process of clinical research, the events that in hospital treatment, hospitalization period extension, permanent disability, working ability impact, danger to life or death, induction of congenital malformation etc.

Receptors will be evaluated of treatment safety after all regular tests in duty during return visit as the research plan. The safety information is obtained not through the derivational question but initiatively provided by receptor.

Safety of Medicine Group

Common adverse reactions are abdominal pain, abdominal distension, consipation, sickness and other stomach and intestine reactions. Sometimes there is reaction of transaminase, bilirubin and methyl aminoacetic acid enhance, joint pain, platelet reduction etc. Except specific receptor have to stop medicine, most are only sensitive reaction.

No any adverse reaction during test in this group.

Safety of Laser Group

In these several years, low level laser irradiation therapy (LLLI) had been applied on million patients for many years, and up to now no any report for adverse event .

But when the receptor first accept the LLLI therapy, it is kindly noted as followed:

- During first treatment, if blood pressure enhances, just lower output power to below 3mW, and turn up to 5mW only until blood pressure return normal value. This therapy has the function of blood pressure stabilization.
- For the one with high blood viscosity, low level laser irradiates blood, improve the micro-circulation, therefore someone will perhaps feel giddy slightly.
- After 15-min laser irradiation, few secretion generated in the nose cavity, it is normal situation

As Table 4, in laser group, ALT level decrease significantly (P=0.022) after treatment, but not obvious change in medicine group.

Table 4 Liver Function Change before and after Treatment

	Laser Group(U/L)		Medicine Group (U/L)	
	ALT	AST	ALT	AST
Basic Level	22.4±11.2	23.9±6.7	27.9±10.7	26.1±6.2
20 th Day	17.0±10.7	24.0±7.5	27.7±6.9	28.9±7.2
P Value	0.022	0.942	0.933	0.345

Safety Comparative Analysis Result of Two Groups

After adjust age, sex, smoke, drink and waistline and other factors which may influent the result. ALT reduced distinctly in laser group and more obvious than medicine group (P=0.070), ALT changes in two groups are similar.

Table 5 Comparison of Liver Function between Two Group *

	Laser Group	Medicine Group	P Value
ALT (U/L)	-23.1±28.2	6.9±27.7	0.070
AST (U/L)	0.5±15.6	15.0±40.1	0.340

*Reduction Rate of transaminase of comparison with basic level

13.Data Statistics Analysis

All results are wrote on case report form, only through check and confirm by main conductor as evaluated case and be recorded into database; Quantity data adopts T check, Number data adopts χ^2 check; analyze blood fat level and liver function difference of two groups before and after treatment, adopt pair T test comparison of blood fat level and liver function difference in the same group before and after treatment; all statistics analysis is conducted on SPSS statistics software.

14.Conclusion

- 1) On basis of adjusted diet, low level laser nose cavity irradiation lower serum total cholesterol level by 5.8% (P=0.031), triglyceride lowered by 8.8%.
- 2) Low level laser nose cavity irradiation therapy can effectively adjust blood fat, and also

lower ALT level lowered by 23.1% (P=0.022), as well as protective function to liver.

3) Compared with ShuJiangZhi, fat adjust function by low level laser nose cavity irradiation therapy is relative weak, but on consideration of safety, laser nose cavity irradiation has a significant applicable value for those of ineffective diet control and abnormal liver function.

15. Cooperation and Work Division

- Guilin Kangxing Medical Instrument Co., Ltd provides instruments for research.
- China South Normal University Hospital take charge of receptors selection, provides medicine, laboratory test, case record.
- China South Normal University Information Photoelectron Technology Institute take charge of manages low level laser cure instrument, TTM test, case record, clinical case data statistic analysis in research.
- Beijing Liferun Medical Science Tech. Co., Ltd. afford fee and take change in organization

Above sides cooperate to make this clinical research project and write the conclusion report.

16. Main Researchers Signature

I am the main researcher of “Low Level Laser Irradiation Therapy”, agree with above report contents of clinical research conclusion, hereby sign as following:

Cooperation Unit	Signature of Main Researchers
China South Normal University Information Photoelectron Technology Institute	Zi-ru Li
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Beijing Liferun Medical Science Tech. Co., Ltd	Lei Hou

2004/9/2

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