

Bio-psychology review on Low Level Laser Therapy management to overcome the condition of elephantiasis in chronic filariasis

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Abstract. Although lymphatic filariasis treatment programs have been implemented in Indonesia over the past decade, chronic impact of this disease in the form of elephantiasis remains a problem. This study aims to find a solution to reduce the volume of elephantiasis through innovation Low Level Laser Therapy (LLLT) and acupressure biopsychology. Quasi-experimental methods were used in this study with pre- and post-control designs. Subjects in this study were 20 chronic filariasis patients with lymphedema stage III. The control group was given standard treatment for lymphedema. The treatment group was given basic treatment standard plus LLLT on accupoin and bio psychological approach. The study was conducted in Bandung, Cimahi, and Karawang regencies, West Java, Indonesia. The results showed that the mean decrease of lymphedema volume in the group of $823,89 \pm 588.14$ ml was significantly different with the control group ($p = 0,001$). Methods of administration of LLLT and acupressure biopsychology may be considered to be developed as a complement therapy of chronic filariasis management.

1. Introduction

Low Level Laser Therapy (LLLT) which has a synonym for phototherapy, low dose laser, laser bio activation, laser bio stimulation, laser irradiation, laser photo stimulation, or photo-bio modulation is the use of photons in non-thermal radiation to alter biological activity. LLLT is a special type of laser that affects the biological system through non-thermal means. LLLT uses a light source consisting of a filtered lamp or a light-emitting diode (LED) or, sometimes, a combination of both [1]. When a photosensitizer molecule is present, as in LLLT, it is photographed back to the right excited state of the molecule, by the classical and photo physical photochemical path determined by the Jablonski diagram. The resulting specific reaction can accelerate the addition of ATP, the most common production of ROS (Reactive Oxygen Species) including superoxide anions (O_2^-) and hydrogen peroxide (H_2O_2). The photosensitizer in the ground state (S_0) absorbs the photon and is very interested in the singlet condition (S_1). The S_1 molecule can return to its ground state as emission of luorescence or move to a triplet excited state (T_1) through intersystem crossing, then form a free radical species with Type I reactions or transfer energy (Type II reactions) to oxygen molecules in a triplet state to a singlet state. The photosensitizer T_1 molecule can also return to S_0 through a process that lasts longer than the fluorescence known as glow [2].



The use of LLLT as a therapeutic modality originated in Eastern Europe since 1967. Professor Mester, an employee of Semmelweis University in Budapest, Hungary, observed and reported that the Helium-neon (He-Ne) laser has the ability to promote wound healing in rats [2].

In the process of wound healing, if it is not perfect, it will cause fibrosis. Any fibrosis causes the phenomenon of hyper proliferation and thickening of the extracellular matrix. The process of occurrence of fibrosis through several stages of inflammation, synthesis of extra cellular components of collagen and non-collagen, cell hyper proliferation and the formation of new tissue. The histopathology skin character suggests that the progression of fibrosis of the lymph vessels and surrounding tissues occurring in chronic filariasis results in a keratinocyte hyper proliferation feature that causes epidermal thickening, collagen settling, and mononuclear cell accumulation. The use of LLLT to reduce epidermal thickening, increased collagen density, and the accumulation of mononuclear cells have been performed by various researchers separately [3]–[7].

The researches that attempt to reveal the mechanism of LLLT in the wound healing process have been done. In the last decade's study it was found that the mechanism of LLLT in the wound healing process is to restore the balance between mRNA expression of metalloproteinase matrix (MMP) -2 and MMP-9. The mechanism of action of LLLT indirectly as anti-inflammation is through Reactive oxygen species (ROS) by phagocytes, lymphokines and cytokines produced by various lymphocyte subpopulations, or via NO produced by macrophages or as a result of NO-hemoglobin photolysis [8].

In chronic filariasis disease, fibrosis occurs in the lymph vessels and tissue around the lymph. Filarial worms enter the patient's body through vector mosquitoes. Through blood circulation, the filarial worm becomes adult in the lymph vessels. After many years, the adult worm dies. Worms will be wrapped by connective tissue as a reaction of the patient's body so that granulation will occur that will clog the lymph channels. The blockage causes the lymph fluid to not rise again and cause swelling of the distal blockage. The lymphatic channel wall located in the distal congestion over time will develop hyper cellular and its extracellular matrix solidifies and then forms fibrosis. Fibrosis of the lymph vessel wall and surrounding tissue causes damage to the valves in the lymph vessels and the surrounding muscle contractions become less effective in expanding the flow of lymph. Damage to the lymph vessel valves causes macrophage cells, lymph capillary endothelial cells and hematopoietic cells to produce Transforming Growth Factor β (TGF β) which initially aims to overcome the injury that occurs in the lymph vessel walls and surrounding areas. Apart from that the antigen produced by the adult worm also stimulates the macrophages producing the TGF β cytokines. Hyper production of TGF β stimulates the production of various collagen and other extracellular proteins by other mesenchyme cells to form fibrosis. The lymph fluid that collects in the lymphedema area is a fertile place to breed bacteria. Immune reactions to secondary bacteria and endosymbiosis of filarial worms with *Wolbachia* bacteria further trigger fibro genesis. In the skin arise in the form of thickening abnormalities due to increased keratinocytes, fibroblasts, and adipocytes.

Fibrosis occurring in the lymph vessel wall causes the lymph flow to be inhibited so that the fibro genesis process continues in chronic filariasis. This condition is different from the process of fibrosis formation on wound healing in other organs where fibro genesis stops after fibrosis develops. This condition causes the foot form chronic filariasis patients can continue to grow to resemble elephantiasis so called elephantiasis. Elephantiasis leads to a decrease in the patient's mobility ability which results in decreased productivity of individuals and their families. This shame and helplessness creates a prolonged stress impact on the sufferer and family, causing elephantiasis to cause physical and psychological problems. The condition that studies the physical and psychological relationship of man is Biopsychology.

The number of elephantiasis sufferers in Indonesia is second most in the world after India. The government is working with the WHO to try to reduce the number of filariasis sufferers with filariasis free filariasis targets in 2025. Filariasis control program consists of two pillars, namely the termination of the transmission chain through Bulk Prevention of Filariasis Prevention and the management of cases. In chronic cases with conditions of elephantiasis, management is urged to reduce the inability of motion in the patient and to prevent the severity of the disease. Until now there has been no drug or

surgical technique that produces satisfactory results to handle elephantiasis. A more effective solution is needed to reduce lymphedema in chronic filariasis occurring as a result of fibrosis in the lymph vessels and surrounding areas while controlling fibro genesis is ongoing and continuous.

The last two decades of research on the propagation of cell signals and cellular structures suggests that many of the basic biochemical interactions are controlled by electricity, as well as networks between connected cells and proteins. Based on this particular mechanical transmission system that is mechanical transmission in the body becomes an important thing in launching integration between cells [9]. In the human body, has been found dots that have high electrical conductivity that is on the area used in acupuncture treatment. These dots are called accupoint. This study aims to analyze the effectiveness of LLLT integration method on accupoint with bio psychological therapy to decrease lymphedema volume in elephantiasis patients due to chronic filariasis.

2. Method

2.1. Research design

This research design uses pre-post-test experiment with control design. In this study quantitatively analysed differences in lymphedema volume on the subject. The volume of extremities undergoing lymphedema is measured by a method based on the Law of Archimedes. Feet dipped in a vessel filled with water. Spilled water is measured as a measure of the volume of an immersed foot. The volume of lymphedema represents the normal volume of foot lymphedema and leg. In this study used LLLT with red light, wavelength 633 nm, and power 10 mw. The measurement scale is the nominal scale.

2.2. Research subject

The subjects of this research are filariasis patients who meet the criteria of research and are willing to follow the research by signing the informed consent. The target population of this study is all chronic filariasis patients stage III. Affordable population of this study is all chronic filariasis patients stage III recorded at the Health Office District of Bandung, Cimahi City, and District of Karawang. The inclusion criteria for chronic filariasis patients in this study were as follows:

- Based on anamnesis, clinical examination, and data from Community Health Center is diagnosed as chronic filariasis.
- Having lymphedema stage III according to WHO criteria (large volume increase in extremity followed by changes in skin and subcutaneous tissue)
- Lymphedema occurs in the lower extremities.
- The exclusion criteria is in severe disease other than chronic filariasis such as systemic infection (DHF, typhoid fever and others).

The sample is the partial or representative of the population to be studied. The number of samples drawn is determined based on the formula for Categorical-Numerical Analysis of 2 unpaired groups as follows:

$$n_1 = n_2 = \frac{2(Z\alpha + Z\beta)S^2}{X_1 - X_2} \quad (1)$$

Information:

$Z\alpha$: Z score (standard deviation) based on degree of meaning

$Z\beta$: Z score (standard deviation) based on power / test power

S : Standard deviation of both groups

$X_1 - X_2$: Clinical judgement, the desired clinical differences or the mean minimum difference considered meaningful.

n : number of samples.

With confidence in this study 95% ($\alpha = 5\%$), 80% test power ($1 - \beta = 80\%$), standard deviation 15.5 for hyperkeratosis thickness, and average the difference is assumed to be meaningful 20 μm , then based on the calculation of the number of samples obtained the number of samples of 10 people for the control group and 10 people for the treatment group. Subject selection was based on Consecutive Sampling (patient sequence) that has fulfilled the inclusion and sampling exclusion criteria until the minimum sample size was achieved

2.3. Research work procedure

Preliminary data retrieval is carried out at the community health center with the care facility or in the medical center or in the hospital near the patient's residence. For the control group given the standard treatment according to WHO. Patients are given training and exemplified hygiene care, prevention and treatment of comorbid infections, lymph node elevation during the day for 4-5 hours and throughout the night while sleeping, extremity body exercises, use of foot stockings, and appropriate footwear usage. Patients were given data checklist to perform the therapy every day for 2 months starting from the first day after initial data collection. Family sufferers and cadre officers are asked to participate in supervising the patient's compliance and discipline.

To monitor compliance, the researcher performs the examination to community health center/clinic near the patient's residence every once a week for 2 months. To the treatment group was given LLLT He-Ne 633 nm, 10mWatt power with 0.5 Joule energy. This LLLT was administered on accupoint which has been studied by Kanakura and colleagues in 2002 to treat lower extremity lymphedema like ST36, SP6, BL23, BL67, Ki1, CV2, CV3, and CV12 [14]. The accupoint determination was performed using the accupoint guides from WHO and checking using accupoint detectors. ST 36 is located at 5 mm laterally and distally from the anterior tubercle of the tibia. SP6 is located on the inside of the foot just below the ankle. This point is often used for immune system disorders. BL23 is located at 1.5 cun (1 cun equals the sample's thumbnail width) laterally from the midline of the vertebra, as high as the lower border of Lumbal 2 (between the spinal proximal L1 and the spinal proximal L2). BL67 is located 0.2 cm at the corner of the little toe of the lateral toe. Ki1 is located on the sole of the foot, ie at the curve when the plantar of the leg is flexed at the 1/3 anterior and 2/3 posterior meeting at the base of the 2nd and 3rd fingers and the heel. CV2 is located at the midline of the front body, the superior central tip of the pubis. CV3 is located on the center line of the front body, 1 cun above CV2, or 4 cun below umbilicus. CV12 is located in the center line of the front body, 4 cun above umbilicus [10].

Provision of LLLT conducted for 3 months with the frequency of giving 3x a week. Treatment of hygiene, prevention and treatment of comorbid infections, lymphedema extremity elevation, exercise of extremity motion, use of foot stockings, and appropriate footwear usage are maintained during LLLT delivery. After 3 months, re-registration was done to obtain final treatment group data.

2.4. Analysis design

The data collected, grouped and then tested normality. Test normality with Shapiro Wills to know the average of sample data is normal or abnormal distribution. The results of this normality test to determine the next analysis is to use parametric analysis when the data is normally distributed and non-parametric analysis if the data is not normally distributed. In this study used 2-group unpaired comparative-numeric analysis. The data is processed using SPSS.

3. Results

After 2 months treatment, the difference of control group lymphedema and treatment was presented in figure 1.



Figure 1. Differences in experimental and control groups before and after therapy.

Figure 1 shows changes in foot volume of the subjects after treatment for 3 months. Figures 2a and 2b show changes in the subject's foot of experimental group, on the other hand figures 1a and 1b show the control group. In plain view, figure 1 shows the extremities undergoing elephantiasis in the experiment group, condition before treatment (2a) clearly bigger than condition after treatment (2b). On the other side, the control group condition between before treatment (1a) and after treatment (1b) was unclear.

We performed measurements of mean differences of extremity volume before and after treatment in the control group and treatment group. The difference in the average change in extremity volume can be seen in table 1.

Table 1. Lymphedema change after treatment.

Lymphedema Volume	n	Mean \pm SD	p
Control Group	10	-04,5 \pm 55,65	0.001
Experiment Group	10	-819,5 \pm 88,71	

Table 1 shows a decrease in mean lymphedema volume in both groups. Data analysis showed a decrease in mean lymphedema volume of 104.50 mL in the control group and mean reduction of 819.50 mL in the treatment group. Since the normality distribution test (Shapiro-Wilk) showed normal distributed data in both the control and treatment groups, therefore the parametric statistical analysis of paired T test was used for testing the data before and after in each group.

Table 2. Meaning of different volume lymphedema extremity control group compared treatment.

Decrease of Volume	n	Average \pm SD	p
Control group	10	-104,5 \pm 55,65	0.001
Experiment group	10	-819,5 \pm 488,71	

Table 2 shows a significant difference in extremity volume between control and treatment groups ($p < 0.05$).

4. Discussion

The origin of the use of LLLT is based on the theory of Albert Einstein in an article entitled “Zur Quantum Theories der Strahlung” (1917) which sets out the basic principle of emission stimulation. At a nucleus, in which electrons move from one orbit to another, the release or absorption of energy is called a photon. Emission theory is then developed and classified into high potential (destructive) and low potency (without destructive potential [11].

In LLLT, the energy of the photons is transformed into photochemical, photo physical, and photo biological effects. Research by Kalarova et al suggests that penetration of HeNe light with a wavelength of 632 nm can reach up to a depth of 19 mm in the dermis. The energy of the photons depends only on the wavelength. Photons that interact with organ molecules or chromospheres in the tissue will be absorbed. Since photons have a red wavelength, the photon absorbing chromospheres will tend to electronize the electron in the molecular orbital that is increased from the initial position to the above-level position by the delivered quantum energy.

The basic biological mechanisms behind the effects of LLLT occur through the absorption of red light and NIR by mitochondrial chromospheres (cytochrome c oxidase / CCO) contained in the respiratory chain and by photo acceptors in the plasma cell membrane. Consequently, cascade events occur in the mitochondria, leading to bio stimulation of various processes (figure 1). The absorption spectra obtained for CCO in different oxidation states are recorded and found to be very similar to the action spectrum for biological responses to light. The absorption of this light energy can cause photo dissociation oxide nitric inhibition of CCO9 leading to increased enzyme activity, electron transport, mitochondrial respiration, and increase adenosine triphosphate (ATP), LLLT alter cell redox states that induce activation of various intracellular signaling pathways, and alter factor affinity transcription related to cell proliferation, survival, tissue repair and regeneration [1], [12].

The laser has the ability to change the cellular behavior determined by its wavelength. The neon helium laser (HeNe; 633 nm) has the ability to penetrate into the deep dermis layer. The thickness of the dermis varies from 300 μm in the eyelids to 3 mm on the back. The dermis can be divided into papillary, located just below the epidermis, and the reticular dermis, located between the papillary and the hypodermis. The effective rate of light penetration of LLLT into the skin is about 1-3 mm at 630 nm [1]. The location of lymph vessels that are blocked is in the dermis layer of elephantiasis sufferers. LLLT is able to penetrate up to the dermis layer, degrading the dermis collagen. Since collagen is the main structural protein and constitutes 70-80% of the skin's dry weight, the modulation of collagen metabolism in the skin by therapeutic irradiation has clinical importance. Skin collagen synthesized by fibroblasts consists of 80-85% collagen type I and 10-15% collagen type III [1], [7].

From the bio psychological side, LLLT acts analgesically as it increases the release of endorphins and therefore inhibits the nociceptive signal and controls the pain mediator. LLLT also acts on the oxidation potential of cellular reduction. Cells that are initially acidic in redox state after laser irradiation becomes alkaline and can function optimally. In healthy cells, laser exposure does not lead to increased redox potential; therefore, the laser does not affect healthy cells. It is known that LLLT stimulates lymphocytes, activates mast cells, and increases the production of adenosine-triphosphate in mitochondria and the proliferation of various cell types thus acting as anti-inflammatory. Further, this laser stimulates the microcirculation that results in changes in the hydrostatic pressure of the capillaries which in turn results in absorption of edema and the elimination of an intermediate metabolite [13]. Biophysical activation of LLLT in accupoin can accomplish effects which are manifestation of the nervous (peripheral, autonomous, and central) and endocrine systems, owing to interaction and integration of sensitive stimuli. Stimulation of accupoin can activate enkephalin, b-endorphin and endomorphin [14]. The release of endorphins acted as morphine, decreases anxiety and increases the body's immune system [15]. This speeds up the cure of disease.

The effects of histologic changes and molecular levels post-LLLT delivery are a reduction in the amount of collagen, fragmentation of collagen fibers, elastic degeneration of elastic fibers, increased regulation of metalloproteinase matrices (MMPs), especially MMP-1 and MMP-2, widening and dermal vessels, and atrophy and disorientation of the epidermis [1]. In this study LLLT rays are given to the sensitized areas of accupoints (acupuncture points). Accupoint has high conductivity and low inhibitory power. The energy of LLLT is absorbed primarily by hemoglobin and mitochondria which ultimately increase ATP, decrease collagen density and other extracellular matrices that impact on decreased lymphedema volume.

5. Conclusion

LLLT decreases the lymphedema volume in elephantiasis through collagen reshaping mechanism, increased ATP, improved apoptotic mechanism, increased endorphin hormone leading to increased immunity of elephantiasis. LLLT may be considered for chaperone treatment of chronic filariasis treatment.

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