

Role of Gallium Arsenide Laser Irradiation at 890 nm as an Adjunctive to Anti-tuberculosis Drugs in the Treatment of Pulmonary Tuberculosis

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ABSTRACT

Background. Tuberculosis is a global emergency with about nine million people developing disease every year. The long duration of treatment has emerged as a major obstacle in the control of tuberculosis. There is a need for development of new drugs and or shortened therapy.

Methods. The present study was carried out to explore whether any benefit could be achieved by the addition of low level energy laser therapy (LLLT) to the conventional anti-tubercular chemotherapy. One-hundred-thirty new sputum smear positive patients of pulmonary tuberculosis were enrolled to evaluate the bio-stimulatory effects of Gallium Arsenide laser irradiation at 890 nm, as an adjuvant therapy. These patients were randomly divided into two groups to receive either LLLT or sham irradiation (control) concomitantly with anti-tuberculosis chemotherapy.

Results. The patients treated with semiconductor laser as an adjuvant therapy along with anti-tuberculosis drugs had a faster clearance of tubercle bacilli from the sputum as compared to the control group (P value at: 45 days=0.1392, 60 days=0.0117, 75 days=0.00805, 90 days=0.00739).

Conclusions. These findings provide preliminary evidence that low level laser therapy with Gallium Arsenide laser may be a promising adjunctive therapy for patients with tuberculosis. Faster conversion of sputum should prevent the development of resistant mutants.

Key words : Tuberculosis, Treatment, Low level laser therapy.

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INTRODUCTION

Tuberculosis is a deadly disease and challenging in its management. About one third of the world population (two billion people) is already infected with tubercle bacilli. It is estimated that about nine million people develop tuberculosis every year. By 2020, another 200 million people

are expected to become sick and about 70 million will die from tuberculosis. Short course chemotherapy is the most effective treatment available for tuberculosis¹. In spite of this one fifth of half of all these patients with tuberculosis do not complete treatment. This is serious for both patients and community. Direct observation helps many patients to complete six

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to eight months treatment². WHO advocates the use of Directly Observed Treatment with a short course drug regimen as a part of the DOTS strategy.

Recently the effect of low level energy laser therapy (LLLT) has drawn attention in clinical medicine. Although the exact mechanism of its action is not known a few number of studies have demonstrated the photobiological effect associated with laser therapy. The study of immunomodulator agents in the treatment of tuberculosis is an exciting new area of investigation. The immunomodulators with a capacity to enhance host defense mechanisms and promote the killing of bacilli merit investigation in the treatment of tuberculosis. We have earlier reported the role of intracavitary nitrogen laser (wavelength-337 nm, output 1.5 mw) and endovascular Helium-Neon laser (wavelength-632.8 nm, output 1.5 mw) as an adjunctive treatment for drug-resistant pulmonary tuberculosis³. The possible risks of pneumothorax and haemoptysis associated with the puncture of lung cavity during the procedure of intracavitary nitrogen laser irradiation limited further evaluation of nitrogen laser therapy. The wavelength of semiconductor laser delivers energy to tissues and organs of human beings to the depth of 5 to 6 cm. A few studies have reported the efficacy of semiconductor external laser irradiation in-patients with pulmonary tuberculosis⁴⁻⁶. These studies reported a reduction in the time of cessation of bacterial excretion by 2-4 weeks by the use of semiconductor laser irradiation along with combined drug therapy in patients with disseminated infiltrative pulmonary tuberculosis. The present study was carried out to evaluate the effect of Gallium Arsenide laser (wavelength-890 nm) given concomitantly with anti-tuberculosis chemotherapy.

MATERIAL AND METHODS

The study was approved by the ethical committee of the LRS Institute of Tuberculosis and Allied Diseases and was carried out in the Department of Tuberculosis and Chest Diseases.

New sputum smear positive pulmonary tuberculosis patients were enrolled. A detailed history was obtained and clinical examination was performed. Routine investigations were carried out. HIV testing was not done in these patients. All patients gave an informed consent to participate in the study. Patients with a history of frank haemoptysis, diabetes mellitus, liver disease and alcohol abuse were excluded. These patients were randomly divided into two groups. In the first group (case group), the patients were treated with anti-tuberculosis category-I daily regimen along with semiconductor laser therapy as an adjunctive treatment. In the second group (control group), the patients were treated with anti-tuberculosis category-I daily regimen along with sham irradiation (placebo effect). Anti tuberculosis treatment consisted of two months of daily intensive phase with isoniazid, rifampicin, ethambutol and pyrazinamide, followed by four months of daily isoniazid and rifampicin (2HRZE/4HR). Intensive phase was extended for one more month in those patients whose sputum microscopy result was positive for acid fast bacilli at the end of two months. Semiconductor laser therapy was given using a double channel laser equipment (Gallium Arsenide) with a wavelength of 890 nm, frequency of 1500 Hz and output of 4-6 mW. The site of the field of external laser irradiation was guided by the location of the radiological lesion on chest radiography. At each field laser irradiation was given for 4 minutes by placing the laser probe in the intercostal space corresponding to the site of lesion both anteriorly and posteriorly. The total duration for laser irradiation did not exceed 12 minutes (*e.g.* 3 fields of 4 minutes) per day. The laser therapy was given daily for ten days. The patients were admitted for LLLT. Those patients who consented to come daily were treated from the out patient clinic. Sham irradiation was given for 10 days using the same laser machine without switching it on. The duration for sham irradiation was 4 minutes per field not exceeding 12 minutes (*e.g.* 3 fields of 4 minutes) per day.

Monitoring of treatment was done by clinical improvement in symptoms, weight gain,

haemoglobin and sputum examination for acid-fast bacilli by Ziehl-Neelsen method. The patient was considered sputum negative (*i.e.* sputum conversion) when the sputum microscopy results were negative for acid-fast bacilli and remained negative on subsequent examination.

RESULTS

One-hundred-twenty-six male and four female new sputum smears AFB positive (3+) pulmonary tuberculosis patients were enrolled. Five patients were excluded because four of these developed hepatitis and one developed hypercuricemia. Only 70 patients (53.84%) completed the full anti-tuberculosis treatment. One patient died and 54 patients (41.54%) defaulted. Out of the 70 patients who completed the treatment, 65 patients (92.86%) were cured and five patients (7.14%) failed. Thirty-four patients in the case group who received semiconductor laser therapy along with the anti-tuberculosis treatment were cured and 31 patients in control group who received sham irradiation (no laser therapy, placebo effect) were cured.

Comparison of Sputum Conversion

The sputum conversion rate of the cured patients in both the groups is given in the table. Two patients (5.88%) in the case group and six patients (19.35%) in the control group became sputum smear negative in 15 days. At 45 days

21 patients (61.76%) in the case group and 15 patients (48.38%) in the control group became sputum negative. Thirty patients (88.23%) in the case group and 20 patients (64.51%) in the control group became sputum negative by two months. All the cured patients in the case group became sputum negative for AFB by 90 days and by 135 days in the control group. Statistical analysis showed that patients treated with semiconductor laser as an adjuvant therapy along with anti-tuberculosis drugs had faster clearance of tubercle bacilli from the sputum (earlier sputum conversion) than the control group patients who were treated only with anti-tuberculosis drugs (P value at: 45 days = 0.1392, 60 days - 0.0117, 75 days - 0.00805, and 90 days = 0.00739).

It was observed that the patients in the case group showed sputum conversion almost twice

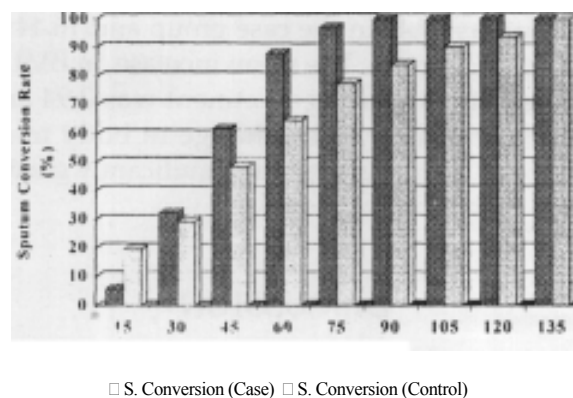


Figure. Cumulative proportion of sputum conversion of cured patients in case and control groups.

Table. Sputum conversion rate of cured patients

No. of Days	Case Group (n = 34)	Control Group (n=31)	P Value	Relative Risk RR (95% CI) with Reference to Baseline
15	2 (5.88%)	6 (19.35%)	0.0493	1.0
30	11 (32.35%)	9 (29.03%)	0.386	1.92 (0.56-6.63)
45	21 (61.76%)	15 (48.38%)	0.1392	2.04 (0.61-6.80)
60	30 (88.23%)	20 (64.51%)	0.0117	2.10 (0.64-6.92)
75	33 (97.05%)	24 (77.41%)	0.00805	2.03 (0.62-6.67)
90	34 (100%)	26 (83.87%)	0.00739	1.98 (0.60-6.53)
105	34 (100%)	28 (90.32%)	0.0316	1.92 (0.58-6.33)
120	34 (100%)	29 (93.54%)	0.0661	1.89 (0.57-6.23)
135	34 (100%)	31 (100%)		1.83 (0.55-6.04)

as fast (RR=2.0) in comparison to the controls who only received anti-tuberculosis therapy (see Figure).

Comparison of Change in Blood Hemoglobin

The mean hemoglobin of the cured patients at the time of enrolment in the study was 11.92 ± 1.47 gm% in the case group and 11.56 ± 1.89 gm% in the control group ($P = 0.392$). The increase in hemoglobin in these patients during treatment was 1.38 ± 1.32 gm% in the case group and 1.64 ± 1.61 gm% in the control group. Using t-test (two samples assuming equal variance), this increase had no significance between the two groups ($P = 0.4858$).

Comparison of Change in Mean Body Mass Index

The Mean body mass index (BMI) of the cured patients at the time of enrolment of the study was 17.42 in the case group and 16.44 in the control group. The mean increase in BMI in these patients during treatment was 2.94 and 2.32 respectively. The change in body mass index in the case group was significantly greater than in the control group.

DISCUSSION

In the present study the role of LLLT as an adjunctive treatment was evaluated in new smear positive patients of pulmonary tuberculosis. To assess the activating effects of low level laser irradiation in a study with this small size would be difficult because the regime in both the groups would be accepted to cure more than 95% of patients. If the bio-stimulatory or immune activity of the body is enhanced by low level laser irradiation at 890 nm, the patient should eliminate the tubercle bacilli from the lung cavities or lesions faster and have early sputum conversion. Therefore, sputum conversion rates were compared in patients of both the groups who were cured. There was a faster clearance of tubercle bacilli in the sputum of patients who were treated with low level laser therapy along with anti-tuberculosis treatment. The exact mechanism of this is not

clear. Interestingly and inexplicably, in the beginning after 10 days of semiconductor laser therapy, two patients (5.88%) in the case group and six patients (19.35%) in the control group were sputum negative ($P = 0.0493$).

The early conversion has important implications because faster killing of the sensitive organisms improves the bacteriological cure and prevents secondary resistance. The greater the number of tubercle bacilli the patient harbors before the start of therapy, the greater is the extent of primary resistant mutants within this population. If the bacterial count can be rapidly and drastically reduced in the intensive phase, the likelihood that new resistant mutants will emerge is greatly reduced. Although these findings provide preliminary evidence that LLLT with Gallium Arsenide irradiation may have bio-stimulatory effect in the treatment of tuberculosis, the exact mechanism is not known. Further studies are warranted for optimal dose schedules and to define the bio-stimulatory effects of Gallium Arsenide irradiation at 890 nm for quick sputum conversion.

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