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PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF THE EFFECTS OF LOW INTENSITY LASER IRRADIATION ON POSTMASTECTOMY PAIN

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Background: *Low intensity laser therapy (LILT) has been tried successfully for the treatment of pain of different etiologies, including postoperative pain. We tried to assess its efficacy in chronic postmastectomy pain, which has a complex nature and a probable functional component.*

Methods: *Forty female patients were allocated into two equal groups. All have completed adjuvant therapy following Patey's mastectomy for operable breast cancer. We compared the effect of LILT with that of diclofenac sodium 50 mg twice daily. Present pain intensity scale (ppi) assessed pain subjectively, while the drop of diurnal serum cortisol level did it objectively .A goniometer was used to quantify changes in the range of movement at the shoulder joint following treatment.*

Results: *All patients completed the trial, and were compatible in terms of age, type of surgery and adjuvant therapy received. The same surgeon did all operations and the average postoperative period before submission was 4 months. Results of treatment with LILT (n=20) were compared with those of diclofenac sodium (n=20) as follows: pain reduction (ppi mean values) from 72.00% to 21.25% and from 75.00% to 59.00% respectively. Mean diurnal plasma cortisol level (ug/dl) dropped from 22.71 to 15.82 and from 21.26 to 18.26 respectively. Improvement in the range of movement at the shoulder joint (mean values in degrees) flexion: from 20.25 to 71.00 versus 23.25 to 33.50, abduction: from 18.00 to 81.00 versus 20.25 to 36.70, horizontal adduction: from 42.90 to 115.00 versus 38.15 to 72.75. $p<0.05$ in all tested parameters.*

Conclusion: *LILT significantly reduces postmastectomy pain subjectively & objectively, and significantly improves the range of movements at the shoulder joint. The degree of improvement is statistically significant.*

Key words: LILT, Laser therapy, Mastectomy, Postoperative pain

INTRODUCTION

Knowledge about postmastectomy pain has accumulated considerably in the last decades. The pain which occurs after mastectomy for operable breast cancer is chronic and stays for a long time and occurs at the operation site, shoulder, lower neck and upper limb [1]. Like all other types of late postoperative pain, it is inadequately recognized, inadequately monitored and inadequately treated (the report of the Joint Commission of the Royal College of Surgeons of England and the College of Anesthesia, 1990), and to the moment it remains an unsolved problem. It is in part dependent on the psychological make up of the patient, as a decrease of pain tolerance may be present.

There is no conclusive evidence to suggest the exact organic cause of postmstectomy pain, but trauma and compression to the nerves, trauma and ischaemia to the muscles, fibromyalgia, and fibromyositis are among the proposed causes [2-10]. Toxic polyneuropathy (due to adjuvant chemotherapy), and brachial plexus or intercostal neuralgia may also contribute [8,11].

The conventional treatment of postmastectomy pain (similar to other types of traumatic and inflammatory neuromuscular pain) is by nonsteriodal anti-inflammatory drugs. Diclofenac sodium a member of this group, is effective, and in the recommended dose (50 mg. twice daily), patients are less likely to discontinue treatment due to side effects or lack of a convenient response [12]. In addition it has analgesic properties [13], which -like aceclofenac- are more prolonged than those of paracetamol and aspirin. An improvement up to 87% is expected if the pain is moderate or mild, with a 50% excellent to good tolerance. Complete relief occurs in 10% of cases only.

Analgesic Laser Therapy

The analgesic effect of laser was well known in the early days of laser science, but the attempts to get benefit from this effect in surgical practice gained momentum only in the 1980s. One of the pioneer studies was that of Walker[14] who documented this effect on various types of chronic pain of multiple diagnoses. He also drew the attention to the possible involvement of serotonin metabolism in its action.

The results of laser therapy in different painful syndromes were variable, but it was very effective in myofascial and postoperative pain, and to a lesser extent in low back pain [18,21,22,25].

Nd-YAG laser has been used to relieve pain in rheumatoid arthritis, particularly for small joints, with an appreciable improvement in 60% of cases [15]. Similar results were obtained in osteoarthritic patients [16,17] and in other types of arthritis and periarthritis [19] even if calcification is present [20]. Recently moderate reduction in muscloskeletal backpain with improvement in function was obtained using 1 .06 μm laser irradiation. The benefits were limited and decreased with time [21].

CO_2 laser has been used to treat mastalgia [23] and laser acupuncture was a substitute for anesthesia in minor oromaxillofacial operations, and in dental practice [24].

Low Intensity Laser (LIL) was tried to treat pain of trigeminal neuralgia, radicular pain and for occipital neuralgia. Its use to relieve postoperative pain was reported by many [18,22].

The rational for the clinical application of LILT to relieve pain was not clearly evident, but recent data on laser tissue interaction have started to suggest some possible identifiable mechanisms. It has manifold biological effects, and its efficacy has been documented by clinical studies. Martino et al. [23] found in an open trial, a significant pain reduction in one third of patients having mastalgia. They attributed the analgesia to the photobiomodulatory effects of laser upon neural function. There is also evidence to suggest that it may have significant effects on the synthesis, release and metabolism of a range of neurochemicals including serotonin and acetyicholine. In addition, it has proven effects upon the pharmacology of nociceptive process at the level of the primary pain receptor, and also on nerve conduction latency.

Some workers [19] directed the attention to the cumulative effects of this line of treatment and its long lasting results. and others pointed to the possible implication of serotonin metabolism, as a mechanism of laser mediated analgesia.

Assessment of Effect

Although subjective assessment of treatment is not difficult using different pain scales [27], objective one is always so. Estimation of plasma beta-endorphine level seems to be very useful and ideal [16,26].

Beta-endorphine, an endogenous opiate, is released into the blood by the pituitary gland in response to pain. Its release is associated with a gradual onset of both analgesia and elevation of pain threshold that lasts for a long period. The rapidity with which analgesia occurs suggests a neural mechanism for its action. Estimation of plasma beta-endorphine level is possible by a specific radioimmunoassay that is sensitive to 5 pg./ml. The normal level by this method is 33.66 pg/ml at night with a diurnal increase parallel to the circadian rhythm of ACTH secretion[26].

The secretion of beta-endorphine is accompanied by the secretion of ACTH from the pituitary gland, with consequent alteration of plasma cortisol level. These alterations may be used as an accurate indirect index of beta-endorphine level. Patients with chronic pain tend to have high plasma cortisol levels that drop after analgesia.

PATIENTS AND METHODS

Between January and October 1999, forty female patients were enrolled in the study. The patients were chosen from those recently treated of breast cancer by surgery and adjuvant therapy, and presenting because of post treatment pain. A written consent was obtained for all patients and all were informed about the possible use of laser in their treatment. Patients having gastric or gastroesophageal troubles and those with hepatic or renal impairment were not included in the study. Also excluded were those having light sensitivity or having cardiac pace makers[26].

The patients were investigated for recurrence of their tumor by chest X-ray, liver ultrasound, bone scan and

estimation of the tumor marker Ca 15-3. Their post treatment pain was intractable, in the shoulder and breast regions, not present before operation, and persistent for the last 3 months. There should be no history of osteoarthritis, cervical spondylosis, cervical rib syndrome, supraspinatus tendenitis, carpal tunnel syndrome and other similar conditions.

The patients were randomly divided into two equal groups (according to the hospital serial number), each is 20 patients. Group 1 received laser treatment, while group 2 received oral diclofenac sodium 50 mg twice daily for ten consecutive days. The design was double blind.

Differences in mean values of parameters were assessed by Student's unpaired *t* test and statistical significance was assumed at $p<0.05$.

Laser Device and Dosimetry

The equipment used delivers He-Ne laser combined with infrared diode laser. It gives the option of using spot He-Ne laser alone (using a hand piece) or both combined together using a scanning technique. There is a special device, which makes it possible to modify the laser beam from point to line and to move it longitudinally at the speed desired.The infrared beams are focalized and projected parallel to the He-Ne rays so that they operate together on a wide area in an automatic sweeping action. The patient and operator wear goggles glasses to protect the eyes from the laser beam and the equipment is preadjusted to deliver laser beam with the following specifications: output wave length 632.8 nanometers, power 15 mW, energy density 2 Joules /cm^2 frequency 5000Hz., pulse duration 200 nanoseconds and pulse energy 10 nanojoules, area of treatment (20 X 20) cm^2 and a total treatment time of 200 minutes (16,26)

Testing Procedures

1. Determination of pain intensity, using the present pain intensity scale [27] which is a graphic rating scale with numerical values placed equidistantly from 0 to 4. Pain intensity was scored as being: no=0, mild=1, moderate=2, severe=3, and unbearable=4.

2. Estimation of diurnal plasma cortisol level (a proxy for beta-endorphine) before the start of treatment and after its termination, by radioimmunoassay. The plasma is separated from heparinized venous blood samples and stored refrigerated at 5° C. The tubes were then dealt with using Gamma Coat ™ ^{125}I kits. The expected normal value by this method is 7-25 μg/dl with a sensitivity standard of 0.21 μg/dl.

3. Determination of range of movement at the ipsilateral shoulder joint: flexion, abduction and horizontal adduction using a single goniometer for all patients to reduce error.

RESULTS

The overall mean age at presentation was 53 years (range from 38 to 66 years). All patients in both groups (who were comparable in terms of age, type of surgery, and type of postoperative adjuvant therapy), completed the trial. The same surgeon (first author) did all the operations, and the average postoperative period before presentation was 4 months. The following are the mean values of the tested procedures before and after treatment (summarized in Table 1) and for convenience they are shown in (Fig. 1 (a & b)).

Present Pain Intensity

72.00 & 75.00 for the laser and drug groups respectively before and 21.25 &59.00 after treatment (p = 0 for laser group and 0.02 for the drug group).

Diurnal Plasma Cortisol Level

22.71 & 21.26 μg/dl for the laser and drug groups before and l5.82 & 18.26ugldl after treatment (p = 0.0l for the laser group and 0.03 for the drug group).

Range of Movements at the Shoulder Joint

a) Flexion: 20.25 & 23.25 degrees for the laser and drug groups before, and 71.00 &33.50 degrees after (p = 0 for the laser group and 0.02 for the drug group).

b) Abduction: 1 8.00 & 20.25 degrees for the laser and drug groups before and 81.00 & 36.70 after treatment (p = 0 for the laser group and 0.01 for the drug group).

c) Horizontal Adduction: 42.90 & 38. 15 degrees for the laser and drug groups before and 115.00 &72.75 degrees after treatment (p = 0 for both groups.).

Table (1): ***Mean and standard deviation (SD) of the tested parameters in both groups (each n=20 & p< 0.05)***

Parameter	*Before*		*After*		
	Value	*SD*	*Value*	*SD*	*t*
Laser Group					
Pain (ppi%)	72.00	21.42	21.25	15.00	8.46
Dpc (ug/dl)	22.71	6.42	15.82	3.38	4.14
Movement*					
F	20.25	6.78	71.00	7.18	-22.40
Abd	18.00	6.38	81.00	5.28	-33.16
H Ad	42.90	9.75	115.00	12.03	-20.30
Diclofenac Group					
Pain (ppi%)	75.00	20.48	59.00	18.61	2.52
Dpc (ug/dl)	21.26	4.47	18.26	3.52	2.30
Movements*					
F	23.25	8.16	33.50	15.40	-2.56
Abd	20.25	9.39	36.70	14.89	-4.07
H Ad	38.15	10.44	72.75	18.53	-7.09

* : at the shoulder joint in degrees | F :flexion
ppi :present pain intensity | Abd :abduction
Dpc :diurnal plasma cortisol level | H Ad :horizontal adduction

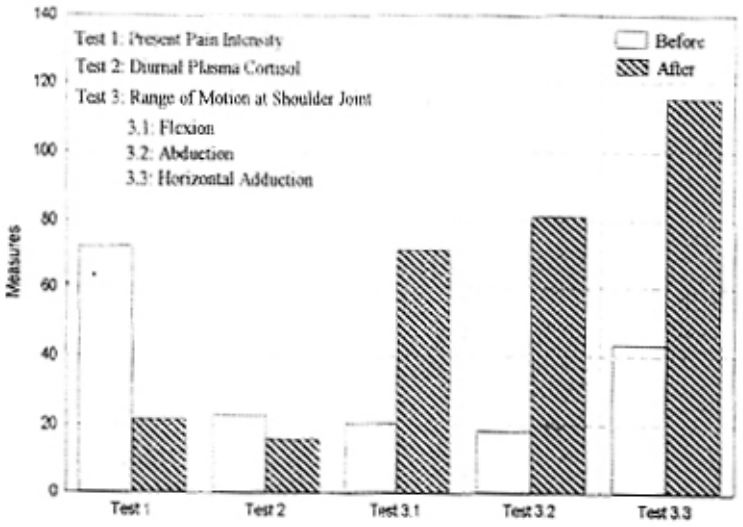

Fig (1a) : Results of the laser group

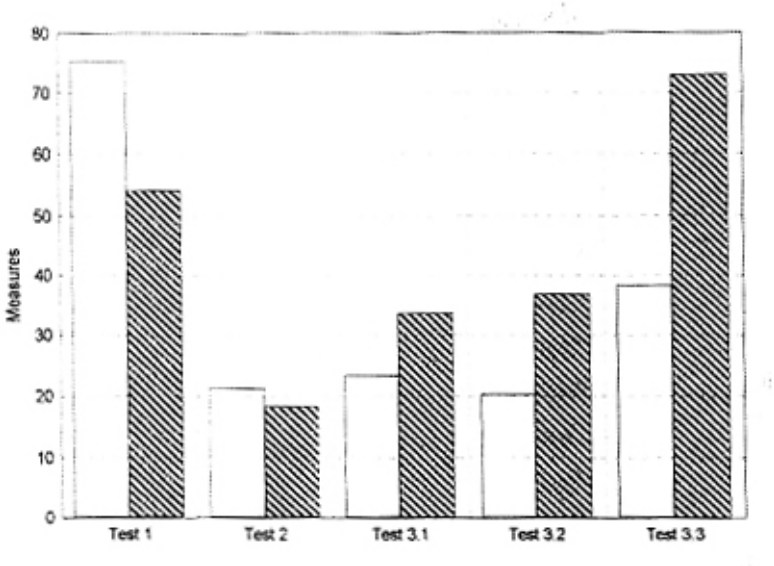

Fig (1b) : Results of the diclofenac group

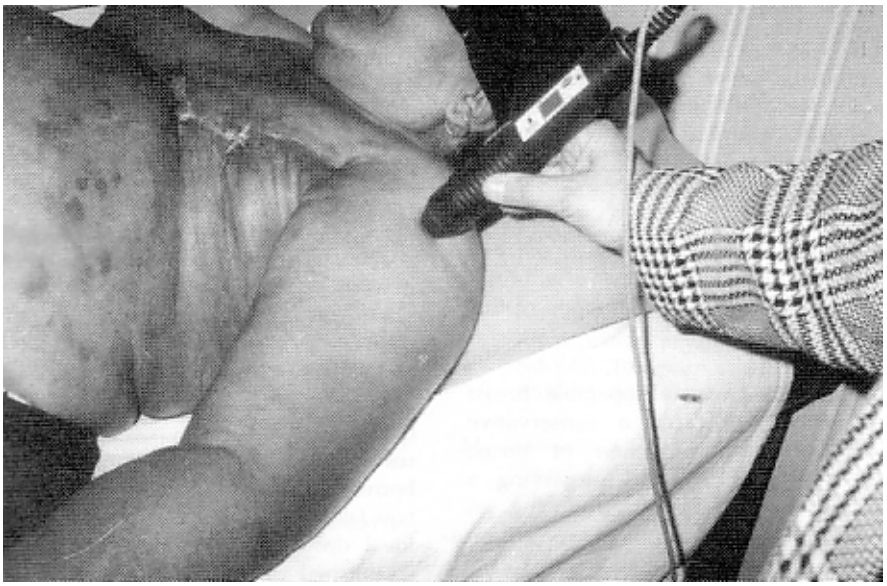

Fig (2) : Spot technique : He- Ne laser alone delivered by a handpiece

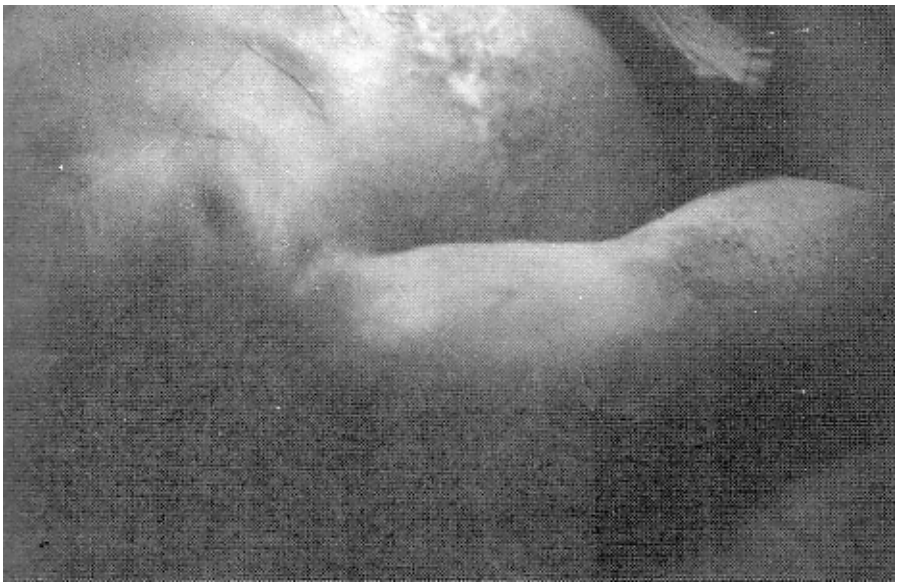

Fig (3) : Scanning technique : He-Ne and infra-red diode laser delivered by an automatic sweeping action.

DISCUSSION

Previous studies have shown that low intensity laser is effective in the symptomatic relief of pain of different etiologies. The current interest of this analgesic effect centers on its presumed effectiveness without side effects. Despite this, there is still no enthusiasm to use it in postmastectomy pain.

Official statistics in Egypt [28] as it is in other parts of the world [29], point to an appreciable increase in breast cancer diagnosis. The causes are outside the scope of this study but all are known.

The classical surgical treatment of operable breast cancer, has changed recently towards a conservative attitude [1], crowned by the introduction of breast conservation therapy. The latter aims at preserving a normally looking breast after treatment, producing an acceptable cosmetic appearance and an improvement in patient's body image. But in all surgical procedures, axillary dissection remains an integral part of the operation, and is responsible for the major part of postmastectomy pain. Therefore irrespective of the type of radical surgery applied, half of the patients do suffer from pain, but those asking for treatment are minority. For adherence to the design of the study, we restricted the treatment in both groups to those having performed the classical modified radical mastectomy as described by Patey [30].

One of the important features of postmastectomy pain is the diverse causes responsible, both organic and functional, and in that it is different from other situations in which LILT was applied before. During surgery, trauma to muscles may cause an abnormal increase in the activity of non-nociceptive musculoskeletal afferents that normally serve proprioceptive function [31]. This type of pain is refractory to usual conventional analgesic therapy including NSAIDs and even to surgical procedures for pain relief [6]. It was wrongly attributed to psychological causes, as normal muscle movements tend to be very painful. This new postulation, proven by the wondertul work of Mense[7] , received no attention in the past and the problem was very difficult to treat. In Beric's report of this proprioceptive allodenya [8] muscle pain can occur with normal evryday movements, like writing, wearing of clothes, cooking, combing, coughing and can also be induced by vibration. The unique mechanism of laser action on neuro-transmitters and their local and central release as well as their modification by photoenergy [32,33], may be beneficial in ameliorating the pain of such a functional problem. This presumed action would also explain the statistically better results obtained in the laser treated group than in the drug treated group, as diclofenac sodium has no effect on functional pain.

An obvious limitation to our study is the small sample size, and we are currently enrolling more patients in this trial as a larger sample size might show more significant differences. Yet at this point several conclusions can still be made. In the present study, there was a significant difference between the laser and drug groups in pain attenuation following treatment. This was also observed on the mean values of diurnal plasma cortisol level and the range of movements at the shoulder joint. This may point to the possible efficient effect of LILT on all parameters of postmastectomy troubles particularly pain and limitation of movements. But it is too early to recommend its routine use. There was no evidence in the study to prove that it should be used as a primary treatment. It could be used as a complement to other treatments to reduce their dose. In addition, results of the current study should be interpreted cautiously for several reasons. First. our conclusions are restricted to the laser parameters in this study. This was born in mind from the start, and a laser technique and dose was fashioned to mimic laser therapy in clinical practice, as ideal dosimetry with universal agreement has not been established yet [21] Second: no data are available about the long term results, though almost all patients were regularly seen in the first 6 months after termination of the study, as dictated by the follow-up program of their original disease, and they did not complain of pain recurrence.

One of the outstanding features of laser therapy observed in this work is the excellent patient compliance as the treatment was quick, (10 minutes /day for 10 days), it was painless, and non-of the patients was lost during the trial. Multiple sessions were necessary to obtain optimal results and this goes with the observation of Jensen [18,19] about the possible cumulative effects of laser therapy. Ten sessions were chosen arbitrary, to be close to the usually applied lasers in clinical practice [34].

Recommendation:

The present results suggested that the tested laser would be effective and applicable in clinical practice to treat postmastectomy pain. Available data indicate that it provides an alternative to the conventional treatment with NSAIDs represented by diclofenac sodium, and is superior in its action on functional pain. It lacks side effects, is painless and is relatively cheap.

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