TREATING CHRONIC POST-MASTECTOMY LYMPHOEDEMA WITH LOW LEVEL LASER THERAPY: A COST EFFECTIVE STRATEGY TO REDUCE SEVERITY AND IMPROVE THE QUALITY OF SURVIVAL

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While there are some controversies and uncertainties about the effectiveness of LLLT in acute tissue disease and damage situations and some uncertainty about penetration, scatter and reflection effects of laser light, most do not apply to the progressive condition of chronic lymphoedema. In this study patients with moderate to severe chronic lymphoedema associated with axillary clearance and radiotherapy received 16 LLLT treatment sessions each of 2~4 J/cm² over a period of 10 weeks. Each patient was their own control with the contralateral arm being used as a base reference point. The progression of LLLT was monitored fortnightly by circumference measurement, plethysmography, tonometry and bio-impedance as well as by subjective questioning of the patients. At the end of the 10 week period, oedema volumes decreased by an average of 19%, the lymphoedematous tissues progressively softened, the ECF volume significantly decreased and patients reported significant progressive improvements in aches and pains, tightness, heaviness, cramps, pins and needles, mobility and perception of circumference. The results show that when we are dealing with evaluation of treatment efficacy, we must not only present and interpret quantitative results but also the qualitative ones relating to the patient's quality of life. With declining health budgets, the cost of treatment is also a crucial issue. The cost of LLLT treatment in a public hospital was estimated at AU \$16 per percentage point reduction compared with approximately AU \$60 per percentage point reduction with the multifaceted complex physical therapy programs. LLLT is thus a cost effective strategy for the treatment of chronic lymphoedema.

Key words: lymphoedema; laser therapy; mastectomy; axillary clearance

Introduction

Any form of surgical intervention, particularly that involving the removal of lymph nodes and vessels, will impair the functioning of the lymphatic system resulting in post surgical oedema. This usually resolves as other lymphatics remove the accumulated lymph, however there may be longer-term progressive changes occurring in the remaining lymph vessels and surround-

ing tissues. At times when the load of lymph awaiting removal from the area is close to the carrying capacity or when the lymph vessels are overloaded, lymph (containing protein) will begin to accumulate in the perilymphatic area.⁽¹⁾ This results in a perilymphatic metabolic disturbance whose end result is a subtle yet progressive fibrosis of the lymphatic vessel walls and surrounding tissues through radial spreading.⁽²⁾ Lymph collectors become constrained and are unable to pump effectively. Radiotherapy will further exacerbate lym-

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Manuscript received: October, 1995

Accepted for publication: November, 1995

phatic pumping effectiveness by causing further fibrotic tissue formation. Since lymphatic vessels can only recanalize through 0.5 mm of scar tissue these events significantly reduce the ability of the lymphatics to regenerate.⁽³⁾ While lymph loads remain normal (or near normal) this failing system may be able to handle the load. This phase is called the latent phase.⁽¹⁾ In situations where the load is increased through infection, trauma or strenuous exercise the system may rapidly fail, precipitating the limb into a stage of overt swelling which is detectable by circumference measurement and plethysmography as well as by tonometry and bio-impedance.⁽⁴⁻⁶⁾ It is noteworthy that the later two forms of measurement are able to detect changes in the tissues long before the lymphoedema becomes measurable by circumference measurement or plethysmography and are thus useful in determining progression of changes through the latent phase.^(1,2,4)

While the incidence of postmastectomy lymphoedema has decreased over the years to between 14%^(7,8) and 29%,⁽⁹⁾ it is still unacceptably high. A similar situation also applies to the incidence of lymphoedema following groin dissection where it ranges between 20%,⁽¹⁰⁾ to 29%.⁽¹¹⁾

Once lymphoedema is clinically manifest, it will rarely resolve without some form of continuing external intervention, be it in the form of pressotherapy (sleeves and bandages), massage, pharmacological treatment or a combination. All of these are time consuming, and relatively expensive to the patient and health care system. They are not well suited to lymphoedema treatment and management programmes in public hospitals where patients who are without private health insurance are in the majority.

As well as dealing with the problem of the oedema volume, we should also attempt to treat the many associated problems such as functional impairment, anxiety, pain, sensory deficit (following damage to the intercostobrachial nerves⁽⁹⁾) and scar adhesions. Any treatment which can improve the quality of life of a patient by reducing any or all of the problems associated with the above as well reducing the lymphoedema is likely to be welcomed especially if it is cost effective as well.

Experimental evidence has indicated that Low Level Laser Therapy (LLLT) may be an effective method the treatment chronic lymphoedema. This exploratory clinical study aimed investigate this possibility. Experimental evidence also indicated that the mode of action of LLLT on lymphoedematous tissues would be multifaceted in some aspects similar to the actions of the benzopyrones which already have been well documented.⁽¹²⁾ Not only should LLLT reduce the amount

of tissue protein and fluid, (facilitating a return to normal tissue functioning), but it should restore immunocompetence and facilitate a return to near normal tissue functioning.

The term LLLT is often used interchangeably with such misnomers as 'low power laser' and 'cold laser,' however the term LLLT will be used throughout this article as suggested by Ohshiro and Calderhead^(3,6) and followed by Kert and Rose.⁽⁶⁾ LLLT systems include the helium-neon (visible red) and gallium arsenide (infrared) lasers which are used in this study.

Materials and Methods

A total of 11 subjects entered the study, however one was excluded during the study due to a severe bout of erysipelas associated with an injury.

Inclusion Criteria

All subjects had a unilateral standard or modified/radical mastectomy with subsequent radiotherapy. Lymphoedema arm volume was between 130% and 160% of the normal arm and a clinically discernable lymphoedema duration of between 3 and 10 years. All showed significant fibrotic induration of the tissues (indicated by tonometry). In pretrial questioning all subjects indicated a level of 3 or above on a 5 point Lichert scale for the following; Aches and pains, range of arm movement, tension, heaviness, numbness and pins and needles. Van Dam⁽⁹⁾ has reported the incidence of the above mentioned problems to occur in about one third of all patients, which concurs with our recruitment data.

Exclusion Criteria

Presence of metastasis, any chronic inflammatory conditions in the last three months, any medication regime known to alter fluid balance, current massage or compression therapy within the last month, a history or condition of venous thrombosis, current radiotherapy, wearing of a sleeve or compression garment or current compression treatment.

Apparatus

A Space Mid M#-UP laser with a scanning head, comprising a 9.0 mW HeNe laser emitting at a wavelength of 632.8 nm and four semiconductor diode infrared (IR) laser diodes each emitting a peak power of 27 W with a pulse width of 180 nsec at a wavelength of 904 nm, was used. The average power output under these conditions was 7 mW. The 904 nm wavelength penetrates cutaneous and subcutaneous barriers without increasing the temperature and has an effect on tissues up to 5 cm below the surface. The 632.8 nm wavelength penetrates only to about 0.8 mm, although

in each case there is some uncertainty about reflection and scatter properties.

Assessment Schedule

Each patient was their own control. The contralateral limb was used as a baseline indicator for changes. During treatment the patient remained supine. Treatment was administered for approximately 10 minutes on the axillary region, followed by approximately 10 minutes each on the upper and forearm. Times varied slightly since the main concern was delivery of an appropriate level of energy to each site. There were 16 laser treatment sessions. The dose range was 24 J/cm² per treatment.⁽¹³⁾ There were 2 sessions in each of the first 6 weeks followed by a single further session each week for a further 4 weeks. The total duration of the therapy was 10 weeks.

Evaluation of Therapy Effect

The following were performed on the contralateral control arm and on the side of the mastectomy prior to the first laser treatment and thereafter at fortnightly intervals until the completion of treatment. (A follow up report will deal with progression of the limbs at one, three and 6 months after the completion of treatment).

- Limb circumferences to 0.1 cm using a tape measure, at seven anatomically based points on the arms, being 10 cm and 20 cm proximal and distal to the antecubital fossa, at the wrist and mid palm.^(1,5)
- Volume determination made by using a plethysmographic tank using previously standardized procedures.⁽¹⁴⁾
- Tissue tonometry (resistance of the tissues to compression), three estimations at each of four sites, at 10 cm proximal and distal to the antecubital fossa and over the anterior and posterior thoracic area at the mid points of the respective lymphotomes using a digital electronic tonometer.⁽⁵⁻⁶⁾
- Bio-impedance to determine local oedema and in particular to distinguish between extracellular and intracellular fluid volumes.⁽¹⁵⁻¹⁶⁾ To measure this, electrodes were placed at the wrist, 10cm proximal and 10cm and 20 cm proximal to the antecubital fossa.

In addition all patients were interviewed and their subjective comments regarding mobility of the limb, tightness, heaviness, aches and pain, cramps, pins and needles, arm circumference and sensation of heat/burning in the limb were recorded on 5 point Lichert scales.

Other than basic information about skin care, and a list of "do's and don'ts", patients did not receive any other indications about how to manage their lymphoedema.

Results

All parameters were measured prior to the study and fortnightly during the study. Follow-ups will be made at 1, 3 and six months and reported in a subsequent study. However in the present study only the corrected initial and final results are presented for simplicity of presentation and since the majority of individual values showed similar trends over the measurement period.

Circumference changes

The greatest change in circumference over the 10 week treatment period was a reduction of 2.0 ± 3.3 cm, 20 cm proximal to the antecubital fossa ($P < 0.05$). Other reductions of 0.7 ± 2.2 cm, 10 cm proximal to the antecubital fossa; 0.2 ± 1.9 cm at the elbow; 0.1 ± 1.5 cm, 10 cm distal to the antecubital fossa; and 0.4 ± 0.5 cm at the wrist were obtained although these were not significant due to the small sample size.

Volume changes

The equations used to calculate volume changes were those suggested by Casley-Smith, which take into account the volume changes in both the lymphoedematous and contralateral limb. Using these, the volume reduction over the 10 week period was $19.3\% \pm 19.5$ with a range from 40% reduction to 15.7% increase.

Tonometry

Tonometry basically measures the distance that a plunger depresses the skin under a standard weight applied for a standard time after a fixed time interval. Results are expressed in units of compressibility. Higher values indicate less resistance to compression (softer tissue). Thus for a situation with a large amount of freely moving interstitial fluid the tonometer will depress the tissue more showing a higher value. For oedema with fibrosis, depression of the plunger will be less showing a lower value.

Tonometry of the upper arm (10 cm above the antecubital fossa) showed a significant ($P < 0.05$) softening of 82 ± 39 arbitrary units (on a 500 point scale). Tonometry of the lower arm (10 cm below the antecubital fossa) also showed significant ($P < 0.05$) softening of 106 ± 46 units. Tonometry of the anterior thoracic area showed a significant hardening of 153 ± 48 units while tonometry of the posterior thoracic area showed a non significant softening of 292 ± 101 units.

Bioimpedance

Multi frequency bioelectrical impedance has been used recently to assess changes in the fluid, fibre and fat content of tissues.⁽¹⁵⁻¹⁷⁾ However in this instance the only interest was with changes in compartmental water content. Over the 10 week treatment period, the calculated impedance values associated with the extracel-

Table 1: Tabulated results for patient perceptions of indicated problems over the 10 week treatment period. Values indicate significance of change. The values for 'r' and 't' are calculated according to Pearson

Problem	r	t	P
Bursting aches/pain	-0.92	4.8	0.01
Tightness	-0.97	8.0	0.01
Heaviness	-0.99	13.7	0.01
Cramps	-0.93	5.3	0.01
Pins & needles	-0.99	16.0	0.01
Burning sensation	+0.23	0.5	NS
Mobility	-0.95	5.9	0.01
Circumference	-0.92	4.9	0.01

lular fluid (ECF) indicated a large and significant reduction in its volume. The Pearson *r* was -0.84 and *t* 3.0 (*P* < 0.05). Intracellular fluid (ICF) compartment volumes also showed a reduction over time but they were non significant.

Patient perceptions

As mentioned in the introduction all patients who entered into the trial had significant perceived problems with respect to aches and pain, limb tightness, limb heaviness, cramps, pins and needles, burning (heat) sensations, mobility, and circumference. (All greater than 3/5 on a 5 point Lichen scale) Each fortnight, all patients were asked whether they had noticed any changes in the above parameters compared with the previous fortnightly interview. If there was no change then the previous score held, if it greatly improved the score was decreased by 1 and if it greatly worsened it was increased by 1, if the patient reported a slight improvement or slight worsening then the score was decreased or increased by 0.5 respectively. Table 1 indicates these changes and shows that in all but the area of burning sensations that there were statistically significant (*P* < 0.01) improvements.

The results thus show a significant reduction in the oedema volume of the lymphoedematous limb, a significant softening of the tissues, and a position dependent reduction in circumference. In addition the patients' subjective comments showed the limb to be less of a problem in terms of aches and pains, heaviness, tightness, cramps pins and needles, mobility and circumference.

Discussion

There has been considerable discussion regarding the efficacy and effectiveness of LLLT.⁽¹⁸⁾ This has mainly revolved around the lack of use of control groups in

situations where there is a high spontaneous or natural repair rate of the tissues (sprains and strains) and where the chronic conditions under investigation show fluctuating severity as well as doubt about the depth of penetration and scatter and reflection of the beam in the tissues.⁽¹⁸⁻¹⁹⁾ A chronic condition such as lymphoedema however is not subject to a high spontaneous resolution rate and the condition is progressive, thus to some extent the absence of a control group in this study is partly vindicated. Also lymphoedema is a problem confined to the epifacial compartment and thus issues relating to scatter and reflection of the beam into deeper tissues are not as relevant.

LLLT has been shown to increase lymph vessel diameter, increase their contractility, and facilitate their regeneration in half the normal time of untreated but otherwise damaged tissues.⁽²⁰⁾ These actions should mean that the development of collateral vessels will be easier and perhaps more rapid. This aspect of the mode of action of LLLT will be investigated using lymphoscintigraphy in a forthcoming trial. Low level laser therapy also stimulates the phagocytic activity of neutrophils and monocytes;⁽²⁷⁾ it has been shown to stimulate the release of agents from macrophages which can in turn stimulate or inhibit fibroblasts;⁽²⁸⁾ LLLT also stimulates the immune system, restoring immunocompetence;⁽²⁹⁾ and it helps to restore neural function.^(30,37)

Experimental studies have confirmed both histologically and from the gross anatomical perspective that LLLT has an effect on the reabsorption of oedema fluids.⁽²⁰⁻²³⁾ Others have shown LLLT to benefit wound healing⁽²⁴⁾ as well as demonstrating a strong relationship between wound healing and lymphatic and vascular regeneration.^(25,26) Just as important is the indication that LLLT can reduce scar adhesion to underlying tissues.⁽²⁰⁾ In lymphoedema the enhancement of the ac-

tivity of members of the phagocytic system has been shown to be a crucial factor in facilitating the reduction of lymphoedema.^(2,4,12) This stimulation not only facilitates proteolysis of the abnormally accumulated proteins freeing up any osmotically held fluid but also shifts the balance between collagen lysis and deposition towards lysis, resulting in the gradual removal of fibrotic tissues.^(4,31) Thus the effect of LLLT on lymphoedematous tissues should facilitate collagenous fibre, protein and fluid removal. The stimulation of the immune system and enhanced immunocompetence should additionally reduce the incidence of infections which to date has been recognised as one of the main exacerbating influences on the lymphoedematous limb.⁽³²⁾

Most of the above problems which the experimental information indicate can be improved by LLLT are those which beset patients with chronic lymphoedema. There are a build up of protein rich fluid in the tissues, the presence of scar tissues through surgery and radiotherapy, progressive fibrotic induration of the epifacial tissues (which leads to reduced lymphatic pumping abilities and an inability of lymphatic vessels to regrow and recanalize), and intermittent chronic grumbling inflammation and infections (which create a higher load on the compromised lymphatic system) associated with a compromised immune system.

While Manual Lymph Drainage, Complex Physical Therapy and those multi faceted regimes certainly can achieve greater reductions of oedema,⁽³³⁾ they are rather expensive, costing up to AU \$3000 in the first year. While we are certainly interested in more than just the reduction of oedema (i.e. holistic care),⁽³⁴⁾ using this oedema reduction as an example, we can make a cost effectiveness comparison. The 50% average reduction that the Complex Physical Therapies/Manual Lymph Drainage achieve⁽³⁵⁾ in oedema over the first year means a cost of about AU \$60 per percentage point of reduction. Such expense is becoming hard to justify in a public hospital system where budgets are declining and there is a decreasing proportion of patients with private health insurance. The 16 laser treatments given to the patients in this trial cost a total of AU \$300. These treatments gained a 19% average reduction in oedema over the first 10 weeks at a cost of AU \$16 per percentage point of reduction. Since the completion of this pilot study we have seen that 16 laser treatments was far too many and now we are trialing patients with between 2-4 treatments with similar oedema reductions. In view of the similarity in action between LLLT and benzopyrones we also now have a group of patients who are given benzopyrones for two weeks prior to their LLLT, continuing until the course is complete. Preliminary

results of this work indicate a 24% reduction in oedema for an approximate cost of AU \$4.50 per percentage point reduction. Of course so far there are no results of longer term follow up nor of the cost of this.

Overall however, the authors' preliminary findings are that the volume of the oedema is reduced, the tissues are softened, the ECF volume is decreased and the patients reported significant reductions in aches and pain, pins and needles, tightness, heaviness, and improvements in mobility. These encouraging results certainly give considerable clinical support to the experimental findings regarding the beneficial effects of LLLT.

Acknowledgements

This project was in part supported with a grant from Flinders 2000 and from the Flinders University URB.

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