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Low-Level Laser Therapy in fat reduction: what evidence do we have?

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Abstract

Low level laser therapy (LLLT) dates to early '70 to induce hair and wound regeneration then to reduce inflammation, edema and chronic pain and in present times is widely used for cosmetic fat reduction but despite the presence of many LLLT devices on the market the exact biochemical mechanism to explain its therapeutic effects is yet to be fully understood. Published data from treatments used to achieve fat layer reduction were pooled and reviewed to assess efficacy, safety and patient satisfaction and proposed models of LLLT biological action are discussed.

Introduction

Low level laser therapy was first attempted in early '70 when Mester and other Authors found that applying a laser light on shaved mice induced a quicker hair regrowth and regeneration than in

unexposed mice (1-2). Later the same Authors reported that HeNe laser could stimulate wound healing also in humans and has a beneficial effect in inflammation, edema, and chronic pain (3).

The main mechanism of this therapy is to expose tissues to low energy levels (if compared to those used for ablation) of near infrared (NIR) light, levels of energy low enough to not produce an important heating of the tissues.

The exact biochemical mechanism to explain LLLT's therapeutic effects is yet to be fully understood. Under LLLT stimulation a cascade of events at molecular level are reported, probably due to absorption of NIR light by mitochondrial chromophores, in particular cytochrome C oxidase (CCO): an increase of enzyme function with adenosine triphosphate (ATP), a reduction of reactive oxygen species (ROS) and increase of transcription factors like cAMP-response element–binding protein (ATF/CREB), redox factor-1 dependent activator protein-1 (AP-1), hypoxia-inducible factor (HIF)-1with HIF-like factor and p53 (4-6).Those molecular effects also have strong consequences at cellular level with degranulation of some immune cells like mast cells with release of chemotactic, growth and inflammatory factors (7-9).

LLLT in Fat Reduction

LLLT was proposed to assist surgical lipectomy first by Niera et al. (10) because caused a certain amount of fat liquefaction that helped surgical aspiration; further evidence showed that wavelengths between 630 and 640 nm were the best to assist lipoplasty (11-12). Jackson et Al. in a controlled, randomized, multicentered clinical study confirmed that laser assisted liposuction decreased operating room times, increased fat extraction volume and improved overall patient recovery (13).

Most studies use in vitro models of human adipose tissue like the work by Niera et Al. that after an external irradiation with a 635-nm laser with total energy values between 1.2 and 3.6 J/cm2 for up to 6 minutes showed that the amount of fat liquefaction was time dependent: after 4 minutes of laser exposure 80% of the fat was released from the adipose cells and after 6 minutes all the fat was released from the adipocyte. The lipolythic effect was attributed to the creation of micropores that allowed intracellular lipids to come out of the cell without destroying it and those micropores were reported to be present at electron scan microscopy (11). Caruso-Davis et Al. in a randomized study demonstrated that laser don't activate the complement cascade, do not kill adipocyte and increase triglyceride release but not lipolysis. After irradiating human subcutaneous fatty tissue with 635–680 nm for 10 min, there was no increase of glycerol and fatty acids in cell culture medium, suggesting that fat loss in laser treatment was not due to a stimulation of lipolysis, but could be caused by pores in adipocytes as Niera suggested (14). The phenomenon was explained with the increase of ROS levels that caused a peroxidation of lipids in cellular membranes thus damaging only

temporarily them (15-16). Also, it is possible that LLLT stimulation with a subsequent ATP synthesis increase leads to an cAMP upregulation that could activate a cytoplasmic lipase causing pores in cellular membrane and loss of fatty acids (17). Unfortunately, other attempts to replicate Niera's experiment by other Authors failed to spot micropores with electron scan microscopy (18-19) also another work, questioning the ability of red light (635 nm) to penetrate effectively under the skin to ipodermic level where the fat is located, added more uncertainty to any possible explanation of LLLT effect in fat reduction (20).

Materials and methods

A search on PUBMED online library with the query "LLLT fat reduction" and "LLLT body conturing/ shaping" found 72 works but only 16 contained original, prospective clinical trials. Data from LLLT clinical and pre-clinical treatments used to achieve fat layer reduction were pooled and reviewed to assess efficacy, safety and when feasible patient satisfaction.

Results

We identified 16 prospective clinical trials based on in vivo evaluation, only one based on bioptic samples and two based both on in vivo measurements compared with bioptic samples with a total of 1211 patients involved. All studies are summarized in table I (11, 14, 21-34). As expected, the laser equipment used is never the same and there are some differences in treatment methods used between studies as reported in Table I, mostly regarding number of applications and timing of applications. Nearly all studies were performed on people with a body mass index lower than 30 and without age, sex, or ethnicity exceptions.

Table I. *Summary of LLLT clinical works.*

Author	Journal	Patient N.	BMI Eval.	Circumf. Eval.	Other Eval.	Result	Patient Satisf.
Elm CM 2011	Las. Surg. Med.	5	yes	yes	US	NO difference	no
Neira R 2002	Plast. Rec. Surg.	12	no	no	US/ Biopsy	80% reduction	
Carniol PJ 2008	J. Cosmet. Las. Ther.	10	no	yes		NO diff	yes
Jackson RF 2009	Las. Surg. Med.	67	no	yes		Significant reduction	
Mostafa MS 2016	Las. Surg. Med.	15	yes	yes	MRI	NO difference	no
McRae E 2013	Las. Surg. Med.	86	no	yes		Significant reduction	
Vas K 2019	J. Biophotonics	10	yes	yes	US	Significant reduction	
Caruso-Davis MK 2011	Obes surg.	40	yes	yes	Biopsy	Significant reduction	yes
Wallander ID 2011	Las. Surg. Med.	5	yes	yes	US	NO difference	no
Jankowski M 2017	Las. Med. Sci.	24	yes	yes	US	NO difference	
Jackson RF 2012	Las. Surg. Med.	689	no	yes		Significant reduction	
Lach E 2008	J. Cosmet. Las. Ther.	74	no	yes	MRI	NO difference	32% satisfied
Gold MH 2011	J. Cosmet. Las. Ther.	83	no	yes		Significant reduction	

Nearly all studies (except the bioptic one) used body circumference as the main outcome indicator and there was no significant weight change in subjects enrolled over the study period, thus allowing any circumference change to be attributed to the treatment itself.

All in vivo studies performed abdomen treatment and most report a circumference reduction: overall reduction is reported in 1011 (83.5%) of the total 1211 patients pooled in this review, with 10 works showing a significant reduction (11, 14, 22-24, 26, 28, 30, 31, 34) and 6 works showing no reduction or a not significant one (21, 25, 27, 29, 32, 33). We decided to not compare reduction measurements because of the different treatment protocols applied, mostly by the number of applications and the total time of treatment, that made such comparison obviously meaningless but reduction as much as 6,86 cm of abdomen circumference were recorded (28), however, most works reported a reduction between 2 and 3 cm (14, 21, 24, 34). In different body areas, the same results were studied and shown a common circumference reduction of 1.9-2.5 cm for hips and 2.9-3.9 for thighs. One study (22) reported a mean combined reduction of 3.7 cm of circumference in both arms.

Because the technique used is described as noninvasive most works did not record adverse effects and the few that did, recorded only mild and transient effect that resolved spontaneously. One work reported serious adverse effects on 2 patients that developed skin ulcerations upon area of laser application (29). Common side effects recorded are mild discomfort during the application, erythema lasting few hours and swelling or tingling sensation always of short duration.

Only 8 out 16 of our chosen studies reported patient satisfaction and only 3 reported a certain percentage of unhappy patients; of the 286 patients pooled from studies that recorded patient satisfaction 195 (68.2%) expressed satisfaction after completion of treatment and 91 (31.8%) expressed no positive or an utterly negative evaluation.

Discussion

All studies made to investigate such devices have different treatment protocols, so it is very difficult to directly and accurately compare their results and it is impossible to compare effectiveness of different devices. In our work we excluded all papers that used simultaneously laser treatment and diet to reduce fat to remove another possible confounding factor.

The most important evidence is that all trials, with the exclusion of the one performed on bioptic specimens, required many applications (mean 7 applications, SD 2, 9) to indicate that LLLT needs weeks of time to exert and develop its biological effects and this is consistent with all the proposed models of action: in Neira's model of adipocite's cell membrane disruption by LLLT and lipids spillage (11) even if the effect is almost immediate it requires time to deplete adipocyte and thus be noticed. In the alternative hypothesis of triglyceride mobilization proposed by Caruso-Davis, (14) with unharmed or only temporarily damaged cells, the time lapse is even

more self-evident since it might require days to activate all the metabolic pathways necessary for the fat reduction effect to be evident. The model of metabolic activation is supported also by the study of Jackson et al. (24) that suggest an autocrine/paracrine activation and corroborated by animal studies made by Aquino et al. (35) where in sedentary animals LLLT increased fat volume while decreasing it in active and trained animals. This effect could explain the failure of LLLT treatment in some patients and the reported paradoxical "fat increase" effect reported in few patients by some authors (29, 34).

Despite the mechanism involved lipid in excess are expected to be cleared through lymphatic system but there has been recorded no increase in serum lipid levels but rather cholesterol and leptin levels have been observed to decrease after the treatment (36-38) and this can also be considered supportive to the metabolic activation model. There's a large body of evidence to suggest that vascular oxidative stress induces obesity and metabolic syndrome (39) and oxidative stress in adipose tissue decreases adiponectin secretion with a reduction of adiponectin-induced energy expenditure associated with protein uncoupling (40, 41). Since it is demonstrated that LLLT reduce oxidative stress in other tissues like neural and muscular, another model has been proposed: LLLT-induced reduction of adipose tissue thickness as result from decreased oxidative stress and consequently an increased adiponectin secretion and decreased insulin resistance (29).

Conclusions

Overall evidence shows that LLLT used to for reduce subcutaneous fat tissue is safe and, in most cases, effective but lack of standardized protocols and, most importantly, the exact knowledge of its biological mechanism made it difficult to assess its exact clinical indications and for what kind of patients is best suited for. Further standardized studies are required to make LLLT a powerful tool in aesthetic fat reduction.

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