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Abridged introduction to Low Level Light Therapy (LLLT)

for dentists (first 8 of 80 pages only)

Full version includes 59 clinical trial abstracts

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Introduction to Low Level Laser / Light Therapy (LLLT) for dentists

Introduction

Low Level Light / Laser Therapy (LLLT) is the application of light (usually a low power laser or LED) to promote tissue repair, reduce inflammation or induce analgesia. LLLT has been the subject of several systematic reviews for a range of musculoskeletal pathologies with favorable conclusions reported by The Lancet [1], BMJ [2], International Association for the Study of Pain [3] and the World Health Organization [4]. Unlike other many laser treatments LLLT is not an ablating or heating based therapy, it is more akin to photosynthesis.

There is much encouraging data published in about 100 papers for a wide range of endodontic, periodontic, postoperative, orthodontic, maxillofacial, chronic pain and non healing bone or soft tissue applications in the oral cavity and maxillofacial region.

The laser or LED devices are typically in the 600nm - 1,000nm spectrum (red an near infrared), in the power density range 5mW - 5W/cm2, produced by devices as little as 1mW and even up to 10 Watts. Sometimes pulsed and sometimes continuous beams are used. Treatment time is typically the range of 30 - 60 seconds per point. As little as one point ay be treated but maybe a dozen or more points may be treated. For acute and post operative pathologies as little as one treatment is all that is necessary but for chronic pain and degenerative conditions as many as ten sessions may be necessary. Whilst other wavelengths have similar effects they do not penetrate nearly so far as the red and near infrared range [5]. The maximum depth is probably 5cm (2”).

The following is a brief overview of how LLLT works, the clinical benefits and treatment parameters.

History

In 1967, a few years after the first working laser was invented, Dr Endre Mester in Semmelweis University Budapest, Hungary wanted to find out if this new ‘ray of light’ might cause cancer. He took some mice, shaved the hair from their backs, divided them into two groups and gave a laser treatment with a low powered ruby laser to one group and not the other. The treatment group did not get cancer and, to his surprise, the hair on the treated group grew back more quickly than the untreated group. He described the effect as "laser biostimulation" [6]. Forty-five years later, thousands of papers have been published with over 30 papers being published every month on the mechanism of action, the downstream physiological changes, the clinical benefits (RCTs) and pooled effect sizes in several systematic reviews with meta-analyses. [1-4, 7]

To-date more than 200 randomised double blind placebo controlled clinical trials have been published with some professional guidelines suggesting LLLT is used as part of standard care, including :

- World Health Organisation (WHO) Task Force on Neck Pain systematic review [4]
- The Lancet Systematic review of LLLT for Neck Pain [1]
- International Association for the Study of Pain (IASP) fact sheets for Myofascial Pain Syndrome , osteoarthritis and neck pain [3]
- British Medical Journal (BMJ) Systematic review and guidelines for treating tennis elbow [2]
- American Physical Therapy Association (APTA) Systematic review and clinical practice guidelines for achilles tendinopathy: [8]
- British Journal of Sports Medicine (BJSM) Systematic review for frozen shoulder [7]
- European Society for Medical Oncology (ESMO) Clinical practice guidelines for oral mucositis [9]
- Multinational Association for Supportive Cancer Care (MASCC) Clinical practice guidelines for oral mucositis [10]

Applications

Category	Application	Expected LLLT effects	Refs
Endodontics	Dentinal Hypersensitivity	Reduced tactile and thermal sensitivity	[91-93]
	Pulp	Improved dentin formation in the dental pulp Promotion of HDP cell mineralization	[88-90]
Maxillofacial	BRONJ	Reduced pain, reduced edema, pus and fistulas, improved healing	[85-87]
	Mandibular distraction Mandibular advancement	Improved bone trabeculation & ossification Improved bone formation in condylar region Improved osteogenesis	[64, 83, 84]
	TMJD	Reduced pain Improved range of mandibular movement	[80-82]
	Trauma to the mandibular	Improved bone healing	[79]
Oral Pathology	Burning mouth syndrome	Reduced symptoms, reduced pain	[76-78]
	HSV	Improved healing and reduced reoccurrence	[73-75]
	Lichen planus	Reduced lesion size, less pain As effective as corticosteroids	[70-72]
	Oral Mucositis	Reduced incidence, duration and severity	[56, 68, 69]
	Xerostomia / dryness	Regeneration of salivary duct epithelial cells Improved salivary flow, improved antimicrobial characteristics	[65-67]
Paediatric	Cavity preparation Mandibular distraction Gingivitis	Reduced pain Faster healing	[49, 63, 64]

Category	Application	Expected LLLT effects	Refs
Oral Surgery	Healing	Improved healing after gingivectomy, Reduced gingival Inflammation	[49, 53, 114]
	Paresthesia / alveolar nerve	Improved mechanical sensory perception.	[111-113]
	Third Molar extraction	Reduced pain, reduced swelling, improved trismus	[60, 61, 110]
Orthodontics	Orthodontic pain	Reduced pain Faster remodeling	[36, 106, 107, 109]
	Titanium implants	Improved healing Improved attachment Improved osseointegration	[94, 96, 108]
	Tooth movement	Accelerated tooth movement Improved osteoblast / osteoclast activity Improved collagen deposition	[51, 106, 107]
Paediatric	Cavity preparation Mandibular distraction Gingivitis	Reduced pain Faster healing	[49, 63, 64]
Periodontics	Chronic gingivitis	Reduced inflammation Improved healing	[49, 50, 105]
	Periodontal ligament	Increased early hyalinization	[51, 103, 104]
	Periodontitis	Improved pocket depth Less inflammation	[100-102]
Prosthodontics	Denture stomatitis	Reduced yeast colonies Reduced palatal inflammation	[97-99]
	Implants	Faster bone formation Improved bone-implant interface strength Improved osseointegration	[94-96]

Mechanism of action

Most of the effects of LLLT can be explained by light absorption in the mitochondria [11-13]. Every cell in the body has lots of mitochondria (hundreds or thousands per cell). Mitochondria to make cellular energy (ATP) from oxygen and pyruvate. In stressed or ischemic tissues, mitochondria make their own nitric oxide (mtNO) [14-16] which competes with oxygen. The mtNO binds to Cytochrome c Oxidase (CcO) (the terminal enzyme in the electron transport chain) and displaces oxygen [17]. This displacement of oxygen has two negative effects;

- Reduced ATP synthesis
- Increased oxidative stress (leading to inflammation via the inflammatory "master switch" NF-kB) [14-16, 18-20].

The effect of LLLT on hypoxic / stressed tissues can be described in four stages:

Primary effect of LLLT: Absorption by cytochrome c oxidase

Cytochrome c oxidase (CcO) absorbs red and near infrared light, the transfer of light energy by this enzyme triggers a series of downstream effects [11, 21-23].

Secondary effect: Modulation of ATP, nitric oxide & reactive oxygen species

Changes in ATP, reactive oxygen species and nitric oxide follow light absorption by CcO. These effects are redox state and dose dependent. In hypoxic or otherwise stressed cells it has been shown many times that following LLLT, nitric oxide is released, ATP is increased and oxidative stress is reduced [24-28].

Tertiary effect: Downstream intracellular responses (gene transcription, and cellular signaling)

The downstream effects of LLLT released nitric oxide, increased ATP and reduced oxidative stress are many. They are context and cell type specific. Either directly or indirectly these biochemical intermediates affect components in the cytosol, cell membrane, and nucleus that control gene transcription and subsequently cell proliferation, migration, necrosis and inflammation [24-28].

Quaternary effect: Extracellular, indirect, distant effects

Tissues that have not absorbed photons can also be affected indirectly via secretions from cells that have absorbed light. Cells in blood and lymph can be activated and they travel significant distances from the treatment area to have distant (systemic) effects [29]. These can be autocrine, paracrine, and endocrine effects (sometimes known as a "bystander" effects).

Edema / Lymphatic flow

There is good evidence that LLLT also improves lymphatic flow. A systematic review of eight clinical trials of LLLT for post mastectomy lymphoedema concludes that “There is moderate to strong evidence for the effectiveness of LLLT for the management of breast cancer related lymphedema” [30]. A controlled clinical trial on soccer players with second degree ankle sprains, found a significant reduction in edema volume for the laser group compared with placebo laser (both groups also had rest, ice, compression and elevation) [31]. A laboratory trial on Carrageenan-induced edema in the mouse paw found that treating lymph nodes alone was enough to reduce edema in the mouse paw [32]. The mechanism of action is unknown.

Analgesia

Analgesic effects are probably via a different mechanism from the increased ATP / reduced oxidative stress model described above. According to a systematic review of laser analgesia mechanisms by Chow et al [33], higher power density laser light > 300mW/cm^2, when absorbed by nociceptors, have an inhibitory effect on Aδ and C pain fibers. This high power density LLLT treatment slows conduction velocity, reduces amplitude of compound action potentials and suppresses neurogenic inflammation. Chow’s own laboratory studies show that LLLT blocks anterograde transport of ATP-rich mitochondria in dorsal root ganglion neurons. Varicosities result from this inhibition, this is normally associated with disruption of microtubules. This effect is completely reversible and lasts only 48 hours [34-36]. More work is needed to fully understand the complete mechanism of action.

Myofascial Trigger points

Myofascial trigger points are palpable nodules in taut muscle bands and contraction of muscle fibers that lead to muscle spasms and limited joint movement. They are a component of several pain conditions, including migraine, tension-type headaches, temporomandibular disorder and neck pain. The motor end plate is central to the etiology of trigger points and EMG studies have shown abnormally high electrical activity over trigger points. Electrical activity is reduced after after LLLT and clinical studies have shown that LLLT has immediate and cumulative effects on reducing pain [37-40], however the mechanism of action is not yet fully understood.

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