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Low Level Energy Laser in Oral Mucositis: A Pilot Study

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ABSTRACT

Purpose: The goal of this pilot study is to investigate the capacity of pain relief and wound healing of the low level energy laser therapy (LLEL) in chemotherapy-induced oral mucositis (OM) in an adult oncology population group.

Methods: 50 patients were recruited from Southwestern Regional Medical Center, suffering from chemotherapy induced oral mucositis. OM grade was assessed using the WHO classification. All patients were treated with an 830 nm wavelength laser multiple times per week. Energy delivered (joules) was determined based on severity and number of lesions (3 joules per 33 sec cycle). Treatment time estimates ranged from 3-15 minutes. Side effects of treatment and concomitant medications and therapies were recorded at each visit. Subjective pain was recorded immediately prior and following treatment using a visual analogue scale (VAS). Functional impairment was recorded and all data was charted in an electronic healthcare record.

Results: After 12 months, medical records were evaluated. In many patients, pain relief was noted immediately after receiving treatment. LLEL contributed to healing of mucositis lesion, with the number and duration of treatments corresponding to the severity of the lesions.

Conclusion: Low level energy laser is an exciting new tool that significantly improves quality of life for many cancer patients. It is beneficial in treating chemotherapy induced oral mucositis and was shown to provide immediate pain relief for some patients. No side effects were noted with LLEL therapy. This is a therapy that should be made available to oncology patients experiencing mucositis. More research needs to be done in understanding how LLEL may affect cancerous lesions.

INTRODUCTION / BACKGROUND:

Mucositis is the painful inflammation and ulceration of the mucous membranes lining the digestive tract, usually as an adverse effect of chemotherapy and radiotherapy treatment for cancer.[1] Mucositis can occur anywhere along the gastrointestinal (GI) tract, but oral mucositis (OM), commonly referred to as "stomatitis" or "mouth sores", refers to the particular inflammation and ulceration that occurs in the mouth. Oral mucositis is a common and often debilitating complication of cancer treatment.[2,3] OM affects many patients undergoing high-dose chemotherapy and hematopoietic stem cell transplantation (HSCT), 80% of patients with malignancies of the head and neck receiving radiotherapy, and a wide range of patients receiving chemotherapy. For most cancer treatment, about 5-15% of patients get mucositis. However, with 5-fluorouracil (5-FU), up to 40% get mucositis, and 10-15% get grade 3-4 oral mucositis.[4] Poor oral hygeine, pre-existing mouth damage, impaired immune status and high levels of pro-inflammaory cytokines predispose patients to severe OM[5]. In grade 3 oral mucositis, the patient is unable to eat solid food, and in grade 4, the patient is unable to consume liquids as well.[6]

SIGNS AND SYMPTOMS:

Cancer patients undergoing chemotherapy usually become symptomatic four to five days after beginning treatment, reaching a peak at around day 10, and then slowly improving over the course of a few weeks. Ulcers may range from 0.5 cm to greater than 4 cm [Figure 1]. Oral mucositis can be severely painful. The degree of pain is usually related to the extent of the tissue damage.

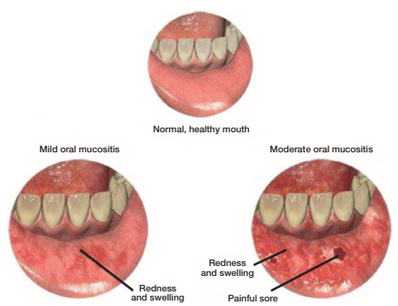

Figure 1 – Development of oral mucositis.

COMPLICATIONS:

Sores or ulcerations can become infected by virus, bacteria or fungus. These may act as a site for local infection that may cause septicemia especially in immunosuppressed patients. Pain and loss of taste perception make it more difficult to eat, which leads to weight loss. Approximately 50% of all patients who receive chemotherapy develop such oral mucositis that results in oncology treatment planning delays, dose reduction or even discontinuation of treatment that may affect oncologic treatment response.[7]

LOW LEVEL ENERGY LASER (LLEL) DEVICE:

A diode laser, with a continuous wavelength (A) 830 nm (infrared) and an output of 90 mW, 30 mW at each of the three aperatures, was used in this study. Treatment time (t) for each application patient is given by the equation T (sec) = D (J/cm^2) x A (cm^2) / P (mW) x 1000. This means that the longer the irradiation is used the greater the energy is released. Energy delivered (joules) was determined based on severity and number of lesions (3 joules per 33 sec cycle). This laser belongs to the class III-B for safety measure, which means that the direct beam is dangerous for direct eye contact but is not hazardous for diffuse reflections. As a protective measure, patients are asked to wear appropriate goggles that are affected in the 800-850 wavelength spectrum.

Patients were assessed for response to the laser based according to standardized grading criteria by evaluating development of the lesions and time needed for healing. The impact of laser therapy on pain control was evaluated using the VAS scale. Prior to and immediately after laser treatment, a pain evaluation was recorded.

MECHANISM OF ACTION:

The mechanism by which LLEL affects cells is not well understood but it seems to be based on bio-stimulation.[8] It is believed that low level radiation is absorbed by intracellular photoreceptors in the membrane of the mitochondria. The effects include a reduction in pain due to increased endorphins, reduction in inflammation via reduction in interleukin-1 and C-reactive protein and tissue healing effects as a result of increased neovascularization and macrophage activity.[9]

The specific parameters of laser therapy that can affect biological response include: 1. Wavelength (nm) 2. Laser power (mW) 3. Amount of energy to be delivered to tissues per square area (J/[cm^2]), and 4. Rate of energy or intensity (W/cm^2)[10]

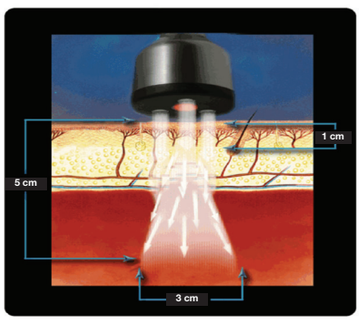

Figure 2 – LLEL tissue penetration.

PATIENTS AND METHODS:

Chemotherapy experienced patients diagnosed with cancer between the ages of 18 and 80 undergoing chemotherapy with symptoms of oral mucositis participated in this study. There were no ECOG performance status restrictions to this study. Patients were assessed for response to the laser therapy based on the World Health Organization (WHO) Oral Toxicity score[11]. The WHO scale is based on subjective, objective and functional outcomes. A single score that grades the severity of the condition from 0 (no oral mucositis) to 4 (swallowing not possible such that patient needs supplementary nutrition). The impact of laser therapy on pain control was evaluated using a visual analogue scale. Patients, as part of the CTCA Patient Empowered Model of Care (PEC) model, met with various medical disciplines during their course of treatment and many were offered the following recommendations:

I. Medical Oncologist: dexamethasone, maalox, ranitidine, carafate, benadryl, and/or lidocaine rinses.
II. Naturopathic Physicians: supplements including L-glutamine, probiotics, honey and aloe.
III. Registered Dieticians: plenty of liquid intake. Avoid citrus fruits, alcohol, and foods that are hot which are all known to aggravate mucositis lesions.
IV. Patient Education/Care Management/Wound Care Nurses: clean their mouth every four hours and at bedtime. Water-soluble jellies to lubricate the mouth and salt mouthwash to help soothe the pain and keep food particles clear so as to avoid infection.

Blood cell counts of the platelets and absolute neutrophils were registered. The laser was to be applied every 48 hours, repeating the procedure at each visit until complete healing of the lesion occurred. Number of joules administered: 18-36 joules per treatment session (approximately 3.5–7.0 min). For many patients a reported clear progress in healing was observed. All patients tolerated the laser treatment without any adverse effect or reactions.

RESULTS:

50 adults were treated with the LLEL. Some patients suffered from reoccurring lesions due to ongoing chemotherapy. During those episodes the patients suffered from different grades of lesions; 50% were diagnosed with grade 1, 48% grade 2 and with 2% grade 3. At each new visit the scoring in pain and severity of lesion was recorded. Pain was often described as a burning sensation and the patient may experience trouble speaking, eating, or even opening the mouth. All patients tolerated the laser treatment without any adverse effects or reactions.

As Figure 3 shows, 35 (70%) patients reported resolution of mucositis symptoms within 1-4 treatments, often within a single week. Overall, 41 patients showed resolution of symptoms and improvement of pain, while 9 patients showed no improvement.

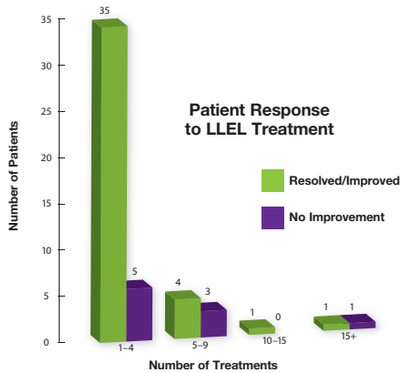

Figure 3 – Patient response to LLEL treatment.

As Figure 4 shows, the majority of patients with mucositis were receiving 5-FU chemotherapy or a taxane based regimes, 19 and 13 patients respectively.

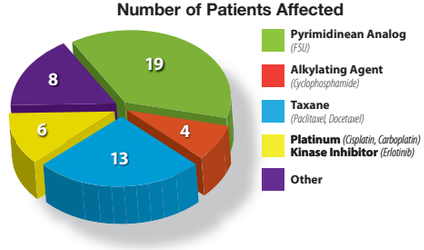

Figure 4 – Offending chemotherapy by type- number of patients affected.

DISCUSSION:

Prevention of ulceration can minimize pain, risk of infection, use of feeding tubes and length of stays in hospital. In immunocompromised patients, there is a risk that intact bacteria may invade submucosal vessels to produce bacteremia or sepsis. No standard therapy is known for OM and if therapy exists it is mostly supportive; basic oral care, bland oral rinses, analgesics, cryotherapy, antibiotics, growth factors and cytokines, biologic mucosal protectants and anti-inflammatory agents [12].

We had opportunities for study improvement. There were multiple providers delivering the therapy which may have contributed to inter-operator variability. Many of our patients were utilizing a variety of concomitant medications and supplements and we did not control for this in the study. Taking pictures of the lesions would have helped to grade the mucositis and track more objective progress. It is not known whether patients received visits to dentist for routine odontologic treatment. There is some research to show benefit using the laser preventatively and we did not use it that way in this study.

CONCLUSIONS:

The three main effects applicable to LLLT are: 1) analgesic effect, 2) anti-inflammatory impact and 3) a fast wound healing. These results were confirmed in this study along with other studies[13, 14, 15]. New guidelines could be developed supporting the use of LLEL in treating oral mucositis. A more extended study is needed to further confirm this promising result.

FUTURE DISCUSSION:

In a 2012 randomized controlled pilot study involving pediatric patients, topical application of honey was found to reduce recovery time in grade 2 and 3 chemotherapy-induced oral mucositis to a degree that was statistically significant. In grade 3 oral mucositis, honey was as effective as a mixture of honey, olive oil and propolis, while both treatments were found to reduce recovery time compared to the control.

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Poster Submission #7