Photobiomodulation Therapy with Low Level Laser Therapy (LLLT) in Pediatric Oncology Patients and Patients Undergoing Hematopoetic Stem Cell Transplantation (HSCT) for Prevention of Oral Mucositis (OM)

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Background

Oral mucositis (OM) is one of the most frequent complications of hematopoietic stem cell transplantation (HSCT) and other aggressive cancer treatments. OM occurs when different therapies break down rapidly dividing epithelial cells lining the GI tract leaving mucosal tissue free to ulceration and infection (1). The incidence of OM can be as high as 40% in patient's receiving chemotherapy and 85% in patient's receiving HSCT with myeloablative conditioning (1).

Several studies have utilized low level laser therapy (LLLT) for prevention of oral mucositis in the pediatric population (3-4). Results support a reduction in mucositis and a decrease in the average severity of OM (3). At present, there is no consensus on a guideline of verified protocol for the use of LLLT in the prevention of OM.

The purpose of this non-randomized pilot study aims to investigate the feasibility of implementing LLLT as preventative therapy for OM in pediatric patients with cancer who have received chemotherapy or HSCT, while inpatient or outpatient at Children's National Health System (CNHS).

Methods

- IRB approval was obtained, and the prevention arm of the study was completed.
- Inclusion criteria includes:
  - Children of appropriate age to tolerate eye protection throughout therapy
  - Planning to undergo transplant or at high risk of developing OM as determined by the treating team
- Diode laser Protocol: diffuse non-surgical handpiece (940nm), low energy level 0.5 W, continuous wave, defocused 5mm away for 3s from 33 defined locations in the oral cavity. Performed every other day beginning on day one of conditioning and continuing for 15 days after transplant.
- Patients will be surveyed by a validated tool, the Children's International Mucositis Evaluation Scale (ChIMES) every other day (5).
- Additional descriptive statistics to evaluate effectiveness of treatment over time; CTCAE-OM grading, relative size of lesions, intraoral photographs, pain medication use, and total parenteral nutrition (TPN) use.
- Feasibility of protocol will be determined by assessing number of LLLT sessions attempted vs completed, satisfaction scores derived from post treatment surveys of patients, parents, and medical staff, and presence of adverse events.

Results

- The study complied 8 sessions in the prevention group.

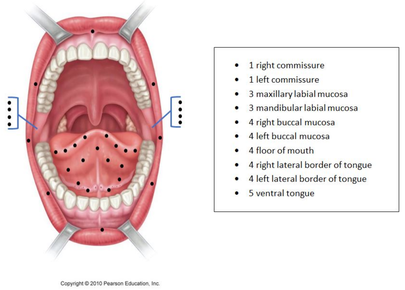

Figure 1: Anatomic locations for laser procedure.

Two patient's from prevention arm of study:
Patient 1: 9 y/o F with HbSS disease
Conditioning regimen: MSD–BMT with busulfan and cyclophosphamide
- Sessions completed: 10 out of 10
- Developed OM: No
- Frankl: 4

Patient 2: 15 y/o F with de-novo RUNX-1 mutation and low-grade myelodysplastic syndrome
Conditioning regimen: haploidentical PSCT with alpha-beta t-cell depletion using rATG, Busulfan and Cyclophosphamide conditioning on ONC1401
- Sessions completed: 5 of 10 (due to development of OM)
- Developed OM: Yes
- Frankl: 4

Patient	Easy to Tolerate?	Reducing Pain?	Overall Experience?	Recommend to Others?
Pt 1	5	5	5	5
Pt 2	5	5	5	5
Pt 3	5	4	5	5
Pt 4	5	5	5	5
Pt 5	5	4	5	5
Pt 6	5	5	5	5

Table 1: Patient Survey Scores; 1 - Very Poor, 2 - Poor, 3 - Average, 4 - Good, 5 -Very Good

Discussion

Mirroring previous studies, the LLLT protocol was well accepted by all parties (6-7). Families overall were receptive and willing to participate in treatment, and patients were cooperative for treatment. Patient, parents and medical staff post study questionnaire resulted in positive response choices. Similar to prior findings, no adverse events were reported in this study (6-7).

Differences in both the treatment arm and prevention arm were noted throughout the study. During the treatment arm patients were typically admitted due to pain. For some of the patient's included in the prevention arm admission was possible. A few patients had their treatments conducted at an outside facility or their regimens did not require admission. Patient's being treated in the outpatient setting demonstrated issues with compliance and ability to come to the hospital for LLLT treatment. Pain was a limiting factor for one patient receiving care in the outpatient setting. The feasibility of conducting LLLT in an outpatient setting proved difficult.

There are several limitations to this study. Most notably, mucositis affects the entire gastro-intestinal tract, not just the oral cavity (8). If our protocol was able to prevent OM, areas such as the pharynx and esophagus still cannot be reached with LLLT. Pain from these lesions leads to the usage of systemic analgesics and TPN dependence. Previous studies have concluded that LLLT appears to be a safe therapy and reduce the severity of OM in pediatric patient's undergoing HSCT (6-8). No conclusion was formulated confirming a decrease in severity and duration of oral mucositis.

Conclusion

- It is often difficult and not feasible for patients to have LLLT performed in outpatient setting.
- Future research directions should explore additional locations for delivery of care including the patient's dental home or oncology treatment center.
- Ideally there will be future implementation of LLLT into patient's overall treatment regimes when undergoing these described procedures .

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