Multicenter randomized, double-blind controlled trial to evaluate the efficacy of laser therapy for the treatment of severe oral mucositis induced by chemotherapy in children: LaMPO RCT

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Gobbo M¹, Ottaviani G¹, Rupel K¹, Poropat A¹, Di Lenarda R¹, Zacchigna S², Biasotto M¹

¹ Division of Oral Medicine and Pathology, University of Trieste, Trieste, Italy

² Molecular Medicine Laboratory, ICGEB, Trieste

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Introduction

Oncology patients undergoing cancer treatment are prone to a series of toxicities, of which oral mucositis (OM) is one of the most frequent and debilitating. OM can occur after standard and high dose chemotherapy (CT) and is commonly encountered in patients receiving hematopoietic stem cell transplantation. Children and adolescents are even more susceptible to OM due to the rapidity of cellular mitosis and to specific intensive CT regimens for pediatric cancer, with incidence varying between 40% and 81% of cases. Class IV diode laser photobiomodulation (PBM) has proven efficacy in the treatment of severe oral mucositis (OM) in paediatric oncologic patients compared with placebo.

Methods

This study was a randomized, prospective, multicenter, double-blind trial investigating the effectiveness of laser therapy (PBM) against placebo (sham therapy). A total of **101 eligible paediatrics** suffering from a WHO grade >2 chemotherapy-induced OM were enrolled in **8 Italian hospitals**. Patients were randomized into either PBM group or SHAM treatment group. PBM or sham treatment were performed for four consecutive days (days +1-+4). On days +4,+7 and +11 OM grade, pain and need for analgesics were evaluated by an operator blinded to treatment.

The study was designed as a superiority trial. Given the results of the previously published RCT in children, we estimated *a priori* that the enrollment of 100 subjects (50 in each group) would provide us a power of 80% to detect a between-group difference of 30% in the primary study outcome (i.e., a 70% success rate in the laser treatment group vs. 40% in the sham treatment group) with a two-sided type I error of 0.05.

Study Design

Inclusion/Exclusion Criteria

- ✓ 3-18 years
- ✓ OM (WHO) grade 3 or 4
- ✓ antineoplastic CT
- Previous PBM
- ✗ Dysplastic oral lesions
- ✗ Reduction of mouth opening (< 1 cm)
- ✗ Head and/or neck RT
- ✗ Use of keratinocyte growth factor

Protocol

PBM TREATMENT

51 patients

(class IV, K-Laser Cube series, Eltech K-Laser, 660 and 970 nm-combined wavelengths, 3.2 W peak power, 320mW/cm² irradiance, 36.8 J cm² fluence, and 50% frequency.

OR

SHAM (Same sound and screen, inactivated laser light)

50 patients

Objectives

Primary study outcome: evaluation of OM grade on day+7 (WHO scale).

Secondary outcomes : OM grade on day +4 and day +11, reduction of pain (0-10 NRS scale), reduction in the use of analgesics, and presence of adverse events.

Results

ACHIEVEMENTS IN SHORT

PBM GROUP

Reduction of pain
Reduction of OM (WHO grade)
Reduced use of analgesics

BOTH GROUPS

No side effects
No differences in neutrophil counts

Baseline demographics

	Laser Therapy	Sham Therapy	P
Age, median (IQR)	11.9 (7.0-14.7)	11.7 (8.0-14.8)	0.67
Male,Sex, number (%)	24(47%)	30 (60%)	0.17
Grade of Mucositis			
Grade 3	30 (59%)	27(54%)	0.63
Grade 4	21 (41%)	23 (46%)	
Neutrophil Count, median (IQR)	40.00 (0.0-201.0)	67.5 (0.0-300.0)	0.65

Pain (NRS)

Oral Mucositis grade (WHO)

	Laser Therapy	Sham Therapy	P
ACUTE LYMPHOBLASTIC LEUKEMIA	20 (39%)	21 (42%)	
BONE MARROW TRANSPLANT	13 (26%)	13 (25%)	
LYMPHOMA	14 (28%)	9 (18%)	0.52
ACUTE MYELOID LEUKEMIA	2 (3.9%)	2 (4.0%)	
OTHER SOLID TUMORS	2 (3.9%)	5 (10%)	
TOTAL BODY IRRADIATION, NUMBER (%)	5 (9.8%)	8 (16%)	0.06

Systematic Review and Metanalysis

Conclusions

PBM is safe and effective and should be introduced as standard therapy for paediatrics patients affected by OM as it accelerates recovery and reduces pain.