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Guest Editorial

Efficacy of Low-Level Laser Therapy (LLLT) in Oral Mucositis: What Have We Learned from Randomized Studies and Meta-Analyses?

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Oral mucositis (OM) is an inevitable complication of radiation therapy (RT) of the head and neck region, as part of gastrointestinal toxicity in chemotherapy and hematopoietic stem cell transplantation (HSCT), causing severe morbidity and affecting the patient's quality of life. Duration and severity of OM, especially in higher grades, are critical, as it hampers the cancer treatment, affects duration of hospital stay, and to a certain extent, predicts success of treatment and complications such as graft-versus-host disease (GVHD) in transplantation patients. There is no consensus on a single agent or agents that can be used either prophylactically or therapeutically in OM. The frequency of OM varies from 12% in patients receiving adjuvant chemotherapy to 80% and 100% in patients undergoing HSCT and RT of the orofacial region, respectively.[1,2] The art and science of photomedicine or phototherapy involving low-level laser therapy (LLLT) or near-infrared light-emitting diodes (NIR-LED) have become promising and effective tools in prophylactic and therapeutic interventions for OM and associated orofacial pain.[3–7]

First reports on LLLT on OM originated from Nice, France in 1992, and since then there have been reports of several randomized control studies with promising outcome.[4–8] In 2007, Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC-ISOO) Mucositis Guidelines have upgraded LLLT as a "recommended" method for the prevention of OM during HSCT.[9]

LLLT of an output power range from 5 to 200 mW with helium/neon (He/Ne) laser of wavelength 632.8 nm or diode lasers of various wavelengths ranging from 630 to 680 nm, 700 to 830 nm, and 900nm is an efficacious, simple, and atraumatic technique in the treatment of OM, with no known toxicity in clinical setting.[8,10,11] In addition, LLLT has been found to reduce the total duration and severity of OM in all the studies, with a few exceptions in which the laser parameters were, perhaps, inadequate. Another debilitating effect of OM is orofacial pain, which often depends upon existing oral health; underlying disease, type of treatment, severity of OM, and pain threshold. It has been shown that there is considerable reduction in orofacial pain in those patients who underwent LLLT. Although side effects were reported, none of them was different from those experienced by the control group, which is a clear indication of how well LLLT was tolerated by cancer patients, irrespective of their mode of cancer treatment.[5–7,10]

Perhaps one of the main pitfalls in past reports of studies with LLLT is the inconsistency in the parameters used, the calibration of the laser device, and the manner in which LLLT was delivered to the site. It is vital to formulate a protocol on parameters from the existing data on what is best for both a prophylactic dose and therapeutic effect. Briefly, we recommend a fairly simple regimen as follows, when considering a commercially available device: wavelength for a red light source at 633–685 nm, infrared 780–830 nm; output of diode between 10 and 150 mW; dose in the range of 2–3 J/cm^2 for prophylaxis, and not less than 4 J/cm^2 for therapeutic effect; application on single spot on a lesion rather than a scanning motion over the entire lesion. Also one should follow a simple formula such as

$$t(s) = D\ (J)\ x\ Surface\ (cm^2)/Power\ (W)$$

Lesions must be evaluated and therapy should be provided by a trained clinician and should be repeated daily or every other day during RT or other chemotherapy regimens and HSCT, or a minimum of three times per week until resolution.

Options on commercially available devices are of *extra-oral* devices and *intra-oral* devices (Fig. 1) targeting structures such as cutaneous and oral mucosal surfaces, respectively. Effects of an *extra-oral device* (Fig. 2) for LLLT over the cutaneous surface of the affected face may well reach the intra-oral structures such as the buccal mucosae, vestibule, and inner epithelial surfaces of the lips, with wavelengths ~830 nm, but not with 630–660 nm. A combination of the above two devices must be considered while managing the head and neck RT-induced effects, but not necessarily for chemotherapy induced intra-oral effects, for which an intra-oral device would suffice.

Finally, following good practice guidelines, such as therapeutic optimization of a commercially available device by calibrating according to the need, such as RT of the head and neck, chemotherapy, or a combination of the foregoing by following the previously mentioned recommendations is critical. We acknowledge the clinical trials, recent reviews, and

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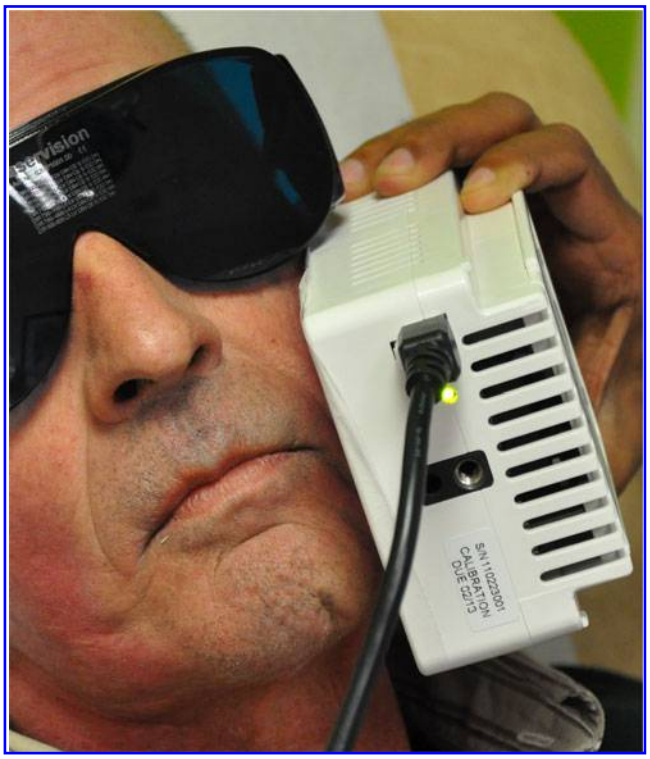

FIG. 1. Transcutaneous laser application.

FIG. 2. Intra-oral laser application.

guidelines on LLLT and the solid research data generated, which has tremendously helped us, but it is beyond the scope of this Editorial to list them all.

The emerging role of phototherapy in OM is clear, and it is pragmatic to envisage LLLT in prophylactic and therapeutic intervention protocols of OM in cancer patients. A joint consensus on this is perhaps the next step, from the wider community of clinicians such as radiation oncologists, medical oncologists, hematologists, oral medicine specialists, nurses, and other professionals involved in supportive care in cancer.

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