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Letter to Editor

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Critically Ill Patients With COVID-19: Are Phototherapies Advantageous for Managing Orofacial Lesions? Our Experience With Brazilian Hospitals

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Dear Editor,

Orofacial lesions in patients with the novel coronavirus (COVID-19) have been gaining attention due to the high prevalence rates, which reach 78.4%.[1] According to a recent review, the most common orofacial manifestations are presented as ulcerative, vesiculobullous, or macular erythematous lesions, and the hard palate, dorsum of the tongue, and labial mucosa are the most affected sites.[2]

It has been suggested that poor oral hygiene, coinfections, stress, underlying diseases, systemic conditions, trauma, vascular compromise, and a hyper-inflammatory response secondary to viral infection would be predisposing factors for these COVID-19-related orofacial lesions,[3] but the knowledge concerning the etiophysiopathology and treatment is still quite limited.[4,5] In this sense, our research group has recently published some case reports on the use of photobiomodulation therapy (PBMT) and antimicrobial photodynamic therapy (aPDT) for managing these lesions, giving a new perspective on the role of lasers in daily practice during the COVID-19 pandemic.[4,5]

The rationale for combining both phototherapies in COVID-19-related orofacial lesions is based upon some well-known benefits. Concerning aPDT, its antimicrobial effect against a vast range of bacteria, fungi, and viruses (including those enveloped such as coronaviruses) would be advantageous for inhibiting either local replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or other opportunistic coinfections.[4,5] PMBT, on the other hand, would modulate substances (e.g., nuclear factor-kappa beta, tumor necrosis factor-alpha, prostaglandin E2, cyclooxygenase-2, and interleukin-1 beta) involved in pain and inflammation processes,[4,5] leading also to faster healing. Moreover, both of them are non-invasive, cheap, safe,[4] and easy to handle.

In light of these facts and considering our wide experience with COVID-19 patients in Brazil, this paper aims to briefly present some multicenter cases in which PBMT and aPDT were used concomitantly to manage orofacial lesions in critically ill patients, a condition that has never been addressed in the literature.

Four critically ill COVID-19 patients presenting respiratory failure and the need for invasive ventilation (Table 1) were admitted to the intensive care units of three Brazilian hospitals. Positive real-time reverse transcription nasopharyngeal or oropharyngeal swab

Table 1. Clinical Features of the Orofacial Lesion and Demographic Characteristics of the Patients

Patient	Gender	Age	Immunization	Lesion Aspect	Time for Healing (days)
1	Male	69	No	Aphthous-like with necrotic areas	7
2	Female	76	No	Aphthous-like	3
3	Female	59	No	Hemorrhagic ulcerations with necrotic areas	4
4	Female	63	Yes (1st dose - Coronavac®)	Aphthous-like with necrotic areas	7

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tests confirmed the diagnoses. All the patients presented lesions on the lips during their hospital stay, but two had also their tongues affected concomitantly. The overall features of the lesions included bleeding ulcers that had progressively presented crusts over time. Given the severity of the patients' systemic conditions, a combination of aPDT and PBMT was proposed. No further systemic or local medication was used to manage the lesions.

For aPDT, 0.01% methylene blue spray solution was briefly applied over the lesions for 3 min., and 660-nm laser irradiation was performed in contact mode, using either Therapy XT® (DMC, São Carlos, SP, Brazil) or Laser DUO® (MM Optics Ltda São Carlos, SP, Brazil) with 100 mW, 6 J, and 60 s per point. For PBMT, 660-nm laser irradiation was performed with 100 mW and 0.5 J and 5 s per intraoral point and 2 J and 20 s per extraoral point (Table 2). The proposed laser protocol was effective in wound healing in all the cases (Figure 1A-L); however, the degree of improvement and the period required varied substantially.

Taking into account that the current paper is the first one to involve intensive care unit patients undergoing mechanical ventilation, we hope to encourage clinicians to consider using aPDT and PBMT concomitantly for managing orofacial lesions in critically ill patients with COVID-19.

Table 2. Laser (Devices and Treatment) Parameters

Specifications	Information	
	Therapy XT®	Laser Duo®
Type of laser	Diode	Diode
Emission mode	Continuous	Continuous
Time on/Time off	-	-
Delivery system	Optical fiber	Optical fiber
Energy distribution - aPDT	6 J	6 J
Energy distribution - PBMT	0.5 and 2 J	0.5 and 2 J
Peak power	0.1 W	0.1 W
Average power	0.1 W	0.1 W
Spot diameter at the focus	-	-
Focus spot area	0.028 cm^2	0.03 cm^2
Spot diameter at the tissue	0.028 cm^2	0.03 cm^2
Focus-to-tissue	In contact	In contact
Spot area at the tissue	0.028 cm^2	0.03 cm^2
Peak power density at spot area	3.57 W/cm^2	3.3 W/cm^2
Peak power density at the tissue	3.57 W/cm^2	3.3 W/cm^2
Average power density at spot area	3.57 W/cm^2	3.3 W/cm^2
Average power density at the tissue	3.57 W/cm^2	3.3 W/cm^2
Beam divergence	No	No
Water irrigation	No	No
Air and aspirating airflow	No	No

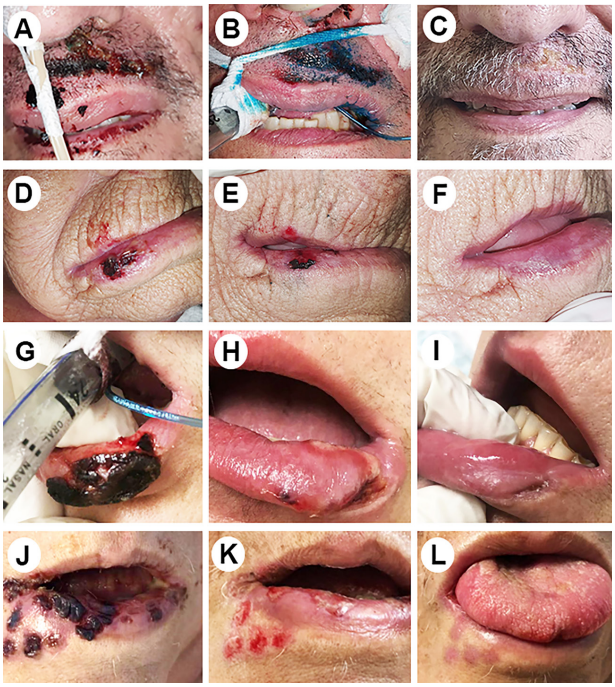

Figure 1. Clinical Aspects of the Orofacial Lesions. (A) Case 1: initial clinical presentation; (B) Case 1: clinical presentation within 72 hours, showing the lesions stained for an aPDT session; (C) Case 1: clinical presentation after 7 laser sessions; (D) Case 2: initial clinical presentation; (E) Case 2: clinical evaluation within 24 hours; (F) Case 2: clinical presentation after 72 hours from the first laser session; (G) Case 3: initial clinical presentation; (H) Case 3: clinical presentation after 3 laser sessions; (I) Case 3: clinical presentation after 4 days from the first laser session; (J) Case 4: initial clinical presentation; (K) Case 4: clinical presentation within 24 hours; (L) Case 4: clinical presentation after 7 laser sessions.

Competing interests

The authors declared no conflict of interest.

Ethical Approval

The patients gave informed consent. Patient anonymity was assured.

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Nothing to declare.

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