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Management of orofacial lesions with antimicrobial photodynamic therapy and photobiomodulation protocols in patients with COVID-19: A multicenter case series

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ABSTRACT

Several oral lesions related to COVID-19 have been described in the scientific literature. The COVID-19 pandemic highlights the importance of supportive protocols, which can reduce inflammation and aid in tissue repair in severe cases. Photobiomodulation therapy (PBMT) alone or in combination with antimicrobial photodynamic therapy (aPDT) can be used to manage orofacial lesions in confirmed cases of COVID-19. Here, we sought to describe the clinical presentation and specificities of three cases in which aPDT and PBMT were used to manage orofacial lesions in patients with COVID-19. The laser protocols were effective with improvement of the orofacial lesions within a few days.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes the coronavirus disease (COVID-19). Typical manifestations of COVID-19 include fever, sore throat, fatigue, cough, and dyspnea. Although there is still no consensus on whether oral manifestations could be a direct result or systemic consequence of SARS-CoV-2 infection, oral lesions related to COVID-19 have been described in the scientific literature [1].

The COVID-19 pandemic highlights the importance of supportive protocols that can reduce inflammation and aid tissue repair in severe cases [2]. Photobiomodulation therapy (PBMT) alone or in combination with antimicrobial photodynamic therapy (aPDT) can be used to manage orofacial lesions in confirmed cases of COVID-19 [2]. In view of the above, we sought to describe the clinical presentation and specificities of three cases in which aPDT and PBMT were used to manage orofacial lesions in patients with COVID-19.

1.1. Case 1

A 55-year-old Brazilian man with a medical history of arterial hypertension sought medical help due to symptoms suggestive of COVID-19, which was confirmed using the reverse transcriptase-polymerase chain reaction (RT-PCR) test. The patient was admitted to the intensive care unit (ICU) and underwent orotracheal intubation. Lesions in the left nostril (Fig. 1A) with no associated oral lesions were observed. An association of aPDT and PBMT with a low-level diode laser device Therapy XT (DMC®, São Carlos, SP, Brazil) was used to detect infection and improve healing (Table 1). The PBMT was initiated 5 days after aPDT (Fig. 1B). There was a marked improvement in healing within 7 days (Fig. 1C), and the patient was transferred to his hometown.

1.2. Case 2

A 58-year-old Brazilian woman with a medical history of type 2 diabetes and hypertension sought medical help due to symptoms suggestive of COVID-19, which was confirmed using the reverse transcriptase-polymerase chain reaction (RT-PCR) test. The patient was admitted to the ICU and underwent orotracheal intubation. Lesions in the left nostril (Fig. 1A) with no associated oral lesions were observed. An association of aPDT and PBMT with a low-level diode laser device Therapy XT (DMC®, São Carlos, SP, Brazil) was used to detect infection and improve healing (Table 1). The PBMT was initiated 5 days after aPDT (Fig. 1B). There was a marked improvement in healing within 7 days (Fig. 1C), and the patient was transferred to his hometown.
diabetes and hypothyroidism had COVID-19 confirmed using RT-PCR. Ten days after the onset of symptoms, the patient was sent to ICU and 2 days later, received orotracheal intubation. An evaluation by the oral medicine team was requested due to lesions in the mucosa of the oral cavity and tongue edema (Fig. 1 D). The aPDT protocol (Table 1) was performed on the first day (Fig. 1 E and F). On days 2 and 3, PBMT was performed (Table 1). After 2 days without laser treatment (Fig. 1 G), the patient underwent tracheostomy and received both laser protocols immediately after. One last laser irradiation was performed the next day, and an important tissue healing and edema reduction were observed (Fig. 1 H).

1.3. Case 3

A 55-year-old man complained of pain and delayed healing of the oral lesions. He also reported a diagnosis of COVID-19, confirmed by rapid chromatographic analysis. The patient developed odynophagia, dysphagia, oral ulcers, and oropharyngeal candidiasis. He reported using nystatin 100,000 IU/mL, miconazole gel 2%, and fluconazole 150 mg (oral), which had improved fungal lesions; however, failed to inhibit the remission of oral ulcers. The patient had no comorbidities or history of allergies and was under treatment with dexamethasone, colchicine, acetylcysteine, apixaban, omeprazole, and mirtazapine and supplemented with vitamins (B12, C, and E); zinc; selenium; and magnesium.

On oral examination, the patient presented with an ulcer in the upper right labial semimucosa measuring approximately 0.5 cm along its longest axis, an extensive ulcer with slightly raised edges in the palatine gingiva, from the region of tooth 26 to the maxillary tuber; another lesion close to the palatine raphe measuring approximately 1.5 cm along its longest axis; and shallow, punctate ulcers on the lingual dorsum. A pseudomembrane overlying the intraoral lesions was also observed (Fig. 1 I–K). His blood count revealed a global leukocyte count of 24,750/mcL (segmented = 86%), alanine aminotransferase count of 95.00 U/L, aspartate aminotransferase count of 25.00 U/L, and creatinine count of 1.23 mg/dL. Owing to the clinical findings, the diagnostic hypotheses were either oral lesions due to COVID-19 or opportunistic manifestations of the herpes simplex virus.

To decontaminate and stimulate wound healing, aPDT was performed using a low-level diode laser device, TwinFlex Evolution (MMOptics®, São Carlos, SP, Brazil) (Table 1). Next, 400 mg of acyclovir (every 12 h/7 days) was prescribed along with sodium lauryl sulfate-free toothpaste and the use of an extra-soft toothbrush and dental tape. After 48 h, the patient began accepting a solid diet. After 72 h, lesions on the palate were shallower, and pain had reduced (visual analog scale = 3);
thus, PBMT for analgesia and wound healing was initiated (Table 1) and repeated on days 5 (Fig. 1L–N), 8, and 12 (Fig. 1O–Q) post-aPDT. The patient is currently undergoing stomatological follow-up with PBMT and progressive pain reduction and healing of the oral lesions.

2. Discussion

There is extensive debate regarding the etiology, prognosis, and significance of oral manifestations of COVID-19, which might be attributed to the direct or indirect action of SARS-CoV-2 over the oral mucosa cells, the presence of coinfections, immunodepression, and reactivation of the oral human papillomavirus [1,3,4]. Thus, aPDT was used to treat oral lesions, based on its capacity to inactivate the virus and, in turn, reduce pain and stimulate healing.

An in vitro study demonstrated the effectiveness of aPDT in the inactivation of SARS-CoV-2 [2]. Additionally, the potential positive effects of PBMT and aPDT on the regeneration of damaged tissues of patients with COVID-19 have been highlighted in case reports in the literature [2,4–8]. In the reported cases, introducing aPDT for its antimicrobial effect and PBMT for its analgesic, inflammation-modulating, and repairing effects may have helped to decrease the viral load, reduce pain, and heal wounds.

The available evidence suggests the importance of oral healthcare in hospitalized patients with COVID-19, which can contribute to the reduction of morbidity and mortality. Although randomized controlled trials are needed to assess the potential benefits of aPDT in managing orofacial lesions directly or indirectly related to COVID-19, case reports provide descriptions of the symptoms, signs, diagnosis, treatment, and follow-up of an individual patient reflecting clinical experience and support medical and research progress.

The most frequently used parameters of PBMT for wound healing and analgesia (Table 2) were 660 nm wavelength, 100 mW power, 1 J energy, and 10 s per point of application. Regarding antimicrobial photodynamic therapy, the most used protocol was methylene blue at 0.01%, 3 min of pre-irradiation time, 100 mW of power, 4.5 J of energy, and 40–50 s per point of irradiation. Since these lesions are related to a viral infection, it is recommended to start with aPDT (one to two sessions), followed by PBMT until complete healing of the lesions. The current consensus is that this is the optimal combination of PBMT and PDT for the treatment of orofacial lesions in patients with COVID-19 and should be used as a basis for future randomized studies.

Declaration of Competing Interest

None declared

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