Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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CASE REPORTS

Intranasal photobiomodulation therapy for COVID-19-related olfactory dysfunction: A Brazilian multicenter case series

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ABSTRACT

Olfactory dysfunction is commonly seen in COVID-19 patients; however, little is known about the pathophysiology and management. The present study aimed to report a series of cases in which three protocols of intranasal photobiomodulation therapy (PBMT) were used for COVID-19-related olfactory dysfunction. Irrespective of the PBMT protocol, olfaction recovery was noted in all cases but with varying degrees of improvement. Although intranasal PBMT seems to be a promising therapeutic modality, more research is needed to better define effectiveness.

1. Introduction

Olfactory dysfunction is commonly seen in many viral diseases in which respiratory epithelium is the primary site of both viral attachment and infection. The mechanisms of olfactory dysfunction are generally nonspecific and based on inflammatory reactions on the nasal mucosa that leads to subsequent rhinorrhea; however, the exact pathophysiology related to the novel Coronavirus Disease 19 (COVID-19) remains poorly understood [1]. Other possible explanations for olfactory alterations during COVID-19 rely on direct or indirect neurologic injuries via angiotensin-converting enzyme 2 (ACE2), the functional receptor for the virus [1,2].

From 5.14% to 98.33% of patients with COVID-19 suffer from complete (anosmia) or partial (hyposmia) loss of olfaction [2]. Considering the sudden onset of impairment of smell and/or taste during the disease course, some advocate including these symptoms in the diagnostic criteria for COVID-19 [3]. Moreover, it has been reported that COVID-19 patients with mild or no symptoms may not fully recover their ability to detect odors within four months or more from the viral infection. Certain odors (e.g., strawberry, lemon, and soap) seem to be exaggeratedly affected, raising the hypothesis that a permanent smell reduction may occur [4].

The management of COVID-19-related olfactory dysfunction varies widely. For cases that improve spontaneously, no specific treatment is needed; however, when the impairment lasts beyond 2 weeks, some therapeutic modality should be considered. Despite very little robust scientific evidence regarding efficiency, the available treatments consist of either olfactory training or medications such as oral or intranasal corticosteroids, intranasal sodium citrate, intranasal vitamin A, and oral omega-3 [3].

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Table 1
Data on the initiation of COVID-19 signs and symptoms and the biomolecular infection confirmation, in days, at first laser irradiation.

Group	Patient	Days from the initiation of the symptoms	Days from the biomolecular confirmation
1	A	52	45
	B	277	270
	C	34	30
	D	62	60
	E	40	36
2	F	33	25
	G	56	63
	H	14	14
	I	103	103
	J	28	26
	K	66	67
3	L	17	9
	M	2	1
	N	88	90

Considering this background, it was hypothesized that photobiomodulation therapy (PBMT) would be beneficial for olfaction recovery, since it is capable of modulating inflammatory processes and improving tissue healing in a general manner. Moreover, this laser modality, also considered simple, low-cost, and non-invasive, has already been successfully used for different purposes in COVID-19 patients, including the treatment of orofacial lesions [5]. Thus, the present study aims to report a series of clinical cases in which intranasal PBMT was administered for the management of COVID-19-related olfactory dysfunction.

1.1. Case series

Twelve female (from 20- to 59-year-old) and two male patients (from 25- to 37-year-old) from five different Brazilian Health Centers and suffering from smell loss (either partially or completely) after COVID-19 infection were clinically accompanied.

Data about the exact initiation of all signs and symptoms related to COVID-19, as well as its biomolecular infection confirmation, were gathered by a simple questionnaire (Table 1). Furthermore, at the first clinical appointment and before the subsequent ones, olfaction was evaluated using a visual analog scale (VAS) ranging from 0 (normal smell) to 10 (complete absence of smell - anosmia).

Three intranasal PBMT protocols were applied (Fig. 1) using either Therapy EC® (DMC, São Carlos, SP, Brazil) or Laser DUO® (MM Optics Ltda São Carlos, SP, Brazil) at 660 nm, on contact mode, with 100 mW of power, and 18 J of energy on the nasal mucosa, corresponding to 3 min of irradiation per nostril. The PBMT protocols were as follows:

Group (1) 10 laser sessions, twice a week and with a 48-hour interval;

Group (2) 5 laser sessions, twice a week and with a 48-hour interval;

Group (3) 10 laser sessions, with a 24-hour interval.

Fig. 2 depicts the olfactory scores obtained at baseline and before every laser session and grouped according to the PBMT protocols. It was noted improvements in smell loss for all the patients, regardless of the laser protocol used.

2. Discussion

According to the current cases, intranasal PBMT resulted in clinical improvements in smell loss for all the patients; however, neither individual nor group patterns were identified over time. To the best of the authors' knowledge, there is no study on the use of PBMT to manage olfactory dysfunction in COVID-19 patients both during and after the viral infection.

Up to now, there is weak evidence to support the benefits from the available therapeutic modalities for cases of COVID-19-related persistent olfactory dysfunction, either pharmacological or not [3]. It was hypothesized, therefore, that PBMT would be beneficial for olfaction recovery, since it is capable of modulating the local inflammatory processes and improving tissue vascularization [5]. Furthermore, systemically through blood cells and components, intranasal irradiation could provide neuroprotection via anti-inflammatory and antioxidant pathways once the nasal cavity presents abundant blood capillaries with relatively slow blood flow [6]. Nonetheless, other possible acting mechanisms can also be proposed, including the potential to activate neural stem cells of the olfactory nerve, bulb, and endothelium, and the autonomic nervous and lymphatic systems [6].

Concerning study limitations, despite presenting three laser protocols, this study lacks a control group (e.g., sham laser) and involved a

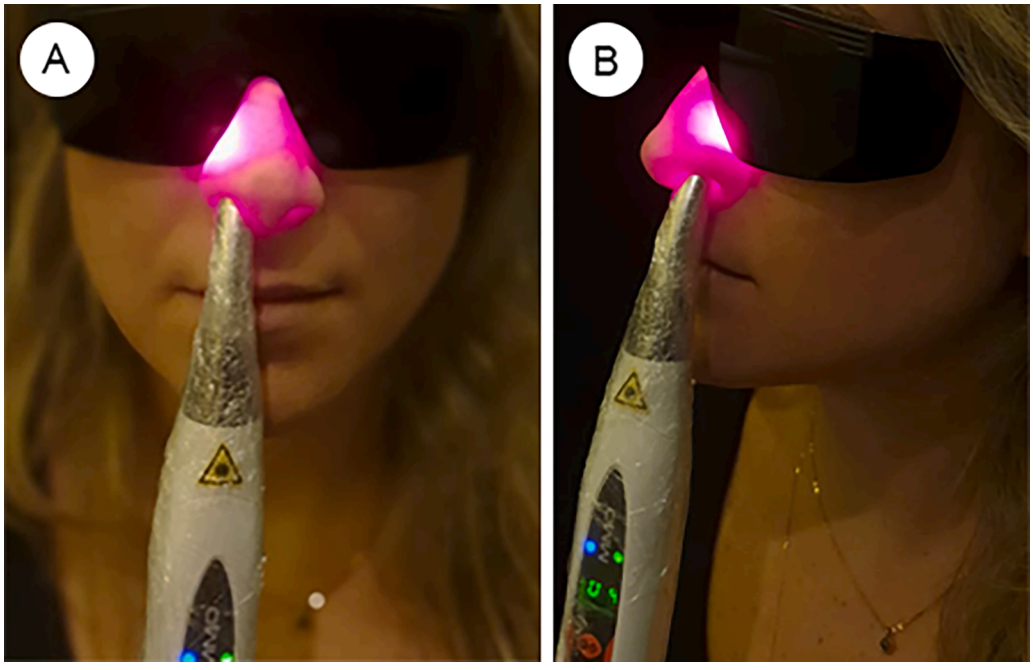

Fig. 1. Intranasal photobiomodulation therapy: frontal (A) and lateral (B) views.

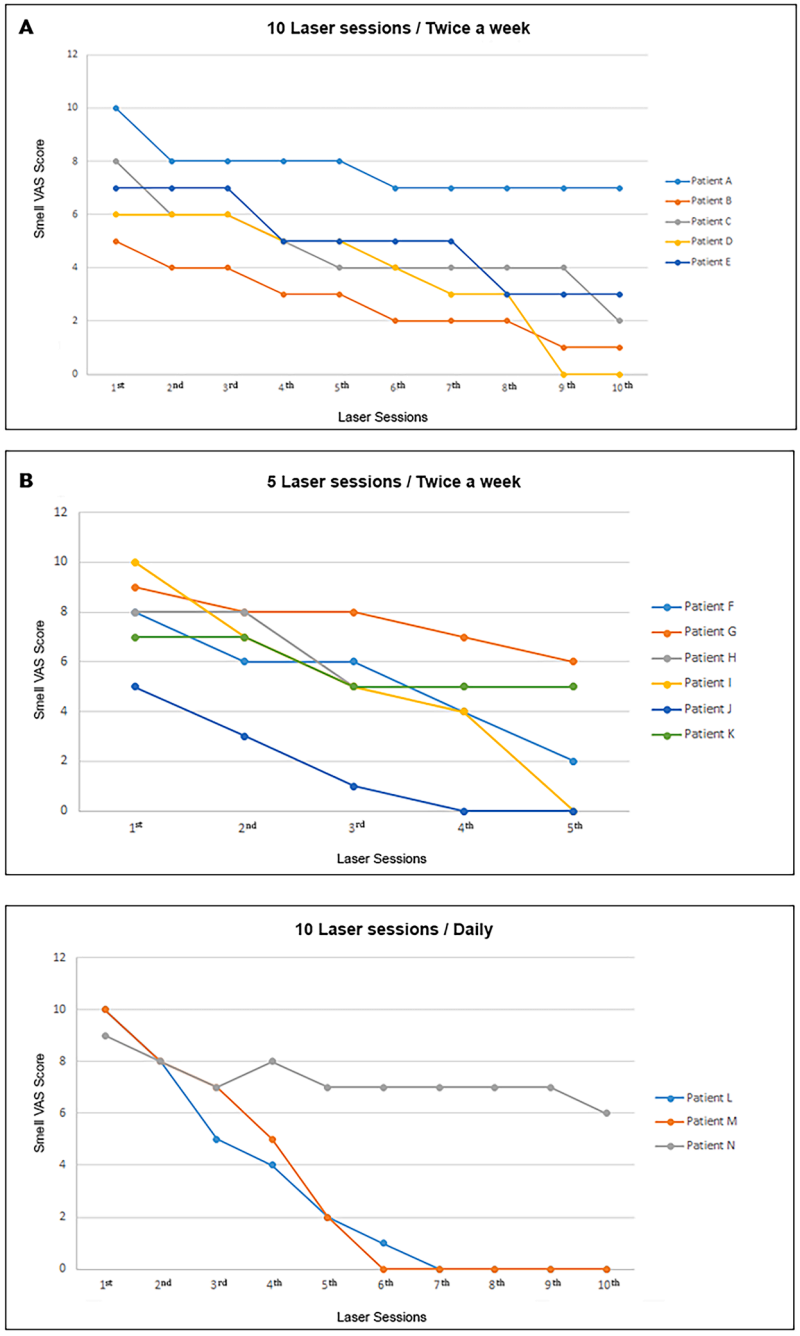

Fig. 2. Olfactory scores at baseline and before every laser session, according to the photobiomodulation therapy protocols.

reduced number of patients. Even being ranked at the lowest level of evidence among clinical studies, case reports and case series are still highly desired, since they may bring early information and novel insights for novel and little-known conditions and diseases such as COVID-19 [5].

Given the unpredictable nature of olfactory dysfunction in COVID-19 patients and the lack of information about the available treatments, intranasal PBMT seems to be a promising therapeutic modality. The choice of the most suitable laser protocol as well as the knowledge of the exact photonic mechanisms, however, demand further clarification.

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Ethics approval

Not applicable.

Consent to participate

written informed consent was obtained from all the patients.

Consent for publication

Written informed consent was obtained from all the patients.

Declaration of Competing Interest

Nothing to declare.

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