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Case report

aPDT for oral decontamination of hospitalized patients with COVID 19

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ABSTRACT

Emerging variants of severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) may have an impact on the virus's transmissibility and pathogenicity and an increased risk of reinfection. Antimicrobial photodynamic therapy (aPDT) is a promising technique to decontaminate the oral cavity to minimize and inactivate microorganisms' load. This article reports through a case series, a proposal for efficient oral decontamination for hospitalized patients with COVID 19 using aPDT. Samples of oral tissues were obtained after aPDT and analyzed using two methods of RT-qPCR to elucidate qualitative and quantitative viral profiles of SARS-CoV-2 RNA in the oral cavity. There was a reduction of viral load in the oral cavity immediately or one hour after the use of aPDT. This method could be a good option to decontaminate the oral cavity to minimize and inactivate microorganism load.

Background

SARS-CoV-2 has already been detected in several organs and tissues, including oral tissues and saliva. The role of saliva in disease spread may be associated with viral replication within salivary gland cells that are reservoirs for SARS-CoV-2 [1]

In addition, patients with COVID-19 may undergo long periods of hospitalization and often need oral care. In intensive care units, oral decontamination needs to be effective to prevent oral bacteremia, viremia, and co-infections. The association of oral bacteremia and viremia with systemic manifestations has been reported in a patient with heart disease and COVID-19 [2]. The clinical management of these patients represents a great challenge for healthcare workers, especially when treatments involve exposure to saliva and/or blood. A fact that places them at greater risk of contamination and virus transmission [3].

Photodynamic therapy (aPDT) is an effective alternative method for decontamination of the oral cavity, as it forms reactive oxygen species that can inactivate enveloped and non-envelope DNA and RNA viruses, which suggest their promising potential against SARS-Cov-2 [4] in reducing the risk of contamination for dentists and patients.

In vitro studies confirmed the effectiveness of aPDT antiviral activity against SARS-CoV-2 [4], but no *in vivo* study was conducted with aPDT and SARS-CoV-2. This article reports through a case series, a proposal for efficient oral decontamination for hospitalized patients with COVID 19 using aPDT.

Case reports

A 42-year-old white man presented himself to the Emergency Military Police Hospital, with a history of nausea, vomiting, cough, and fever (38.8 °C). A chest computed tomography scan was performed revealing a pulmonary consolidation (>50%). A diagnosis of pulmonary infection

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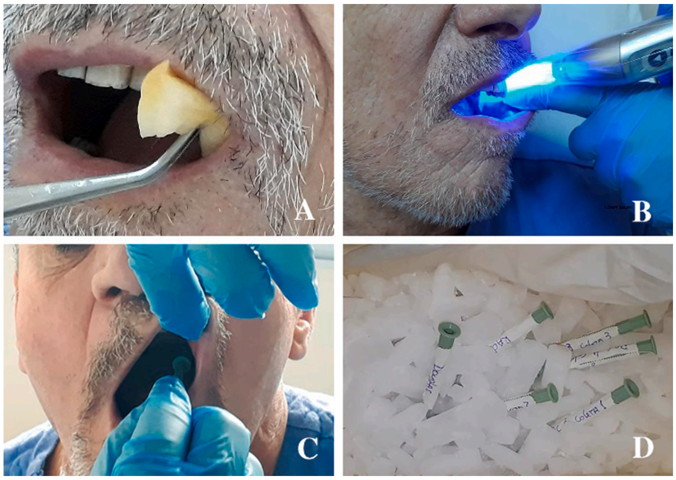

Fig 1. A. Cotton rolls wet with curcumin solution placed in the upper left superior region; B. Blue LED device positioned in the patient's mouth to perform the aPDT technique; C-D. Samples were collected and immediately stored at −80 °C.

was made. Another 82-year-old white man presented himself to the Emergency Department with a history of worsening dyspnea and dizziness. A diagnosis of acute decompensation of chronic heart failure precipitated by pulmonary infection was made. Both men were hospitalized because of the deteriorating respiratory pattern and real-time polymerase reverse transcriptase chain reaction (PCR) confirmed COVID-19.

Oral care and decontamination are important to avoid bacteremia. During the COVID-19 pandemic, these measures can prevent co-infections that could aggravate the general condition. Our protocol was approved by the Committee of Ethics of the Medical Center PMESP (n$^{o.}$ 43,125,520.7.0000.8847), and the patients signed a consent term. The photosensitizer was prepared by diluting (1.5 g/L) curcumin solution (Empório Medicinal Farmácia de Manipulação- São Paulo- Brazil) in dimethylsulfoxide (0.1%) and then in distilled water (980 ml), to obtain the final curcumin solution (30 mg/L) [5].

The oral cavity of both patients was rinsed with 10 ml of curcumin final solution for the 30 s, and cotton rolls wet with the solution were placed in the upper left superior region for 5 min (Fig 1A). The buccal and gingival surface were irradiated with a blue LED (ECEL ®, RD-7, 455 ± 30 nm, 900 mW/cm^2) with a cylindrical diffuser tip, (89 mm in length and 6.73 mm in diameter) for 5 min (Poly Wireless, Kavo-Brazil) (Fig 1B). The buccal and gingival mucosa surface of the left posterior region were scraped with a sterile punch (Kolplast ci LTDA, Brazil) three times (before therapy, immediately after, and 1 hour after aPDT).

The samples were frozen and stored at −80 °C (Fig 1C-D). RT qPCR reactions were performed as previously described [1] All samples were evaluated by the CDC human RNase P (RP) and Charité molecular assays for detection of SARS-CoV-2. The results regarding the effects of aPDT in the Ct values obtained to detect SARS-CoV-2 target genes were descriptive. As the viral load and the Ct values are inversely correlated, we considered a high viral load when Ct≤25, intermediate Ct 26–30, and low Ct ≥31 [6]. Samples from all patients and evaluated periods showed good quality. A detailed description of the Ct values obtained in each patient is shown in Table 1. The patients showed a substantial decrease in the Ct values 1 h after aPDT, indicating a decrease in the viral load in the oral cavity. The results regarding the Ct values were very similar using Cherité and CDC protocols. The patients were followed up for 48 h and no side effects of aPDT were observed or reported.

Discussion

aPDT has emerged as a promising technique to reduce antimicrobial-resistant pathogens [4]. Our study showed that patients had lower levels of SARS-CoV-2 genes immediately or 1 h after a single section of aPDT compared to baseline viral load, deep layers could be achieved. Furthermore, no adverse effects were reported until 48 h after the procedure.

Antimicrobial PDT with methylene blue has been used in different procedures, however, in oral disinfection curcumin has been investigated and presented promising results. It has the advantage of being a colorless natural substance, combined with a LED light, safe for the oral tissues, has low cost, and can promote the reduction of microorganisms in a similar way to traditional 1-minute mouthwash with 0,12% chlorhexidine [7,8].

Our results are corroborated by the findings of Santezi et al. (2016) which demonstrated that aPDT reduced the microbial load, and has no side effect on taste, teeth color, burning sensation, or mucosal desquamation. Oral itching was observed only in a few volunteers in the Araújo et al. (2012) study. These aspects are important principally in patients hospitalized with COVID-19, which may have lesions in the oral cavity due to immunosuppression.

The main targets of the curcumin are external structures of the microorganisms, the adhesion of the photosensitizer is sufficient for its destruction when activated by light. aPDT also has a crucial role in the minimal risk of resistance development, which provides an advantage over the mutation ability of SARS-CoV-2 [4] and conventional antimicrobials [7].

COVID-19 determined paradigm shifts for healthcare workers, whose repercussions have not yet been dimensioned. aPDT is a promising technique for clinical use in the pandemic era, but further clinical trials

Table 1
Description of the Ct values obtained by Charité and CD protocols for SARS-COV-2 detection in patients treated with aPDT at different time points.

Groups/Patients	Charité protocol (Ct)			CDC protocol (Ct)		
	Before	Immediatlly after	1 h after	Before	Immediatlly after	1 h after
Patient 1	17.3	28.8	30.4	17.5	28.1	27.3
Patient 2	26.8	26.3	34.3	25.3	23.3	35.6

must establish a viable, effective, and safe oral decontamination protocol for patients infected with SARS-CoV-2.

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