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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Case report

aPDT for oral decontamination of hospitalized patients with COVID-19

Susana Morimoto a,*, João Luiz Azevedo Rosin b, Bruno Fernandes Matuck c, Gabriella Schröter d, Maria Fernanda Setúbal Destro Rodrigues e, Karen M. Ramalho a, Daniela Procida Raggio f, Maria Stella Moreira a, d, Luiz Fernando Ferraz da Silva c

a School of Dentistry, Ibirapuera University (UNIB), São Paulo, SP, Brazil
b CAES - Military Police of São Paulo State, São Paulo, SP, Brazil
c Department of Pathology, School of Medicine, University of São Paulo (USP), São Paulo, SP, Brazil
d Department of Stomatology, School of Dentistry, University of São Paulo (USP), São Paulo, SP, Brazil
e Postgraduate Program in Biophotonics Applied to Health Sciences, Nove de Julho University (UNINOVE), São Paulo, SP, Brazil
f Department of Pediatrics, School of Dentistry, University of São Paulo (USP), São Paulo, SP, Brazil

ARTICLE INFO

Keywords:
COVID-19
SARS-CoV-2
Photodynamic therapies
Oral decontamination

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...
was approved by the Committee of Ethics of the Medical Center PMESP (n. 125520.7.0000.8847), and the patients signed a consent term. 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 Cherit 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 are indicated.

### 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) Before | Immediately after | 1 h after | CDC protocol (Ct) Before | Immediately after | 1 h after |
|-----------------|-----------------------------|------------------|-----------|--------------------------|------------------|-----------|
| Patient 1       | 17.3                        | 28.1             | 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.

References

[1] B.F. Matuck, M. Dolhnikoff, A.N. Duarte-Neto, G. Maia, S.C. Gomes, D.I. Sendyk, A. Zarpellon, N.P. de Andrade, R.A. Monteiro, J.R.R. Pinho, M.S. Gomes-Gouveia, S.C. Souza, C. Kanamura, T. Maua, P.H.N. Soldiva, P.H. Braz-Silva, E.G. Caldini, L.F. F. da Silva, Salivary glands are a target for SARS-CoV-2: a source for saliva contamination, J Pathol 254 (3) (2021 Jul) 239–243, https://doi.org/10.1002/path.5679, 2021.

[2] M.S. Moreira, I.L.I. Neves, C.Y.S.M. de Bernoche, G. Sarra, M.A. Dos Santos-Paul, F.C.N. Silva, G.T. Schrotter, T.C.P. Montano, C.M.A. de Carvalho, R.S. Neves, Bilateral paresthesia associated with cardiovascular disease and COVID-19, Oral Dis (2020 Jul 8), https://doi.org/10.1111/odi.13539, 10.1111/odi.13539.

[3] M.M. Alshamrani, A. El-Saied, Y.M. Arabi, M.A. Zunitan, F.M. Farahat, H.B. Bonnie, M. Matalqa, F. Othman, S. Almohrij, Risk of COVID-19 in healthcare workers working in intensive care setting, Am J Infect Control (2022 Jan 23), https://doi.org/10.1016/j.ajic.2022.01.093, S0196-6553(22)00017-7. doi:.

[4] J.F. Besegato, P.B.G. de Melo, P.E. Tamae, A.P.A.R. Alves, L.F. Rondon, L.G. Leanse, C. Dos Anjos, H.H. Casarini, M.A. Chinellatti, G. Faria, T. Dai, V.S. Bagnato, A.N. S. Rastelli, How can biophotonics help dentistry to avoid or minimize cross infection by SARS-CoV-2? Photodiagnosis Photodyn Ther 37 (2021 Dec 12), 102682 https://doi.org/10.1016/j.pdpdt.2021.102682.

[5] D.P. Leite, F.R. Paolillo, T.N. Parmesano, C.R. Fontana, V.S. Bagnato, Effects of photodynamic therapy with blue light and curcumin as mouth rinse for oral disinfection: a randomized controlled trial, Photomed Laser Surg 32 (11) (2014 Nov 627–632, https://doi.org/10.1089/pho.2014.3805.

[6] C. Azabha, V. Patel, V. Bhor, D. Gogoi, Cycle threshold values in RT-PCR to determine dynamics of SARS-CoV-2 viral load: an approach to reduce the isolation period for COVID-19 patients, J Med Virol 93 (12) (2021 Dec) 6794–6797, https://doi.org/10.1002/jmv.27206.

[7] N.C. Araújo, C.R. Fontana, M.E. Gerbi, V.S. Bagnato, Overall-mouth disinfection by photodynamic therapy using curcumin, Photomed Laser Surg 30 (2) (2012 Feb) 96–101, https://doi.org/10.1089/pho.2011.3053.

[8] C. Santezi, J.M. Tanomaru, V.S. Bagnato, O.B. Júnior, L.N. Dovigo, Potential of curcumin-mediated photodynamic inactivation to reduce oral colonization, Photodiagnosis Photodyn Ther 15 (2016 Sep) 46–52, https://doi.org/10.1016/j.pdpt.2016.04.006.