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ORIGINAL ARTICLE

Photodynamic inactivation of *Paracoccidioides brasiliensis* helps the outcome of oral paracoccidiodomycosis

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Abstract The antifungal drug therapy often employed to treat paracoccidiodomycosis (PCM), an important neglected fungal systemic infection, leads to offensive adverse effects, besides being very long-lasting. In addition, PCM compromises the oral health of patients by leading to oral lesions that are very painful and disabling. In that way, photodynamic therapy (PDT) arises as a new promising adjuvant treatment for inactivating *Paracoccidioides brasiliensis* (Pb), the responsible fungus for PCM, and also for helping the patients to deal with such debilitating oral lesions. PDT has been linked to an improved microbial killing, also presenting the advantage of not inducing immediate microbial resistance such as drugs. For the present study, we investigated the generation of reactive oxygen species (ROS) by using the fluorescent probes hydroxyphenyl fluorescein (HPF) and aminophenyl fluorescein (APF) after toluidine blue (TBO—37.5 mg/L)-mediated PDT (660 nm, 40 mW, and 0.04 cm^2 spot area) and the action of TBO-PDT upon Pb cultures grown for 7 or 15 days in semisolid Fava Netto's culture medium; we also targeted oral PCM manifestations by reporting the first clinical cases (three patients) to receive topic PDT for such purpose. We were able to show a significant generation of hydroxyl radicals and hypochlorite after TBO-PDT with doses around 90 J/cm^2; such ROS generation was particularly useful to attack and inactivate Pb colonies at 7 and 15 days. All three patients reported herein related an immediate relief when it came to pain, mouth opening, and also the ability to chew and swallow. As extracted from our clinical results, which are in fact based on in vitro outcomes, TBO-PDT is a very safe, inexpensive, and promising therapy for the oral manifestations of PCM.

Keywords Photodynamic therapy · Paracoccidioidomycosis · Paracoccidioides · Reactive oxygen species · Toluidine blue

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Introduction

Paracoccidioides brasiliensis (Pb) and *Paracoccidioides lutzii* both consist of fungi that are responsible for causing paracoccidioidomycosis (PCM), an important neglected and systemic infection mainly found in Latin America [1, 2]. Throughout their development processes, these fungi developed certain characteristics and mechanisms that allowed for their progression towards an efficacious pathogenicity in the human host; such pathogenicity involves pathogen-host interactions, such as fungal adaptation, adhesion and invasion, as

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