



# Photodynamic Therapy for Oral Herpes Simplex Infections: It can be Possible?



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## Opinion

Herpes simplex virus type 1 (HSV-1) is a member of the Alphaherpesviridae subfamily and its structure is composed of linear dsDNA, an icosahedral capsid with a spikey envelope. HSV-1 infection is characterized by a cycle of primary infection of epithelial cells, on the latency primarily in neurons, and reactivation. HSV-1 involved overall oral mucosa [1]. An HSV infections treatment includes topical acyclovir 5%, penciclovir 1%, dosoconal 10%, lidocaine, sunscreen sticks for herpes labialis [2].

Photodynamic Therapy (PDT) relies on the interaction between a photosensitizer, a light with the appropriate wavelength, and the presence of oxygen. The reaction between the 3 elements generates ROS in cells that take up the photosensitizer, causing cell death by necrosis or apoptosis, but spares the surrounding tissue [3]. PDT was used in literature for the treatment of oral disease, such as oral lichen planus [4], oral pre-cancerous lesions [5] and oral infections.

Some articles on the treatment of HSV infections are present in scientific literature. In vitro studies made by Zverev et al. [6] shown high sensibility of HSV-1 and Type 2 spp to LLLT mediated by Fotoditazine cromophore leading to a reliable decrease of viral agents content [6].

Marotti et al. [7] presented case series and demonstrated the effectiveness of PDT on recurrent herpes simplex infections on the lips [7,8]. All patients treated, were in the vesicular stage, so it was possible to perform PDT treatment on the lesions. The vesicles were carefully perforated with a needle. A methylene blue solution was placed over the lesions, and after 5 min, the excess dye was removed. The lesions were irradiated with a diode laser of 660-nm of wave length [7]. The patients had no recurrences at 6 and 10 months follow-up. Marotti et al. [7] demonstrated also that PDT is effective as the High level laser therapy for HSV infections [8]. Ramalho et al. [9] also proposed the use of Methylen blue as a photosensitizer. Methylene Blue solution was applied topically by

authors in a 0.005% concentration. Five minutes was considered as pre-irradiation time and one point of irradiation was performed over the lesion using a 660 nm wavelength laser. Irradiation time was 2 min for point [9]. Kvacheva et al. [10] wrote an in vitro study on the effectiveness of PDT associated with 5-aminolevulinic acid [10]. Photo inactivation of herpes simplex virus was evaluated in the past, by rose bengal and fluorescein as photosensitizer [11]. Reactivation of HSV and lesions progressions was a strongly debated topic in PDT mediated herpes lesions therapy [12].

Sperandio et al. [13] established a low risk of recurrent HS lesions and vesicles after PDT followed by a constant and repeated low level laser therapy [13].

Kharkwal et al. [14] further studied the effect on phenothiazinium mediated photo-biostimulation on oral tissues in a review and later discovered low risk of lesion's reactivations when a cromophore medium is applied during the photobiostimulation process [14].

Marotti et al. [15] in a 2010 paper later discovered that intensity, applications, and irradiation power does not alternate the final results and healing process. Patients were treated with High Intensity Laser Therapy (HILT) followed by LLLT or Methylene Blue cromophore medium applied before LLLT stabilizing therapy. Stimulation therapy was applied at 24,48,72 h and 7th day. During the six month follow-up period, no patients showed signs or symptoms of recurrent herpes lesions (RHL) [15,16]. The evaluation of new cromophore substances represents a principal issue and a largely debated discussion topic in literature.

In 2017 Remichkova et al. [17] evaluated the effect of Zync-Phthalocyanine complexes in genetic alterations of coxsackie spp. First positive result were raised after bovine applications and a HS evaluation should be considered [17,18].

Latief et al. [19] demonstrated that PDT with a porphyrin derived cromophore medium is effective for eliminating HSV-1

and ACV-resistant HSV-1 without a harmful effect on host cells even in acyclovir resistant agents [19].

Even if the light mediated therapeutic effects in dermatological herpes lesions are increasingly demonstrated, only few papers in scientific literature actually debate on oral HRL applications. Furthermore in vitro and in vivo studies have shown a reliable and significant efficacy of PDT in RHL treatment. Pathogenic mechanisms are far to be widely known and further RCTs and comprehensive reviews need to be performed.

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