# EFICÁCIA DA TERAPIA FOTODINÂMICA NO TRATAMENTO DA HERPES SIMPLES TIPO I

# EFFICACY OF PHOTODYNAMIC THERAPY IN THE TREATMENT OF HERPES SIMPLEX TYPE I

# EFICACIA DE LA TERAPIA FOTODINÁMICA EN EL TRATAMIENTO DEL HERPES SIMPLE TIPO I

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## RESUMO

O presente estudo trata-se de uma série de relatos de caso clínico sobre a aplicação da Terapia Fotodinâmica Antimicrobiana (TFD) no tratamento de lesões causadas pelo Herpes Simples Tipo I (HSV-1). Essa infecção viral é caracterizada por episódios recorrentes, impactando diretamente a qualidade de vida dos pacientes devido à dor, desconforto estético e estigmatização social. Tradicionalmente, o tratamento é realizado com antivirais, como o Aciclovir, os quais apresentam limitações relacionadas à resistência viral e possíveis efeitos adversos. Diante disso, a TFD surge como uma abordagem terapêutica minimamente invasiva, que utiliza um fotossensibilizador ativado por luz de comprimento de onda específico, gerando espécies reativas de oxigênio capazes de destruir seletivamente as células infectadas. Este trabalho teve como objetivo relatar três casos clínicos tratados com TFD, empregando azul de metileno a 0,005% e laser de diodo de 660 nm em pacientes com lesões herpéticas em fase vesicular. Em todos os casos, observou-se melhora significativa dos sintomas, com alívio da dor e diminuição da inflamação em até 24 horas após a intervenção. Os resultados obtidos corroboram os dados da literatura quanto à eficácia da TFD como adjuvante no tratamento da herpes labial recorrente, principalmente em pacientes imunocompetentes. Além disso, o estudo evidencia a praticidade, segurança e ausência de efeitos colaterais relevantes dessa abordagem, o que a torna uma opção viável na clínica odontológica. Conclui-se que a TFD representa uma alternativa promissora, especialmente para indivíduos que buscam terapias complementares, eficazes e de baixo risco. No entanto, reforça-se a necessidade de

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estudos adicionais com maior número de participantes e padronização dos protocolos utilizados, a fim de consolidar a técnica na prática clínica diária.

**Palavras-chave:** Herpes. Herpes simples. Laser. Laserterapia. Terapia Fotodinâmica.

## ABSTRACT

This study presents a series of clinical case reports on the application of Antimicrobial Photodynamic Therapy (aPDT) in the treatment of lesions caused by Herpes Simplex Virus Type I (HSV-1). This viral infection is known for its recurrent episodes, which significantly affect patients' quality of life due to pain, aesthetic discomfort, and social stigma. Traditionally, treatment involves the use of antiviral medications such as Acyclovir, which may present limitations related to viral resistance and potential side effects. In this context, aPDT emerges as a minimally invasive therapeutic approach that combines a photosensitizing agent with light of a specific wavelength, generating reactive oxygen species capable of selectively destroying infected cells. This study aimed to report three clinical cases treated with aPDT, using 0.005% methylene blue and a 660 nm diode laser on patients with vesicular-phase herpetic lesions. All cases showed significant improvement in symptoms, with pain relief and reduced inflammation within 24 hours after treatment. The outcomes corroborate existing literature regarding the efficacy of aPDT as an adjunctive therapy in managing recurrent labial herpes, especially in immunocompetent patients. Furthermore, the study highlights the practicality, safety, and lack of relevant side effects, making aPDT a viable option in dental practice. It is concluded that aPDT is a promising alternative, particularly for individuals seeking complementary, effective, and low-risk therapies. Nevertheless, further studies with larger samples and standardized clinical protocols are needed to support the widespread use of this technique in daily clinical practice.

**Keywords:** Herpes. Herpes simplex. Laser. Lasertherapy. Photodynamic Therapy.

## RESUMEN

Este estudio es una serie de informes de casos clínicos sobre la aplicación de la Terapia Fotodinámica Antimicrobiana (TFD) en el tratamiento de lesiones causadas por el virus del herpes simple tipo I (VHS-1). Esta infección viral se caracteriza por episodios recurrentes, que impactan directamente en la calidad de vida de los pacientes debido al dolor, la incomodidad estética y la estigmatización social. Tradicionalmente, el tratamiento se realiza con antivirales, como el aciclovir, que presentan limitaciones relacionadas con la resistencia viral y posibles efectos adversos. Por lo tanto, la TFD surge como un enfoque terapéutico mínimamente invasivo, que utiliza un fotosensibilizador activado por luz de una longitud de onda específica, generando especies reactivas de oxígeno capaces de destruir selectivamente las células infectadas. Este estudio tuvo como objetivo informar tres casos clínicos tratados con TFD, utilizando azul de metileno al 0,005% y láser de diodo de 660 nm en pacientes con lesiones herpéticas en la fase vesicular. En todos los casos, se observó una mejoría significativa de los síntomas, con alivio del dolor y reducción de la inflamación dentro de las 24 horas posteriores a la intervención. Los resultados obtenidos corroboran la literatura sobre la eficacia de la TFD como adyuvante en el tratamiento del herpes labial recurrente, especialmente en pacientes inmunocompetentes. Además, el estudio destaca la practicidad, seguridad y ausencia de efectos secundarios relevantes de este enfoque, lo que lo convierte en una opción viable en la clínica dental. Se concluye que la TFD representa una alternativa prometedora, especialmente para quienes buscan terapias complementarias, efectivas y de bajo riesgo. Sin embargo, refuerza la necesidad de realizar estudios adicionales con un mayor número de participantes y estandarizar los protocolos utilizados para consolidar la técnica en la práctica clínica diaria.

**Palabras clave:** Herpes. Herpes simple. Láser. Terapia láser. Terapia fotodinámica.

## INTRODUCTION

Infections caused by the herpes simplex virus represent a relevant public health problem in Brazil and worldwide. Thus, it is essential to constantly update studies aimed at improving the treatment conditions and the conducts adopted in the face of these diseases. The dentist must be trained to diagnose and guide patients affected by primary herpes simplex, recurrent herpes (perioral and intraoral), with the aim of reducing the time of clinical manifestations and providing adequate guidelines for the prevention of these conditions. Human herpesviruses (HHVs) represent DNA viruses belonging to the Herpesviridae family, capable of infecting human cells, causing the spread of diseases (Santos et al., 2012).

Human herpes virus (HHV) is part of a family – Herpesviridae and has humans as their host. They are ubiquitous and latent and, once the first infection occurs, they remain in the body of the affected individual throughout his or her life (Santos et al., 2012).

Herpes simplex virus (HSV) is a viral infection caused by the herpes simplex virus (HSV), and is classified into two main types: Herpes simplex virus (HSV) is a common human pathogen, classified into HSV-1 and HSV-2, both of which have similar but antigenically different structures. HSV-1 is characterized by extragenital conditions, disseminating through infected saliva or active perioral lesions, while HSV-2 involves perigenital conditions (Tagliari, Kelmann, Diefenthaler et al., 2012). This infection has a high prevalence worldwide and is characterized by recurrent episodes, causing a significant impact on the quality of life of patients due to pain, discomfort, and social stigmatization (Burocracia Zero et al., 2025).

In this sense, the majority of the population becomes infected by contagion of viral particles present in saliva or in active peroral lesions. With this, it is highlighted that Cold Sores is a recurrent disease that affects about 40% of the world's population. HSV-1 generates peroral lesions, and herpetic gingivostomatitis is often the primary manifestation in infected individuals. Regarding recurrences, for many, it represents a recurrent discomfort with the presence of symptoms, and, for immunosuppressed individuals, such as HIV-positive, this infection is associated with increased morbidity and mortality (Rocha et al., 2024).

The reactivation of the HSV-1 virus in the lips and oral cavity can be triggered by febrile episodes due to diseases of various causes, in women who are in their menstrual period and by inadequate sun exposure. Therefore, patients commonly present with the prodromal stage of pain, burning, itching, and paresthesia. In this way, as long as the vesicles are present with their liquid content, they are infectious, and when the vesicles

rupture, the presence of small ulcerations with subsequent repithelialization of the skin or mucosa appears, and at this stage the disease is asymptomatic (Cabral et al., 2022).

On clinical examination, it is possible to see small yellowish vesicles on the mucosa and skin that are susceptible to rupture at any local stimulus, forming ulcers, covered by a membrane and an erythematous halo. The course time of herpes is approximately 7 to 14 days for complete healing, being a lesion that is repaired by regeneration, leaving no scars at the site (Rocha et al., 2024).

The evolution of HSV virus infection is characterized by the following phases: primary, latency, and recurrent. Primary is the phase in which there is initial exposure to the virus, occurring predominantly in young individuals. Then the latency test, in which the virus is absorbed by the sensory nerves and transported to the associated nerves, remaining latent in the ganglia. Finally, the recurrent phase is the reactivation of the virus, which may be related to factors that predispose to the viral activity of HSV, such as advanced age, exposure to UV rays, stress, pregnancy, mechanical trauma, menstrual period, and systemic diseases (Camargo et al., 2024).

Cold sores are the clinical manifestation of recurrent infection that is characterized by small and numerous erythematous and painful papules, which constitute conglomerates of vesicles that rupture and form crusts. Regarding the manifestation of herpes simplex labialis, they can be evidenced in 3 clinical periods of the disease, they are: prodromal, active clinical and reparatory. In the so-called prodromal period, initial clinical manifestations are observed that precede the lesions, the individual can predict up to 24 hours in advance the reappearance of the active form of the viral infection (Rocha et al., 2024).

Currently, the standard treatment for herpes simplex is usually based on the use of antiviral medications, being applied to both primary and recurrent infections, which can help reduce the intensity and extent of symptoms. Several antiviral drugs are available, such as Valacyclovir, Famciclovir, and Acyclovir (Camargo et al., 2024) that inhibit viral replication and reduce the duration of outbreaks. Although the use of antivirals, such as Acyclovir, is the most widely accepted treatment for Herpes Simplex lesions, low-level laser therapy has gained ground in clinical practice due to its tissue-repairing, analgesic, and anti-inflammatory properties (Rocha et al., 2024).

In this context, antimicrobial photodynamic therapy (PDT) emerges as a promising alternative for the treatment of herpes simplex. PDT is a minimally invasive technique that combines a photosensitizing agent, light at a specific wavelength, and molecular oxygen to generate reactive oxygen species (ROS), promoting the selective destruction of infected cells and reducing viral load. Recent studies have shown that PDT can inhibit HSV

replication and accelerate the healing of lesions, in addition to potentially modulating the local immune response, minimizing the recurrence of the infection.

In view of the need for new, more effective treatments and the growing viral resistance to traditional antivirals, the present study aims to evaluate, through clinical case reports, the efficacy of laser therapy in the treatment of herpes labialis simplex type I.

## CASE REPORT

The three clinical case reports presented were carried out at the Dental Clinic of the UniBH University Center. The patients or their guardians signed the free and informed consent form (ICF) for the treatment of herpes simplex labialis.

The patients had herpes in the vesicular phase and, therefore, the indication was to perform antimicrobial photodynamic therapy (PDT) treatment in the lesions. Table 01 shows the laser irradiation parameters for PDT. The treatment protocol for herpes simplex labialis (vesicular phase) used in clinical cases 1, 2 and 3 are described below:

Table 1 Dosimetry parameters used in Photodynamic Therapy (PDT)

| | |
|---|---|
| Wavelength (nm) | 660 |
| Active medium | InGaAlP |
| Beam Area ($cm^3$) | 0,04 |
| Power (mW) | 40 |
| Power Density (W/cm) | 1 |
| Irradiation time per point(s) | 90 |
| Energy per point (J) | 9 |
| Irradiation mode | Punctual and contact |
| Number of sessions | 1 |

Source: Authorship.

### CASE REPORT 1

An 11-year-old female patient, with a white skin phototype, arrived at the Dental Clinic of the Unibh University Center, complaining of burning on the lower lip and itching at the site, and reported that it began after returning from a beach trip (Figure 1A). Clinical examination revealed the presence of vesicles in the middle of the lower lip (Figure 1A), with painful symptoms. The vesicles were carefully ruptured with a sterile needle and the fluid was carefully drained with the aid of sterile gauze in order to prevent the infection from spreading to adjacent areas. Next, a 0.005% methylene blue photosensitizer (Chimiolux, DMC, São Paulo) was applied to the lesion (Figure-1B).

Figure 1A Initial appearance of the vesicular phase of herpes simplex labialis.

Source: Authorship.

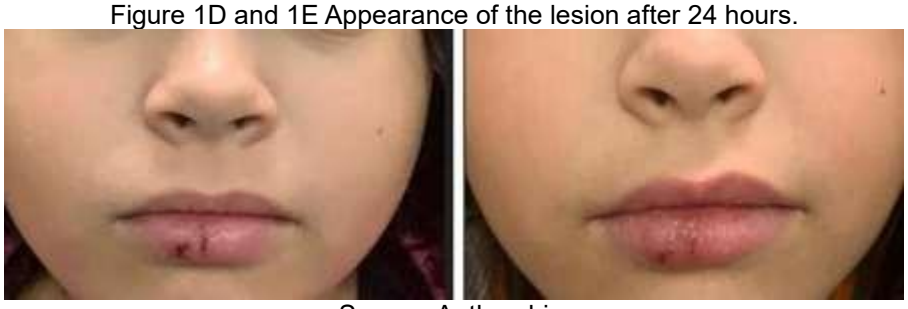
Figure 1B Blue 0.005% methylene photosensitizer on the lesion.

Source: Authorship.

Figure 1C Irradiation with the 660 nm low-power diode laser.

Source: Authorship.

Figure 1D and 1E Appearance of the lesion after 24 hours.



Source: Authorship.

After the recommended time, the excess photosensitizer was removed and the lesion area was irradiated at two different points, using a diode laser equipment (MM Optics, São Paulo), continuous emission, at low intensity, with a red wavelength of 660 nm, output power 40mw, energy of 9 joules, for 90 seconds at each point (Figure 1C). After 24 hours, the patient returned for consultation with a significant improvement in the lesion,

mainly reporting decreased pain sensitivity and burning. (Figures 1D and 1E).

## CASE REPORT 2

A 24-year-old male patient, with brown skin phototype, arrived at the Dental Clinic of the Unibh University Center, complaining of painful lesions on the lower lip. In the anamnesis, she reported no significant systemic alteration or use of medication, however, she was going through a period of stress after changing jobs. Clinical examination revealed vesicular lesions compatible with herpes simplex type I (Figure 2A). The vesicles were carefully ruptured with a sterile needle (Figure 2B) and the fluid was carefully drained with the aid of sterile gauze in order to prevent the infection from spreading to adjacent areas. Subsequently, a 0.005% methylene blue photosensitizer (Chimiolux, DMC, São Paulo) was applied to the lesion for five minutes. The area was irradiated at three different points with diode laser equipment (MM Optics, São Paulo), continuous emission, at low intensity with red wavelength of 660 nm, output power 40mw, energy of 9 joules, for 90 seconds at each point in contact mode (Figure 2C). After 24 hours, the patient returned already reporting a lot of improvement in the condition (Figures 2D and 2E). And he performed a photobiomodulation therapy session using the same equipment, but with an output power of 5 mw, energy density of 3.7 J/cm2, 10 seconds per point, in contact mode. The patient called the dental surgeon reporting that he was much better and did not return for consultation.

Figure 2A Initial appearance of the vesicular phase of herpes simplex labialis.

Source: Authorship.

Figure 2B Piercing of the vesicles with a sterile needle

Source: Authorship.

Figure 2C Irradiation with the 660 nm low-power diode laser.

Source: Authorship.

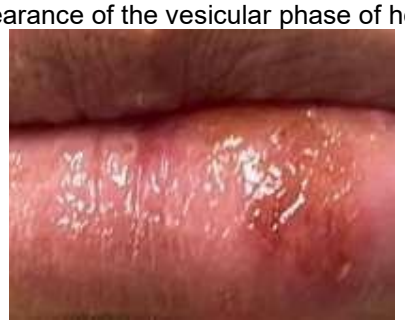
Figure 2D and 2E Appearance of the lesion after 24 hours.

Source: Authorship.

## CASE REPORT 3

A 26-year-old female patient presented to the dental office complaining of a herpetic lesion in the vesicular phase, located on the lower lip (Figure 3). During the anamnesis, the patient reported experiencing a period of stress, attributed to a recent professional transition. To conduct the treatment, we opted for the use of Antimicrobial Photodynamic Therapy (PDT). Continuing the clinical protocol, the vesicles present in the affected region were removed. Subsequently, 0.005% methylene blue (Chimiolux, DMC, São Paulo) was applied for a period of five minutes, corresponding to the pre-irradiation time (Figure 3B). After this interval, the excess of the photosensitizing agent was carefully removed. In continuity with the protocol, the lesion area was irradiated at two different points, using a diode laser equipment (MM Optics, São Paulo), continuous emission, at low intensity, with a red wavelength of 660 nm, output power 40mw, energy of 9 joules, for 90 seconds at each point (Figure 3C). After 24 hours, the patient returned for consultation with a significant improvement in the lesion, mainly reporting decreased pain sensitivity and burning. (Figures 3D and 3E).

Figure 3 A Initial appearance of the vesicular phase of herpes simplex labialis



Source: Authorship.

Figure 3B Blue 0.005% methylene photosensitizer applied to the lesion.

Source: Authorship.

Figure 3C Irradiation with the 660 nm low-power diode laser.

Source: Authorship.

Figure 3D and 3E Appearance of the lesion after 24 h (D and E).

Source: Authorship.

## DISCUSSION

The cases reported with laser therapy are related to the treatment of herpes simplex type 1 (HSV-1). Herpes simplex is a viral infection caused by the Herpes simplex virus (HSV), belonging to the Herpesviridae family. Herpes simplex virus type 1 (HSV-1) infection is a neurotropic viral condition of high prevalence worldwide, affecting approximately two-thirds of the adult population globally (Whitley, Kimberlin, Roos et al.,2023).

A key feature of Herpes simplex virus (HSV) is its ability to establish latency in sensory nerve ganglia, periodically reactivating under stimuli such as stress, immunosuppression, and exposure to ultraviolet radiation (Roizman, Knipe; Whitley R, et al., 2013).

In the clinical cases presented in this study, it was possible to clearly observe the correlation between the triggers described in the literature and the clinical episodes of reactivation. Case 1, an 11-year-old patient, reported the onset of symptoms after a trip to the beach. Intense sun exposure, specifically to UV radiation, is a factor classically recognized for triggering HSV-1 reactivation, since it compromises local immune function and alters the integrity of the epidermis (Wald et al., 2007). The clinical picture, characterized by burning, itching, and clustered vesicles, is typical of the active phase of the virus.

Cases 2 and 3, involving young adult patients, demonstrated the impact of emotional stress as a triggering factor. Both patients reported recent changes in their professional routines, experiencing psychological pressure and significant changes. Stress is known to influence the hypothalamic-pituitary-adrenal axis, increasing cortisol levels and compromising the T-cell-mediated immune response, the main mechanism of control of HSV-1 during its latency. (Segerstrom et al, 2004). With this, viral reactivation is facilitated, manifesting clinically in previously affected areas.

The treatment chosen for all cases was Antimicrobial Photodynamic Therapy (PDT), using 0.005% methylene blue as a photosensitizing agent and a 660 nm diode laser. The choice of this approach was based on its antimicrobial, anti-inflammatory and healing action, described as effective by several recent authors. PDT consists of the application of a photosensitive dye that, when activated by a specific light source in the presence of oxygen, generates reactive oxygen species (ROS), promoting the selective destruction of cells infected by the virus (Pereira et al., 2021).

In all cases, the clinical response to PDT was favorable. The patients reported significant relief of pain and inflammatory symptoms within the first 24 hours after application, in addition to visual regression of the vesicular lesions and the beginning of re-epithelialization. The additional advantage is the absence of systemic side effects, often associated with the use of oral antivirals.

In addition, it is important to emphasize the clinical usefulness of photobiomodulation and PDT in cases of recurrent cold sores, with superior benefits when treatment is initiated in the prodromal or early stages of the lesion. The use of PDT has been shown to be especially useful for immunocompetent patients with recurrent lesions (Neves et al., 2023).

PDT not only reduces the local viral load, but can also modulate the inflammatory response, reducing the frequency of relapses in patients with recurrent episodes (Rocha et al., 2024). This aspect is particularly relevant in the dental context, where frequent recurrences directly affect the aesthetics and well-being of patients.

However, despite the promising results, it is necessary to recognize that part of the current literature still considers PDT as an adjuvant therapy, and not as a definitive replacement for traditional antivirals. Therefore, PDT should be seen today as an excellent complementary therapeutic alternative, especially in patients seeking minimally invasive approaches, with few adverse effects and good cost-benefit.

Thus, the clinical cases presented in this study reinforce the applicability of PDT in dental practice and its efficacy against recurrent HSV-1 infections. The direct relationship between the clinical triggers described (sun exposure and stress) and viral reactivation, associated with good response to PDT, suggests that this therapeutic modality deserves to be more widely explored and standardized in clinical dental protocols.

## CONCLUSION

Laser therapy has stood out for its analgesic, anti-inflammatory, and healing effects in several clinical conditions, without presenting relevant side effects. In the treatment of herpes simplex type 1 (HSV-1), a significant reduction in pain, accelerated tissue repair, and a decrease in recurrences are observed, suggesting that this approach may be more effective than conventional methods. However, although the advances provided by this therapy are promising, the literature points to the need to establish a universal protocol, which requires further studies focused on the standardization of procedures.

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