


## USE OF PHOTOBIOMODULATION AS A FORM OF ADJUVANT TREATMENT IN FELINES WITH SPOROTRICHOSIS

### USO DA FOTOBIOMODULAÇÃO COMO FORMA DE TRATAMENTO ADJUVANTE EM FELINOS COM ESPOROTRICOSE

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#### ABSTRACT

Due to the exponential growth of felines diagnosed with sporotrichosis in the state of Espírito Santo, as it is a zoonosis of great importance in public health, this study emerged as a way of quantifying the number of animals with the disease, observing the traditional treatment with antifungals. exclusives is already showing resistance. Objective – The objective of this study was to verify the therapeutic response of photobiomodulation associated with traditional therapies in felines with sporotrichosis, without changing the dosage of medications. Animals - 43 felines already diagnosed with sporotrichosis (*Sporotrix* spp.) were selected, treated in the dermatology sector in clinics and veterinary offices in Espírito Santo, presenting ulcerated, papulo-nodular lesions and intense itching. Method – As a treatment methodology with photobiomodulation, red light was chosen, at a power of two joules, due to its healing action and antiseptic effect, as all patients had already undergone drug treatment between 6 months and 2 years, without success. Results – As a result, it was confirmed that all animals showed wound healing in a few sessions, ranging from 2 to 6 with an average of 3.4 sessions (median of 3 sessions), thus promoting faster clinical healing of sporotrichosis and thus reducing the time of drug treatment. Conclusion – It is concluded that photobiomodulation helps in faster clinical improvement in patients with sporotrichosis, without side effects for the patient.

**Keywords:** Sporotrichosis. Cats. Photobiomodulation.

#### RESUMO

Devido ao crescimento exponencial de felinos diagnosticados com esporotricose no estado do Espírito Santo, por se tratar de uma zoonose de grande importância para a saúde pública, este estudo surgiu como uma forma de quantificar o número de animais acometidos pela doença e observar que o tratamento tradicional exclusivo com antifúngicos já apresenta

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sinais de resistência. Objetivo: Verificar a resposta terapêutica da fotobiomodulação associada às terapias tradicionais em felinos com esporotricose, sem alteração da dosagem dos medicamentos. Animais: Foram selecionados 43 felinos previamente diagnosticados com esporotricose (*Sporothrix* spp.), atendidos no setor de dermatologia em clínicas e consultórios veterinários no Espírito Santo, apresentando lesões ulceradas, pápulo-nodulares e prurido intenso. Método: Como metodologia de tratamento com fotobiomodulação, foi escolhida a luz vermelha, com potência de dois joules, devido à sua ação cicatrizante e efeito antisséptico, uma vez que todos os pacientes já haviam sido submetidos a tratamento medicamentoso por períodos entre 6 meses e 2 anos, sem sucesso. Resultados: Como resultado, confirmou-se que todos os animais apresentaram cicatrização das feridas em poucas sessões, variando de 2 a 6, com média de 3,4 sessões (mediana de 3 sessões), promovendo assim uma cicatrização clínica mais rápida da esporotricose e reduzindo o tempo de tratamento medicamentoso. Conclusão: Conclui-se que a fotobiomodulação auxilia na melhora clínica mais rápida de pacientes com esporotricose, sem efeitos colaterais para o paciente.

**Palavras-chave:** Esporotricose. Gatos. Fotobiomodulação.

## RESUMEN

Debido al crecimiento exponencial de felinos diagnosticados con esporotricosis en el estado de Espírito Santo, por tratarse de una zoonosis de gran importancia para la salud pública, este estudio surgió como una forma de cuantificar el número de animales con la enfermedad y observar que el tratamiento tradicional exclusivo con antifúngicos ya está mostrando resistencia. Objetivo: Verificar la respuesta terapéutica de la fotobiomodulación asociada a las terapias tradicionales en felinos con esporotricosis, sin modificar la dosis de los medicamentos. Animales: Se seleccionaron 43 felinos previamente diagnosticados con esporotricosis (*Sporothrix* spp.), atendidos en el sector de dermatología de clínicas y consultorios veterinarios en Espírito Santo, que presentaban lesiones ulceradas, pápulo-nodulares y prurito intenso. Método: Como metodología de tratamiento con fotobiomodulación, se eligió la luz roja, con una potencia de dos joules, debido a su acción cicatrizante y efecto antiséptico, ya que todos los pacientes habían sido sometidos previamente a tratamiento farmacológico durante períodos entre 6 meses y 2 años, sin éxito. Resultados: Como resultado, se confirmó que todos los animales presentaron cicatrización de las heridas en pocas sesiones, que variaron de 2 a 6, con un promedio de 3,4 sesiones (mediana de 3 sesiones), promoviendo así una recuperación clínica más rápida de la esporotricosis y reduciendo el tiempo de tratamiento farmacológico. Conclusión: Se concluye que la fotobiomodulación contribuye a una mejora clínica más rápida en pacientes con esporotricosis, sin efectos secundarios para el paciente.

**Palabras clave:** Esporotricosis. Gatos. Fotobiomodulación.

## 1 INTRODUCTION

Among the zoonotic dermatological diseases, sporotrichosis is a subcutaneous mycosis, with papulo-nodular characteristics, having as its causal agent the fungus *Sporothrix schenckii*, which is monospecific and dimorphic, that is, it presents different micro and macro morphological aspects, depending on the substrate and temperature, being filamentous in the environment (25 °C) and at 37 °C it is similar to yeast, and can be acquired by animals or humans.<sup>1,7</sup>

Epidemiologically, subacute or chronic infection has a cosmopolitan distribution, being more frequent in tropical and subtropical climatic conditions<sup>2</sup>. The most common form of transmission that occurs between animals and humans is through scratches or bites, by sick or asymptomatic cats<sup>1</sup>. Furthermore, there is no interrelationship between feline sporotrichosis and FIV and FeLV<sup>1</sup> retrovirus infections.

It is extremely important to differentiate sporotrichosis from other dermatological diseases through tests such as: leishmaniasis, cryptococcosis, feline leproid, bacterial abscesses, atypical cutaneous mycobacteriosis, foreign body granulomas, and neoplasms<sup>1</sup>.

The most commonly observed macroscopic characteristics of the lesions are: crusts, ulcerations and the presence of pus and blood, and regarding the location of the lesions, these animals were most affected on the head, followed by the thoracic and pelvic limbs. areas, and these locations can indicate which regions are most exposed during fights or even when they come into contact with soil or plants<sup>3</sup>.

Regarding the tests that conclude the diagnosis of sporotrichosis, the most common and quickest to be performed is skin cytology with the lesion impression technique, which is stained with a laboratory panopticon and it is possible to highlight a large number of rounded and yeast-like lesions and oval shapes<sup>4</sup>.

Patients respond well to treatment with antifungals such as ketoconazole, itraconazole and iodide, but the drug of choice is itraconazole due to its greater efficacy and safety<sup>5</sup>.

Treatment associations proved to be effective in treating refractory animals, being a medicinal alternative when Itraconazole alone does not provide an effective response<sup>13</sup>. However, although the associations present a more satisfactory therapeutic response, there is still the possibility that the fungus may also create new resistance due to the emergence of new strains of *Sporothrix* spp.<sup>14</sup> and, in addition, the more drug associations there are, the greater the side effects on the body<sup>13</sup>.

Integrative therapies have been increasingly studied and used with the aim of reducing conventional treatment time and medication side effects. Photodynamic therapy (or laser therapy) has been widely studied in the health sector in recent decades, and has been widely used as an alternative to conventional treatments in localized injuries as it is very effective in accelerating tissue healing and also in association with low intensity of the Laser with photodynamic therapy induces beneficial actions to the affected tissue, thus reducing local inflammation, causing analgesia and tissue restoration<sup>6</sup>. The response we observed, that is, the reduction of lesions, occurs because the therapy increases vascularization and, thus, generates an increase in the supply of nutrients and oxygen to the lesion site, in addition to promoting the healing stimulus, through a positive proliferation cell, including fibroblasts, which helps in the rapid and organized tissue recovery response<sup>6</sup>.

Currently, there is only one bibliographical source using photobiomodulation therapy for the adjuvant treatment of sporotrichosis in cats, which also confirms that the association of integrative therapy with medications in animals that had already been treated for a long time with medication alone improved much more quickly<sup>8</sup>.

## **2 MATERIALS AND METHODS**

The study was approved by the Animal Research Ethics Committee (CEUA) of XXXXX, under protocol No. 610-2021.

Felines that already had a confirmed diagnosis of sporotrichosis by cytological examination and/or fungal culture were invited to the study, in addition to being on drug treatment for 6 months to 2 years without success in therapy, using medications such as Itraconazole (100 mg cat) and iodide of potassium (dose between 5 and 10 mg/kg), both medicines every 24 hours, being medicines compounded in a veterinary compounding pharmacy or purchased in a pharmacy (medicines for human use), in addition to absolute isolation. All animals were monitored by different veterinarians, but the treatments were the same, so all patients were referred only to photobiomodulation treatment. Furthermore, all of them were in varying general conditions, that is, some were more weakened due to the longer period of drug treatment, and other animals were in normal conditions, and none of the animals in this study presented associated bacterial infection from the moment the treatment began. to clinical cure.

To confirm sporotrichosis, skin cytologies were performed using the imprint or aspiration puncture technique (the choice of collection technique varied according to the type

of lesion), every week until the wound was completely healed (clinical cure). It was always performed by the same professional, a veterinary dermatologist, before each photobiomodulation session. No cytology showed signs of secondary bacterial infection, only yeasts compatible with *Sporotrix* spp.

In total, 43 animals, 41 without comorbidities and two with immunodeficiency due to FIV and FeLV but stabilized, underwent adjuvant therapy with Photobiomodulation (laser therapy) using only red light at a dose of two joules, with weekly sessions aimed at accelerating healing and eliminating the fungus faster. All drug treatment protocols were maintained, in addition to all animals remaining in absolute isolation from the diagnosis of the disease until clinical cure after photobiomodulation therapy, precisely to observe the effect of the laser.

All cats were contained only with stress reduction techniques, such as offering food, disposable toys or scratching posts, or remaining in their own carriers. All materials used were burned before being discarded in the trash. As a result, there was no need for chemical or physical containment, reducing the risk of people in the environment acquiring zoonosis by biting or scratching the animals.

All patients come from the state of Espírito Santo, residing in cities in the Greater Vitória region and aged between 1 and 5 years, with only one being a Persian and the rest being a Brazilian Shorthair. The protocol chosen for all patients was photobiomodulation with red light, with the device setting a dose of  $2\text{J}/\text{cm}^2$  lasting 20 seconds in each lesion on the patient's body. All lesions underwent laser therapy, using a digital caliper to measure the size of each lesion.

The equipment used was from the company ECCO VET®, using a pen (100 mW) or Cluster (450 mW), according to the size of the lesions, which varied from 1 to 6 centimeters in diameter. The distance between the equipment and the skin was 1 cm. The choice of using the pen or cluster depends on the size of the lesion, that is, small lesions can only be used with a single light source (pen – has only 1 light output), while larger and disseminated lesions require a larger light source (cluster – has 3 light outputs).

Regarding statistical analysis, the data were presented descriptively in relation to the frequency of events, as well as the chi-square test was performed for association of variables using the GraphPad Prisma 9.0 program with a significance level of 5%.

### 3 RESULTS AND DISCUSSION

All 43 animals underwent a photobiomodulation session with red light every seven days, always on the same day of the week, and without the use of physical or chemical restraint (with anesthetics).

All animals that did not present comorbidities or secondary infections and animals that had stable FIV and FeLV were approved for the study. Furthermore, all clients (owners) were aware of the study and that their animals would only be discharged from laser therapy after clinical cure (complete healing of the lesions and absence of fungi on the skin accompanied by cytological examination) and the drug treatment should be continued for another 30 days as maintenance and monitored for another 6 months to confirm that the animal would not have a recurrence and none had. As many owners did not have the financial means to carry out the fungal culture test, they were followed up with the cytological test, in which, since clinical cure, they no longer had the fungal structure on their skin, in addition to showing no side effects.

Before starting photobiomodulation, 26/43 animals had been undergoing treatment for six months with antifungals without satisfactory clinical response, while 17/43 animals had been undergoing treatment for more than six months (7 to 16 months) (table 01).

The number of sessions used ranged from 2 to 6 with an average of 3.4 sessions (median of 3 sessions). Clinical cure and negative cytology were observed in 100% of animals submitted to the combination of drug therapy and photobiomodulation.

It was observed that 25/58.1% of the animals began to show improvement in the lesions in the first session, requiring up to 3 sessions, while 18/41.2% of the animals began to show improvement after 3 sessions, requiring up to 6 sessions. Regarding the time of previous treatment and the number of photobiomodulation sessions, there was no association using Fisher's exact test ( $p=0.3443$ ). However, it was observed that a greater number of animals that had been undergoing treatment for six months required up to three sessions (26/65.38%) compared to those that had been undergoing previous treatment for more than six months (8/47, 06%), showing a faster healing response (Table 02).

Analyzing the type of previous treatment, an association was observed between patients who previously received only itraconazole and the number of photobiomodulation sessions ( $p<0.0001$ ). In these patients, a smaller number of sessions were performed for clinical cure to occur, compared to those who received itraconazole with potassium iodide. It is worth mentioning that the faster response of patients who received only itraconazole can



be attributed to the association of potassium iodide, since all animals received the same drug protocol after the start of photobiomodulation, as well as photobiomodulation. Furthermore, it is expected that animals that received itraconazole with potassium iodide would have responded more slowly, given the more resistant nature of the disease and the time at which potassium iodide was introduced since the patients were already chronic. However, in these animals only photobiomodulation was added to the treatment and there was a satisfactory clinical response, which can be directly attributed to the association of photobiomodulation.

The size of the lesions ranged from 1 to 6 centimeters in diameter and were located only on the face (8/18.6%), face and body (17/39.5%), only on the body (10/23.3% ) or only in the nostrils (8/18.6%) (Figure 01), (Table 3). The average number of injuries was 3.6 (median of 3 injuries). Regarding the number of lesions and number of photobiomodulation sessions, there was no significant difference ( $p=0.1136$ ) (Table 02). However, approximately 70% of animals with up to three lesions required only three photobiomodulation sessions, while of those with more than three lesions, only 41% benefited from three photobiomodulation sessions. Furthermore, the lesions of all patients progressively decreased with each session performed.

The medications were prescribed by different veterinarians, as the animals lived in different regions of Greater Vitória in the state of Espírito Santo, but all procedures were the same: keeping the animals in absolute isolation until the disease was completely cured, daily cleaning of the environment with specific products based on quaternary ammonium to eliminate the fungus, medications such as Itraconazole (at a dose of 100 mg for cats) and Potassium Iodide (at a dose of 5 to 10 mg/kg) daily. As a way of standardizing the results, all animals, after starting the laser therapy sessions, tried to use itraconazole and potassium iodide until the disease was completely cured. The medicines used varied between reference medicine and compounded in a veterinary compounding pharmacy, according to the owner's financial condition, with the latter being compounded respecting the ideal correction factor for correct bioavailability in the body.

As all patients had already started the study using one of the antifungals, and there would be no way to suspend it to carry out a control group with laser therapy only, due to the resistance of the fungus<sup>9</sup>, it was then observed from this information that the earlier the association of drug therapy with photobiomodulation, the faster the patient can be cured<sup>9</sup>.

Photobiomodulation therapy has demonstrated positive effects in terms of faster healing and repair of injured tissue<sup>8</sup>. In the literature it was observed that the same therapy

used as an adjunct in the treatment of wounds in horses obtained satisfactory results in terms of the stimulating effect on tissue healing<sup>9</sup>. Furthermore, other authors have also reported that this therapy has positive effects on healing, preventing and reducing the formation of necrosis at the edges of wounds, helping to control local infection, collagen synthesis and deposition, revascularization and, thus, accelerating healing. healing. process. tissue repair (figures 02 to 05).<sup>8</sup>

The use of red light also has an antiseptic effect, contributing to the elimination of fungus on the skin.<sup>10</sup> (figure 06)

In human dermatology, photobiomodulation is widely used for various pathologies and aesthetic procedures, such as: atopic dermatitis, immunological dermatitis (bacterial, fungal, viral), psoriasis, skin rejuvenation, acne and oral mucositis, resulting in quick and effective results<sup>12</sup>.

In this research, photobiomodulation showed extremely positive results, where it accelerated the tissue healing process in patients with sporotrichosis who had been undergoing treatment for a long time without satisfactory response. This result is important because it is a low-cost procedure, does not present side effects as it is a therapy that uses low potency, does not promote microbial resistance, in addition to being non-invasive, standing out as an aid in the treatment of zoonotic diseases that affect animals. Furthermore, it is very common in deep wounds, when the healing process occurs, for the skin to present a scar, but the laser also reduces this characteristic, promoting follicular growth.<sup>11</sup>

#### **4 CONCLUSION**

It is concluded that complementary therapies, such as photobiomodulation, are valid and promising options in the treatment of feline sporotrichosis. Fast and non-invasive results make this technique advantageous in clinical routine. Furthermore, the results achieved, especially in patients who were already using antifungal combinations, refer to a shorter treatment time when photobiomodulation is associated with drug therapies. The data suggest that the sooner photobiomodulation treatment is started, the faster the response will be. However, clinical cure was achieved in all patients and maintained for at least six months, according to follow-up. Furthermore, future studies are needed to validate our results, especially with the addition of a group of patients who did not receive photobiomodulation.



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