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Photodynamic Therapy in Veterinary Medicine: Applications in dogs and cats

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Abstract. The present article represents a critical review focused on the application of Photodynamic Therapy (PDT) in Veterinary Medicine. Presenting an especial highlight to pet area, this manuscript brings together interesting articles on the application of PDT in pets, especially dogs and cats. Evaluating relevant publications that denote the state-of-art of this area, this present work demonstrates the wide potential of PDT application in several veterinary diseases. In fact, this work presents advantages and disadvantages of PDT and the partially positive results that several important research groups have published. We believe that this work can be useful to researchers and clinical veterinary medicine, mainly those that worked mainly with small animals of the PET area. We believe that this work can be useful for researchers and clinical veterinarians, especially those who work mainly with small animals in the pet area.

Keywords: Photodynamic action, clinical optimization, PET area

Terapia Fotodinâmica em Medicina Veterinária: Aplicações em cães e gatos

Resumo. O presente artigo representa uma revisão crítica focada sobre a aplicação de Terapia Fotodinâmica (TFD) em Medicina Veterinária. Com um especial destaque para a área de animais de estimação (área PET), esse artigo reúne interessantes artigos sobre aplicação de TFD em animais de estimação, sobretudo cães e gatos. Avaliando publicações relevantes que denotam o estado de arte dessa área, este presente trabalho demonstra o amplo potencial de aplicação do TFD em diversas doenças veterinárias. De fato, esse trabalho apresenta vantagens e desvantagens de TFD e também os resultados parcialmente positivos que diversos importantes grupos de pesquisa têm publicado. Acreditamos que esse trabalho pode ser útil para pesquisadores e médicos veterinários clínicos, principalmente aqueles que trabalham sobretudo com pequenos animais da área pet.

Palavras chaves: Ação fotodinâmica, optimização clínica, área PET, animais de estimação

Terapia Fotodinámica en Medicina Veterinaria: Aplicaciones en perros y gatos

Resumen. Este artículo representa una revisión crítica centrada en la aplicación de la Terapia Fotodinámica (TFD) en Medicina Veterinaria. Con un especial énfasis en el área de mascotas (área PET), este artículo reúne interesantes artículos sobre la aplicación de TFD en mascotas, especialmente perros y gatos. Evaluando publicaciones relevantes que denotan el estado del arte de esta área, este trabajo demuestra el amplio potencial para la aplicación de TFD en varias enfermedades veterinarias. De hecho, este trabajo presenta ventajas y desventajas de la TFD y también los resultados parcialmente positivos que varios grupos de investigación importantes han publicado. Creemos que este trabajo puede ser útil para investigadores y veterinarios

clínicos, especialmente aquellos que trabajan principalmente con animales pequeños en el área de mascotas.

Palabras clave: Acción fotodinámica, optimización clínica, mascotas

Introduction

Despite Photodynamic Therapy (PDT) is a well-stablished therapeutic methodology in human medicine, its application in veterinary medicine remains less common (Buchholz & Walt, 2013). However, the ease of use, anti-resistance capability, and excellent cosmetic outcomes should be arguments to a higher application of PDT in animal healthcare (Sellera et al., 2016).

In some diseases, the Photodynamic Therapy (PDT) can act as unique therapeutic option, propitiating excellent results, and, in many cases, reaching until the complete cure. On the other hand, there are several diseases in which PDT can be a very interesting coadjutant therapy, to act together with conventional therapeutic strategies, decreasing the invasiveness character of the treatment, the recovery time, and the well-being level of the patients during the clinical treatment. PDT in veterinary medicine has been used in some dermatological tumors in cats, mainly in head pigmented areas. Other indications have been made to neoplasia in urinary tract of dogs and sarcoid equines (Buchholz & Walt, 2013). Novel perspectives for PDT application in veterinary medicine have been proposed and tested in different types of cancer and microbial infectious diseases (Sellera et al., 2016).

The chemical compound 5-Aminolevulinic Acid (ALA) has been applied in Photodynamic Detection (PDD) and Photodynamic therapy (PDT). 5-Aminolevulinic Acid (ALA) is converted *in situ* in the well-stablished photosensitizer (PS) protoporphyrin IX (PpIX) through the physiological mechanisms of heme formation. Osaki and co-workers encountered 5-ALA-PDD sensitivity and specificity for dogs and cats combined were 89.5 and 50%, respectively, being that some small tumors disappeared (Juarranz et al., 2020; Osaki et al., 2019).

Frimberger et al. (1998) applied fifteen treatments on thirteen animals (Frinberger, 1998). These authors developed 9 treatments in 8 cats and 6 treatments in 5 dogs, generally using 400 J of 652 nm light, being that two feline sublingual squamous cell carcinomas (SCCs) responded briefly, i. e., with a minor response; six feline facial SCCs were treated, resulting in two partial responses and four long-term complete responses (Frimberger et al., 1998). Interestingly, novel strategies have been developed to favor the pharmacokinetics of the photosensitizer (PS) in PDT. In fact, Buchholz et al. (2007) related favorable pharmacokinetics of liposomal drug, which resulted in a favorable tumor response.

PDT in dogs

Prostatic carcinoma of the dog is a very aggressive cancer, with metastasis detectable in most dogs in the diagnosis process. Intraoperative radiation therapy for canine prostatic carcinoma results in average survival time of sixteen (16) weeks, being that the dog described in the article published by Lucroy et al. (2003) had stable disease for 34 weeks after treatment with Photodynamic Therapy (PDT), suggesting PDT could be developed into a useful modality for the treatment of prostate cancer in dogs (Lucroy et al., 2003).

Excellent results were also obtained with three dogs with lung cancer treated with PDT. Peripheral lung adenocarcinomas were treated with intravenous porfimer sodium (Photofrin® [Pinnacle Biologics, Inc., Chicago, IL]), i. e. with a porphyrin derivative as photosensitizer (PS), to photosensitize the tumors. Subsequently, it was performed the navigational bronchoscopy to make possible the photoradiation procedure. One week after PDT, the tumors and involved lung lobe were surgically excised and evaluated histologically, with significative results (Musani et al., 2018). It is auspicious this kind of approach, since the use of optical fiber can minimize the affected healthy tissues, which are localized around the tumor, that would be reached in the applications with optical fiber.

Cutaneous hemangiosarcoma is another malignant neoplasia usually observed in dogs, which was also treated by PDT. The effective treatment that is more usually developed is associated to a wide surgical excision of the tumor. In order to avoid mutilating surgeries, photodynamic therapy (PDT)

could serve as an alternative treatment and, indeed, it was efficient in the treatment elaborated by Rocha and co-workers (Rocha et al., 2019).

A very interesting study was performed by McCaw et al. (2000). These authors treated eleven (11) dogs with oral squamous cell carcinomas employing PDT, with Photochlor (HPPH) as photosensitizer (PS), being that eight (8) individuals were considered cured with no tumor recurrence for, at least, 17 months after PDT applications. It is important to notice that these results are similar to those obtained with surgical removal of tumors, being that this PDT procedure generated superior cosmetic characteristics.

There are cases in which the PDT presents a partial effectiveness to applications against cancer in dogs. Jacobs & Rosen (2000) reported an intrathoracic esophageal squamous cell carcinoma in a 11-year-old castrated male Labrador retriever. A partial response to PDT was supported by a reduction in tumor size, which was identified through various endoscopic examinations, and by a return to oral alimentation. However, this dog was euthanized due to recurrent regurgitation and aspiration pneumonia nine months after the photodynamic treatment.

In the presence of recurrent lesions related to chronic gingivostomatitis in dogs, invasive methods are usually necessary to treat lesions and pain. Applications of PDT proved to be effective as coadjutant treatment for chronic gingivostomatitis, restoring the integrity of affected mucosa and gingiva (Villela et al., 2017). PDT has been also applied in external otitis in dogs. Lee et al. (2014) treated four (4) dogs with various concentrations of 5-ALA, obtaining excellent results.

PDT in cats

Studies focused on application of PDT in cats have been developed in several diseases, such as cancer, infectious diseases and vascular disturbs. Indeed, efforts in the PDT application on the vascular diseases, such as thrombosis, have been developed since several decades (Chopp et al., 1987). In single PDT treatments focused on feline superficial squamous cell carcinoma, it was observed 85 per cent of complete response (Stell et al., 2001), which, denotes, one more time, the efficacy of PDT in a several superficial and/or accessible tissues/organs. Indeed, squamous cell carcinomas are common skin tumors in cats, which has been treated with PDT with significant results (Buchholz et al., 2007). On the other hand, in advanced cases, less decisive results have been observed. In any case, therapeutic strategies have been optimized to improve the control or the minimization of symptoms and signals of the disease (Hahn et al., 1998). We could highlight the relevant work of Bexfield et al. (2008), in which they managed 55 cats (superficial nasal planum squamous cell carcinomas). These authors applied PDT employing 5-ALA as photosensitizer (PS) and a red light as electromagnetic radiation. The procedure was safe, well tolerated, and effective in the treatment, offering an alternative to conventional therapy. However, despite the high initial response rates, this strategy of PDT treatment did not lead to a durable remission or cure in all cases.

Conclusions

In this work, it was analyzed the potential of the application of Photodynamic Therapy (PDT) in Veterinary Medicine, discussing several interesting data from the specialized literature. This critical review highlighted the consistent findings that were obtained from this type of treatment in several areas, such as cancer and microbiological diseases, between others. On the other hand, it is possible to infer that a great increase is still possible in terms of applications of PDT. Indeed, if PDT still can be much more applied in human medicine, in veterinary medicine this potential of growth is still higher, considering that the use of PDT in animal healthcare is much lower than its employment in human medicine. Furthermore, this article denotes the very auspicious character of Photodynamic Therapy (PDT) as unique therapeutic option but also reinforces its efficiency as coadjutant therapy of several conventional treatment strategies.

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