CLINIC AND SURGERY

Different approaches to the clinical care and treatment of epileptic seizures in dogs

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ABSTRACT: This survey analyzed data obtained through a questionnaire on the clinical approaches used by veterinarians to treat dogs with epileptic seizures. We found that neurological examinations were performed by 12% of the respondents, blood tests by 85%, and computed tomography by 72%. In addition, serology for infectious disease detection was mentioned by 30% of the respondents, and 72% did not classify epileptic seizures. According to the answers, the treatment of choice was phenobarbital in 100% of cases which was combined with potassium bromide in 19%. Moreover, 51% of the respondents mentioned that they monitored the serum phenobarbital levels. The study results showed disagreements on the conduct and care recommended by the International Veterinary Epilepsy Task Force consensus.
Key words: generalized epilepsy, seizures, canine idiopathic epilepsy, dogs.

Caracterização da conduta clínica no atendimento e tratamento de cães com crises epilépticas

RESUMO: O objetivo deste estudo foi analisar a conduta clínica de médicos veterinários no atendimento de cães apresentando crises epilépticas por meio de um questionário. 12% afirmaram realizar exame neurológico, enquanto 85% realizam exames hematológicos; 72% solicitam tomografia computadorizada e 30% pedem sorologias para investigação de doenças infecciosas. Todos os veterinários prescrevem fenobarbital para o tratamento. O brometo de potássio foi citado por 19% dos entrevistados em associação ao fenobarbital. A dosagem sérica de fenobarbital é realizada por 51% dos entrevistados. Os resultados apontaram que não houve homogeneidade na conduta preconizada pelas diretrizes científicas sobre o tema.
Palavras-chave: Epilepsia generalizada, convulsões, epilepsia idiopática canina, cães.

INTRODUCTION

Epileptic seizures are the most frequent neurological disorders in dogs, affecting approximately 0.6-0.75% of the entire canine population (HESKE et al., 2014). According to the International Veterinary Epilepsy Task Force (DE RISIO et al., 2015), an epileptic seizure is defined as excessive hypersynchronous, paroxysmal, and generally self-limiting neuronal activity that leads to motor, autonomic, and/or behavioral changes (BERENDT et al., 2015). Seizures can be classified as structural or idiopathic.

Idiopathic epileptic seizures can be classified according to their origin as genetic, suspected genetic, or unknown (BERENDT et al., 2015; HÜLSMEYERet al., 2015). Furthermore, epileptic seizures can be classified as focal, generalized, or focal with secondary generalization.

The most efficient drug to control seizures in dogs is phenobarbital (CHANDLER, 2006; CHARALAMBOUS et al., 2014). Any short- and long-term adverse effects of this treatment should be closely monitored, along with laboratory test results and serum concentration dosages (SANDERS, 2015).

The diagnosis, treatment, and evaluation of the therapeutic outcomes in dogs with epileptic seizures depend on the veterinarian's initial clinical approach and the dogs' seizure and disease history (BERENDT et al., 2015; BHATTI et al., 2015). Based on this information, this study verified the clinical approach and care provided by veterinarians when treating dogs with epileptic seizures in the Federal District, Brazil.

MATERIALS AND METHODS

To collect the data, general practice veterinarians were asked to fill out an anonymous

questionnaire (Figure 1) with 11 descriptive questions about the medical care they use to treat canines with epileptic seizures. The survey consisted of three multiple-choice questions to characterize the profile of respondents in terms of professional education and training, as well as eight open questions on four main points: (i) cause exclusion, (ii) epilepsy classification, (iii) recommended treatment, and (iv) monitoring/follow-up of the treatment recommended. Open-ended questions were chosen to neither induce nor limit responses and obtain more reliable data. The questionnaire was answered without researching the scientific materials.

The target population was general practice veterinarians from small animal/pet clinics and hospitals in the Federal District – Brazil who were not necessarily trained in neurology. However, the source population was restricted to professionals working in veterinary clinics and hospitals by randomly drawing from a veterinary clinic database. Thus, the sampling considered a list of consolidated veterinary clinics and hospitals based on a survey conducted between 2017 and 2018. Only one professional from each establishment participated in this survey.

Epitools® software (SERGEANT, 2009) was used to determine that a sample size of 43 veterinary clinics in 31 different administrative regions of the Federal District with a 95% confidence level and 15% absolute precision was required, according to the following equation:

$$n = \frac{z^2 \times p \times (1 - p)}{d^2}$$

Figure 1 - Picture of the questionnaire model with 11 descriptive questions used in the study.

Where "n" is the sample size, "z" is 1.96 (standard normal distribution value corresponding to the 95% confidence level), "p" is the frequency, and "d" is the desired precision.

Appropriate management was evaluated using the consensus of the IVETF (BHATTI et al., 2015; BERENDT, M. et al., 2015; DE RISIO et al., 2015) for diagnostic investigation, treatment, and follow-up.

Simple random sampling was used. Additionally, the samples were replaced when the selected researchers or veterinarians refused to participate in the study. The replacement criterion consisted of selecting another clinic with a working pattern similar to those initially drawn, located in the same geographic region as the discarded sample.

RESULTS

Veterinarians working in clinics in 18 administrative regions of the Federal District – Brazil were included. Seven of the clinics initially selected had to be replaced for two reasons: (i) three veterinarians did not feel comfortable participating in the study, and (ii) four clinics had permanently closed.

Of the 43 veterinarian respondents, 48.83% (n = 21) had graduated >ten years ago, 27.9% (n = 12) five to ten years ago, 18.6% (n = 8) one to five years ago, and 4.65% (n = 2) < one year ago. The majority, 53.49% (n = 23) had not under taken any specialization course, 9.3% (n = 4) had completed a residency, 9.3% (n = 4) had a master's degree, 25.58% (n = 11) had no further training and 3% (n = 1) did not answered.

To determine the possible cause of epileptic seizures, 13.95% (n = 6) performed a neurological examination. Moreover, 86.04% (n = 37) requested blood tests, such as the total blood count and biochemistry, as complementary examinations. Computed tomography (CT) was mentioned by 72.09% (n = 31) of the respondents, and tests to investigate infectious diseases were mentioned by 30.23% (n = 13). Only 11.63% (n = 5) of the respondents said that they requested a cerebrospinal fluid analysis. Other complementary imaging tests, such as radiography and ultrasound, were performed in 23.25% (n = 10) and 11.63% (n = 5) of the cases, respectively.

In routine clinical care, the nature of epileptic seizures was not classified in 72.09% (n = 31) of the cases, while 27.91% (n = 12) of the respondents classified the seizures. Of these, 41.67% (n = 5) were classified according to etiology, 25% (n = 3) according to the type of seizure manifestation (focal or diffuse), and 33.3% (n = 4) were classified

using other parameters such as the seizure severity and/or the number of seizures. Only two respondents used more than one classification: etiology and seizure type.

Furthermore, 51.17% (n = 22) of the veterinarians mentioned that treatment was started immediately after the seizure was first reported by the owner, 48.83% (n =21) considered the frequency and/or severity of seizures, and one veterinarian mentioned that in addition to the frequency of seizures, adherence to the treatment by the owner was also considered.

All respondents reported treating seizures with phenobarbitone as the initial therapeutic approach. Potassium bromide was mentioned by 18.6% (n = 8) of the respondents, while homeopathic treatment and natural food were mentioned by 4.65% (n = 2). Drugs, such as imepitoin, fluoxetine, and paroxetine, were mentioned only once and were always associated with phenobarbital. Despite being included in the questionnaire, only 41.86% (n = 18) of the veterinarians revealed the prescribed dosage, of which 14 reported that they started treatment with 2-3 mg/kg phenobarbital every 12 h. Two respondents started with 4 mg/kg, one with 1 mg/kg, and another with 5 mg/kg every 12 h in all cases.

Treatment was prescribed for life by 58.14% (n = 25) of the respondents, whereas 30.23% (n = 13) withdrew medication after the seizures stopped or were significantly reduced. The remainder, 11.63% (n = 5) of respondents, stopped administering drugs between six months and one year of age.

As a follow-up, the answers show that 51.16% (n = 22) of the veterinarians scheduled a follow-up visit within 15 days after starting the treatment, 20.93% (n = 9) scheduled a visit after one month, and 25.59% (n = 11) scheduled visits at varying frequencies. A total of 48.84% (n = 21) of the respondents requested laboratory tests/exams, such as the serum dosage of phenobarbital for monitoring treatment efficacy, while 41.87% (n = 18) also requested biochemical tests, such as markers of renal and hepatic function, and glycemia.

When the treatment did not adequately control the seizures, 41.87% (n = 18) of the respondents added other adjuvant anticonvulsants to the treatment, whereas 27.9% (n = 12) only increased the dosage, and 27.9% (n = 12) referred the animal to a neurological specialist.

DISCUSSION

A neurological examination should be performed to identify the lesion site as detected by

a set of neurological deficits (TAYLOR, 2014). Since idiopathic epileptic dogs can show normal interictal neurological examination results, other primary causes of the seizures need to be excluded with complementary examinations. The assessment must be thorough to determine the location of the lesion and provide a list of differential diagnoses to guide the veterinarian regarding the additional tests required (SANDERS, 2015). This study revealed that few veterinarians (11.63%%, n = 5) perform a routine neurological examination, suggesting a lack of knowledge on how to perform the examination or that they underestimate its importance in treating dogs with epileptic seizures. Another reason may be related to the fact that dogs do not exhibit neurological alterations during the interictal period (DE RISIO et al., 2015).

The total blood count, biochemical profile, liver function exams (bile acids or ammonia), and the assessment of the thyroid profile are important to determine the health status of the animals and help diagnose some diseases, besides being considered as the baseline parameters after drug treatment, as most antiepileptic drugs alter these parameters (POTSCHKA et al., 2015). In this study, most of the interviewees requested hematological tests, such as a complete blood count and biochemical profile, as recommended for evaluating animal health conditions. Additionally, the IVETF recommends measuring electrolytes, such as sodium, potassium, chloride, calcium, and phosphate, in addition to measuring glucose, cholesterol, triglycerides, and urinalysis (DE RISIO et al., 2015). Such parameters were not mentioned by the respondents; however, it is important to emphasize that the choice of tests can vary significantly according to each case, and it is possible that the interviewees only considered the most used tests in their routine to fill out the form.

Abdominal and thoracic radiographic examinations, as well as abdominal ultrasonography, are not considered essential for dogs with epileptic seizures. Thoracic radiographs may be useful in patients with suspected pulmonary metastases (SANDERS, 2015; DE RISIO et al., 2015). In the present study, 23.25% (n = 10) of the veterinarians indicated plain radiographic examinations as a complementary evaluation, but the region and the projections were not detailed, which may reflect flaws in the planning of the diagnosis steps. Similarly, the abdominal ultrasound exam was cited as a complementary exam by 11.63% (n = 5) of the respondents; although, these examinations are useful in a few cases, such as portosystemic shunts in young

dogs or abdominal metastases (SANDERS, 2015; De RISIO et al., 2015).

Advanced imaging examinations, such as CT, were requested by most respondents. CT is recommended in cases of suspected cranioencephalic trauma, fractures, or anomalies of the cranial bone, and the images allow the identification of extensive lesions by regional contrast enhancement (TAYLOR, 2014). However, magnetic resonance imaging (MRI) is the most commonly used imaging modality for brain tissue assessment, as it provides greater resolution of soft tissue and contrast between tissues (TAYLOR, 2014), thus identifying small lesions with higher precision (RUSBRIDGE et al., 2015). The frequent indication for CT by veterinarians is probably because it was the only advanced imaging method available in the Federal District - Brazil at the time of this study. Furthermore, most professionals recognize the importance of advanced imaging tests to detect or exclude some types of structural lesions and malformations.

Analysis of cerebrospinal fluid presents high sensitivity and low specificity in the alterations found in laboratory analysis and can be an important tool for diagnosing neurological disorders in cases where infections, inflammation, trauma, neoplasms, or degenerative alterations are suspected (DI TERLIZZI &PLATT., 2009). In addition, the examination allows the differentiation of etiological agents that appear similar on MRI (SANDERS, 2015). In the present study, only five veterinarians considered cerebrospinal fluid collection, supposedly due to a lack of technical training for sample collection, invasiveness of the procedure, anesthetic costs, and associated risks.

Classifying epileptic seizures makes communication easier among veterinarians and allows for a better choice of therapy (BERENDT et al., 2015, SANDERS, 2015). The poor adherence to seizure classification in this study may indicate either a lack of scientific updates or an underestimation of its effectiveness. A questionnaire study with veterinary neurology specialists and non-specialists to detect and characterize 100 different seizures in videos showed low agreement in the presence, classification, and motor and/or autonomic signs attributed to minor experience and interest in epilepsy (PACKER et al., 2015).

Immediate initiation of treatment with anticonvulsant drugs is indicated for dogs with cluster seizures or status epilepticus when two or more seizures occur in less than six months or when there are prolonged and severe post-ictus signs (BHATTI et al., 2015). More than half of the interviewed veterinarians

started treatment immediately after the seizure history reported by the tutor, considering the severity and/or frequency of the seizures, thus respecting the criteria determined for starting therapy (BHATTI et al., 2015). Only one participant mentioned considering the owner's commitment before starting treatment, an important fact to avoid treatment failures due to the owner not adhering to the treatment.

All respondents chose phenobarbital as the initial treatment, as it is a low cost, safe drug with good results and is considered the medication of choice in most cases (KLUGER et al., 2009; BHATTI et al., 2015). The recommended initial dose of phenobarbital is 2.5-3 mg/kg orally every 12 h (BHATTI et al., 2015). In this study, 18 veterinarians mentioned that they prescribed phenobarbital at a dosage between 2 and 3 mg/kg. One respondent prescribed phenobarbital at a dosage below the recommended therapeutic efficacy. However, it should be considered that the interviewed veterinarians were general practitioners and did not necessarily remember all dosages of drugs for specific use in neurology. Phenobarbital and imepitoin are considered first-line drugs for the continuous treatment of epileptic seizures (CHARALAMBOUS et al., 2014; BHATTI et al., 2015, MELAND et al., 2019). Imepitoin and phenobarbital have similar effects, but despite being mentioned as one of the treatment options by a professional in the present study, the imepitoin is not yet available for sale.

Potassium bromide was prescribed by eight veterinarians and was always associated with phenobarbital. When administered alone and as the first therapeutic option, potassium bromide is less effective and less tolerated than phenobarbital (BOOTHE et al., 2012) but can be an option for patients with liver disease and puppies,;although, not mentioned for this purpose in this study by the respondents in this study.

Studies conducted in the United States (MELAND et al., 2019) revealed that phenobarbital is indicated in approximately 66% of cases, but 26% of professionals prefer levetiracetam as the main initial therapy. In our study, no veterinarian mentioned prescribing levetiracetam to treat epileptic seizures in their patients.

As an adjuvant therapy to phenobarbital, homeopathic medicines were indicated by two of the professionals interviewed, but there is a lack of studies that confirmed the success of such substances (PODELL et al., 2015).

Despite few studies, a ketogenic diet with medium-chain fatty acids associated with medical treatment has been recommended for dogs with epileptic seizures (LAW et al., 2015). Furthermore, the veterinarians who prescribed homeopathic treatment reported recommending dietary changes to assist in the treatment of epileptic seizures, but they did not detail whether it was a ketogenic diet, homemade, or formulated by a veterinary nutritionist.

As for the treatment duration, without describing which types of diseases would cause epileptic seizures, most respondents recommended maintaining medication for life. Despite recommendations for continuous use, studies infer that in cases of complete remission of seizures (generalized and focal) for approximately one to two years, one can choose to attempt to gradually discontinue the medication (BHATTI et al., 2015).

Fourteen days after starting the treatment or after changing the dose, the serum phenobarbital dosage should be monitored regularly to assess the treatment efficacy, assist in adjusting the dosage, and avoid toxicity, as the pharmacokinetics of the drug vary due to individual metabolic and physiological characteristics (MAGUIRE et al., 2000). The serum phenobarbital dosage as a form of control was requested by 23 veterinarians, while 21 veterinarians did not mention this analysis. Similarly, a study conducted in Australia with 179 respondents reported that despite recognizing the importance of this follow-up, the serum phenobarbital dosage was neglected by 71% of veterinarians, and 26% revealed that the test was performed only when the treatment was considered ineffective (KLUGER et al., 2009). Furthermore, we observed that veterinarians used serum phenobarbital as the main method for evaluating medication effectiveness. Monitoring the serum dosage of drugs used for treatment is also important to avoid the adverse effects of antiepileptic drugs, such as the hepatotoxicity caused by phenobarbital (POTSCHKA et al., 2015; CHARALAMBOUS et al., 2016).

When the initial treatment was not considered effective, 18 veterinarians added a new medication, 13 increased the dose of the same drug, and 12 referred the dog to a specialist. In cases of treatment failure or after maximizing the drug dose to treat an epileptic seizure, an associated new adjuvant drug, such as potassium bromide, is recommended (BHATTI et al., 2015). Referring to a neurology specialist, cited by 27.9% (n = 12) of the respondents, can be a good solution for refractory cases.

Despite correct treatment and identifying the epileptic cause, seizures are not completely eliminated in most patients. The therapeutic approach can be considered satisfactory when the number of seizures, their frequency, severity, and duration

are efficiently reduced, and clustered seizures are successfully prevented (POTSCHAKA et al., 2015).

Systemic data analysis allowed us to conclude that only seven respondents adequately answered all four points in terms of the diagnosis, classification, treatment, and treatment monitoring of dogs with epileptic seizures based on the IVETF. Furthermore, all seven professionals had some type of additional training: two had a residency in veterinary medicine, one had a master's degree and residency, and the other three reported unspecified complementary training. Notably, three of the four participants that had completed a residency responded to the survey in line with the guidelines used as the basis for the study.

As for the time since graduation, it was not possible to associate experience with appropriate conduct in the clinical approach. The financial conditions of the clinics were not evaluated, but no differences were observed between the quality of answers and the apparent financial condition of the clinic according to district area.

Different priorities between the owners of dogs with idiopathic epilepsy, general veterinarians, and veterinary neurologists showed that improvement in the education of generalist vets about epilepsy was the most important failure reported by owners (JONES et al., 2021). Despite veterinary qualifications in veterinary neurology being available in the United States (American College of Veterinary Internal Medicine) and Europe (European College of Veterinary Neurologists), there is no such specialization available in Brazil, limiting the information general veterinarians can access. Although, the volume of medical information has grown, it has significantly outstripped the individual practitioner's capacity for knowledge retention, particularly in general practice veterinarians.

To the best of our knowledge, this is the first study in Brazil to assess the knowledge, attitudes, and practices regarding the clinical care and treatment of epileptic seizures in dogs. Despite our findings, this study had limitations related to the number of participating and local samples, the lack of interest in neurologic diseases by generalist veterinarians, and no specialist veterinary neurology group to compare the results with. Further studies with larger sample sizes may be needed to improve the representativeness of these results in other states.

CONCLUSION

The clinical approach of general practice veterinarians in the Federal District of Brazil to diagnose and treat dogs with epileptic seizures is not homogeneous and consistent. Common practices are important in choosing the best management for canine idiopathic epilepsy, and additional training of non-specialists could be important to improve the treatment of epilepsy in dogs.

DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

AUTHORS' CONTRIBUTIONS

ACM designed and coordinated the experiment, and GSR performed the study.

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Erratum

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In the author', where we read:

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