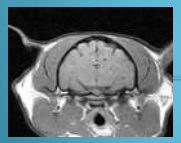
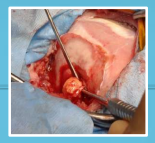
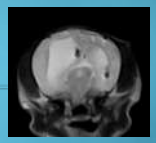
TRATAMIENTO DE EPILEPSIA EN PERROS/ GATOS

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ESPECIALISTAS VETERINARIOS

Crisis epileptiformes (Clasificacion)

Podell 2013, Berg et al 2010

Autolimitante (aislada)
1 crisis 24 h

- **FOCAL (parcial)**
  - Sensorial
  - Motora
    - *Simple (elemental)*
    - *Compleja (automatismos)*
- **GENERALIZADA**

Clusters (>1 en 24h)

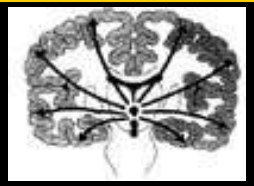
Status epilepticus (continua)
> 5 minutos o no recuperacion a un estado normal interictal entre las crisis.

- **FOCAL (parcial)**
- **GENERALIZADA**

Crisis epileptiformes (Clasificacion)

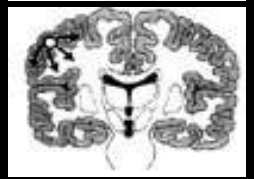
Crisis generalizadas

Origen en ambos hemisferios Cerebrales desde el comienzo.



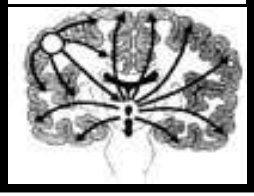
Crisis focales (parciales)

Origen en un area del hemisferio cerebral



Crisis focales (generalizacion 2ria)

Origen en un area del hemisferio cerebral, luego generalizacion.



CRISIS EPILEPTIFORMES AUDIOGENICAS REFLEJAS

Audiogenic reflex seizures in cats

Journal of Feline Medicine and Surgery
2016, Vol. 18(4) 328-336

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DOI: 10.1177/1098612X15582080
jfms.com
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Mark Lowrie[1], Claire Bessant[2], Robert J Harvey[3], Andrew Sparkes[2] and Laurent Garosi[1]

Abstract

Objectives This study aimed to characterise feline audiogenic reflex seizures (FARS).

Methods An online questionnaire was developed to capture information from owners with cats suffering from FARS. This was collated with the medical records from the primary veterinarian. Ninety-six cats were included.

Results Myoclonic seizures were one of the cardinal signs of this syndrome (90/96), frequently occurring prior to generalised tonic–clonic seizures (GTCSs) in this population. Other features include a late onset (median 15 years) and absence seizures (6/96), with most seizures triggered by high-frequency sounds amid occasional spontaneous seizures (up to 20%). Half the population (48/96) had hearing impairment or were deaf. One-third of cats (35/96) had concurrent diseases, most likely reflecting the age distribution. Birmans were strongly represented (30/96). Levetiracetam gave good seizure control. The course of the epilepsy was non-progressive in the majority (68/96), with an improvement over time in some (23/96). Only 33/96 and 11/90 owners, respectively, felt the GTCSs and myoclonic seizures affected their cat's quality of life (QoL). Despite this, many owners (50/96) reported a slow decline in their cat's health, becoming less responsive (43/50), not jumping (41/50), becoming uncoordinated or weak in the pelvic limbs (24/50) and exhibiting dramatic weight loss (39/50). These signs were exclusively reported in cats experiencing seizures for >2 years, with 42/50 owners stating these signs affected their cat's QoL.

Conclusions and relevance In gathering data on audiogenic seizures in cats, we have identified a new epilepsy syndrome named FARS with a geriatric onset. Further studies are warranted to investigate potential genetic predispositions to this condition.

CRISIS EPILEPTIFORMES REFLEJAS COMIDA

Epileptic seizures triggered by eating in dogs

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Abstract

Background: Seizures triggered by eating (STE) behavior are very rare in humans and have not been documented previously in dogs.

Objectives: To document the occurrence of STE in dogs and describe their clinical features.

Animals: Ten client-owned dogs with STE diagnosed at 5 European referral centers.

Methods: A call for suspected cases of STE was made online. This call was followed by a retrospective review of medical records, combined with a questionnaire to be completed by both the owner and the board-certified neurologist who made the diagnosis. Cases were included if >50% of the seizures that occurred were related to eating and if a minimum diagnostic evaluation for seizures had been performed.

Results: Four cases only had STE and 6 cases had both STE and spontaneous seizures. Four of the dogs were retrievers. The most common seizure type was focal epileptic seizures evolving to become generalized. Nine dogs were diagnosed with idiopathic epilepsy. One dog had a presumptive diagnosis of glioma involving the margins of the parietal, temporal, and frontal cortex (the perisylvian region), an area known to have a key role in eating-associated epilepsy in people. Treatment strategies included a combination of pharmacological management and eating habit changes.

Conclusions and Clinical Importance: We have identified a form of reflex epilepsy in dogs, with STE behavior. Further studies are warranted to improve the characterization and management of STE.

- 6 CASOS CRISIS REFLEJAS Y 4 CASOS CON REFLEJAS Y ESPONTANEAS
- 9 CASOS EPILEPSIA IDIOPATICA Y 1 CASO GLIOMA
- FACTOR QUE DA LA CRISIS ES EL ACTO DE COMER

Complex partial cluster seizures in cats with orofacial involvement☆

Akos Pakozdy DVM, DECVN[1]*, **Andrea Gruber** DVM[2], **Sibylle Kneissl** DVM[3], **Michael Leschnik** DVM[1], **Peter Halasz** DM[4], **Johann G Thalhammer** DVM[1]

[1]*Clinic for Internal Medicine and Infectious Diseases, Vienna, Austria*
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[3]*Clinic for Diagnostic Imaging, University of Veterinary Medicine, Vienna, Austria*
[4]*Institute of Experimental Medicine, Budapest, Hungary*

Seventeen cats were presented with acute onset of complex partial seizures with orofacial involvement (salivation, facial twitching, lip smacking, chewing, licking or swallowing), motor arrest (motionless starring) and behavioural changes. In 11 cats hippocampal necrosis (HN) was confirmed by histopathology. In a further six cats hippocampal changes were suggested by magnetic resonance imaging. The mean monitoring time of eight cats which were not euthanased in the acute phase of the disease, was 408 days (60–908): four cats are still alive. In all surviving cases, the owners reported a good quality of life. We conclude that an acute cluster of complex partial seizures with orofacial involvement are often associated with HN and that HN is not necessarily a fatal condition. Supportive and antiepileptic therapy can result in remission. The long-term outcome can be good to excellent; therefore, euthanasia should be avoided in the acute phase of the signs.

Date accepted: 13 May 2011

17 gatos con crisis orofaciales (salivación, chasquido labios, deglución, masticatorios, twitching facial)

11 gatos con necrosis de hipocampo (histopatologia)

Asociación de crisis orofaciales con necrosis hipocampo

TRATAMIENTO DE EPILEPSIA

International Veterinary Epilepsy Task Force consensus proposal: medical treatment of canine epilepsy in Europe

Sofie F.M. Bhatti[1*], Luisa De Risio[2], Karen Muñana[3], Jacques Penderis[4], Veronika M. Stein[5], Andrea Tipold[6], Mette Berendt[6], Robyn G. Farquhar[7], Andrea Fischer[8], Sam Long[9], Wolfgang Löscher[10], Paul J.J. Mandigers[11], Kaspar Matiasek[12], Akos Pakozdy[13], Edward E. Patterson[14], Simon Platt[15], Michael Podell[16], Heidrun Potschka[17], Clare Rusbridge[18,19] and Holger A. Volk[20]

DEFINIR LA CRISIS SI ES EPILEPTICA O NO

TRATAMIENTO DE EPILEPSIA

International Veterinary Epilepsy Task Force consensus proposal: medical treatment of canine epilepsy in Europe

Sofie F.M. Bhatti[1*], Luisa De Risio[2], Karen Muñana[3], Jacques Penderis[4], Veronika M. Stein[5], Andrea Tipold[6], Mette Berendt[6], Robyn G. Farquhar[7], Andrea Fischer[8], Sam Long[9], Wolfgang Löscher[10], Paul J.J. Mandigers[11], Kaspar Matiasek[12], Akos Pakozdy[13], Edward E. Patterson[14], Simon Platt[15], Michael Podell[16], Heidrun Potschka[17], Clare Rusbridge[18,19] and Holger A. Volk[20]

Tratamiento

- Causa identificada (estructural/metabolica):
  - TRATAR LA CAUSA

Drogas antiepilepticas:

Epilepsia genetica/origen desconocido.

Estructural/metabolica (adyuvante)

Contraindicacion enfermedades metabolicas (hepatica, renal)

Imepitoina, fenobarbital, bromuro, levetiracetam, otros

Cuadro 2. Causas metabólicas y estructurales que pueden ocasionar crisis epilépticas o convulsiones reactivas (Podell 2013).

Vascular:
- Isquémico (tromboembolismo, idiopático).
- Hemorrágico (hipertensión, coagulopatía).

Inflamatorio:
- Meningoencefalitis de origen desconocido.

Infeccioso:
- Virus (moquillo, rabia).
- Bacterias (absceso, cualquier bacteria).
- Micóticas (criptococosis).
- Protozoarias (toxoplasmosis, neosporosis).
- Rickettsiosis (ehrlichiosis).

Tóxicos:
- Plomo, organofosforados, etilenglicol.

Traumático.

Anomalía congénita:
- Hidrocefalia, displasia cortical, lisencefalia.

Metabólico:
- Fallo orgánico (hepático, renal).
- Desequilibrio electrolítico (hiponatremia, hipernatremia, hipocalcemia).
- Déficits energéticos (hipoglucemia, déficit de tiamina).

Neoplásico:
- Extraaxial: meningioma, tumores óseos.
- Intraaxial: tumores de la glía, metástasis.
- Intraventricular: ependimoma, tumor de plexo coroideo.

Degenerativo:
- Enfermedades de almacenamiento lisosomal (lípidos, glicoproteínas).

Tratamiento

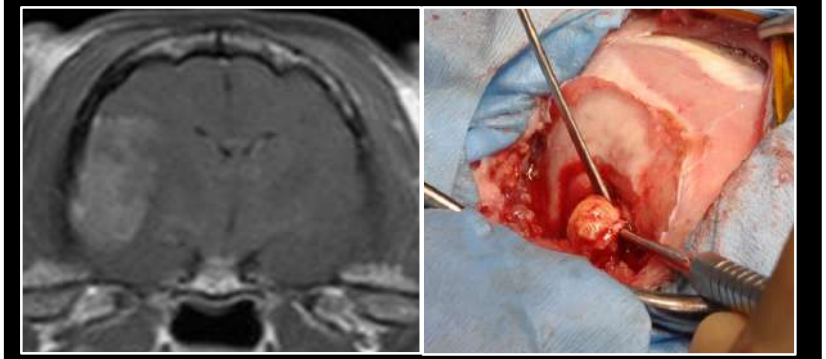
- Causa identificada (estructural/metabolica):
  - TRATAR LA CAUSA

Drogas antiepilepticas:

Epilepsia genetica/origen desconocido.
Estructural/metabolica (adyuvante)
Contraindicacion enfermedades metabolicas (hepatica, renal)
Imepitoina, fenobarbital, bromuro, levetiracetam, otros

Tratamiento

- Causa identificada (estructural/metabolica):
  - TRATAR LA CAUSA



Tratamiento

EPILEPSIA GENETICA/IDIOPATICA

2015 ACVIM Small Animal Consensus Statement on Seizure Management in Dogs

M. Podell, H.A. Volk, M. Berendt, W. Löscher, K. Muñana, E.E. Patterson, and S.R. Platt

- **OBJETIVO DE LA TERAPIA:**
  - Reducir frequencia y severidad evitando efectos secundarios (calidad de vida).
  - Reducir frecuencia > 50% o libre de crisis
  - Educar propietario. No cura de la enfermedad
  - Tratamiento diario de por vida en mayoria de casos.

COMENZAR TRATAMIENTO PERROS

2015 ACVIM Small Animal Consensus Statement on Seizure Management in Dogs

M. Podell, H.A. Volk, M. Berendt, W. Löscher, K. Muñana, E.E. Patterson, and S.R. Platt

International Veterinary Epilepsy Task Force consensus proposal: medical treatment of canine epilepsy in Europe

- **CUANDO EMPEZAR TRATAMIENTO:**
  - Frecuencia (2 o mas crisis en periodo de 6 meses)
  - Presencia de lesion intracraneal o lesion traumatica precedente
  - Cluster , status epilepticus
  - Signos post-ictales severos o duracion mayor de 24 horas
  - Propietarios
  - En general: Cuanto antes, mejor pronostico a largo plazo
  - Frecuencia, duracion, severidad aumentando sobre 3 periodos interictales

Tratamiento

- Seleccion de drogas antiepilepticas (DAE) basado en:
  - ‘Estandard’ vs ‘nueva’ droga
  - Espectro de eficacia
  - Tolerabilidad/enfermedad subyacente (ej, disfuncion hepatic..)
  - Severidad y raza
  - Farmacocinetica
  - Mecanismo de accion

FACTORES EXTERNOS

Seizure-precipitating factors in dogs with idiopathic epilepsy

Johanna A. Forsgård[1] | Liisa Metsähonkala[2] | Anna-Mariam Kiviranta[1] | Sigitas Cizinauskas[3] | Jouni J.T. Junnila[4] | Outi Laitinen-Vapaavuori[1] | Tarja S. Jokinen[1]

animal hospitals.

Results: The prevalence of seizure-precipitating factors in the study population was 74% (37/50). The most frequently reported factors included stress-related situations, sleep deprivation, weather, and hormonal factors. In dogs with focal onset seizures, the number of precipitating factors was 1.9 (95% CI 1.1-3.4) times higher compared to dogs with generalized seizures.

Conclusions and Clinical Importance: Seizure-precipitating factors are common in dogs with idiopathic epilepsy, and the nature of these factors is consistent with those of human patients. Aside from antiepileptic medication, acknowledging and avoiding seizure-precipitating factors could help veterinarians achieve better treatment outcomes.

FACTORES QUE PUEDEN INFLUIR (STRESS, PRIVACION SUEÑO, TIEMPO Y HORMONAL)

EVITAR ESOS FACTORES PUEDEN MEJORAR TRATAMIENTOS

Que antiepileptico usar

Resumen de los fármacos antiepilépticos en el perro

Fármaco	Vida media de eliminación	Nivel estable	Metabolismo	Dosis inicial	Rango terapéutico	Monitorización	Efectos adversos
Fenobarbital	40-90 horas	15 días aproximadamente	Hepático	2,5-3 mg/kg/12 h	15-35 µg/ml	15, 45, 90 y 180 días	PU/PD, PF, ataxia, sedación, hepatotoxicidad, citopenias, pancreatitis.
Bromuro potásico	15-46 días	3 meses aproximadamente	Renal	20-40 mg/kg/24 h	1.000-2.000 mg/l como complementario o 2.000-3.000 mg/l como monoterapia	1, 3 y 6 meses	PU/PD, PF, ataxia, sedación, pancreatitis.
Imepitoína	1,5-2 horas	2 horas	Excreción por vía fecal	10-20 mg/kg/12 h	No determinado	No determinado	PU/PD, PF, ataxia, vómitos, diarrea.
Levetiracetam	3-6 horas	1-2 días	Renal	20-30 mg/kg/8 h	5-45 µ/ml	No determinado	Leve sedación, ataxia.
Zonisamida	15 horas aprox.	3-4 días	Hepático	3-7 mg/kg/12 h	10-40 mg/l	1 semana	Sedación, ataxia, vómitos, hepatotoxicidad.
Felbamato	5-7 horas	1-2 días	Hepático	20 mg/kg/8 h	25-100 mg/l	No determinado	Hiporexia, citopenias, queratoconjuntivitis seca.
Topiramato	2-4 horas	4-8 días	Renal	2-10 mg/kg/8-12 h	2-25 mg/l	No determinado	Ataxia, irritabilidad, sedación.
Gabapentina	3-4 horas	1 día	30 % hepático	10-20 mg/kg/8 h	4-16 mg/l	No determinado	Sedación, ataxia.
Pregabelina	7 horas	1-2 días	Renal	3-4 mg/kg/8-12 h	2,8-8,2 µg/ml	No determinado	Sedación, ataxia.

PU/PD: poliuria/polidipsia; PF: polifagia.

- Tabla de AE en perros

Tratamiento

Table 5. Oral antiepileptic treatment for cats.

Medicine	Dosage	Possible Adverse Effects	Notes	References
Phenobarbital	1–5 mg/kg q12h	Sedation, ataxia, PU/PD/PP, leukopenia, thrombocytopenia, lymphadenopathia, skin eruptions, coagulopathia	Serum level monitoring (100–300 µmol/L, 23–30 µg/mL)	10,24,25,47,60,61,62
Diazepam	0.2–2 mg/kg q8–24h	Sedation, PU/PD/PP, hepatic failure	Liver function monitoring is advisable	9,10,13,25,47,63,64
Potassium bromide	30–40 mg/kg q24h	PU/PD, vomiting, eosinophilic bronchopneumonia	Serum level monitoring	10,25,47,65
Clorazepate	3.75–7.5 mg/kg q6–12h	As diazepam		47
Levetiracetam	10–20 mg/kg q8h	Inappetence, sedation, hypersalivation		66
Gabapentin	5–20 mg/kg q6–12h	Sedation, ataxia	No clinical studies available	67
Zonisamide	5–10 mg/kg q12–24h	Sedation, inappetence, vomiting, diarrhea		68,a
Pregabalin	1–2 mg/kg q12h	Sedation	No clinical studies available	4
Propentophyllin	5 mg/kg q12h		No clinical studies available	10
Taurine	100–400 mg/cat q24h		Inhibitory aminoacid	69
Topiramate	12.5–25 mg q8–12h	Sedation, inappetence	No clinical studies available	70

PU, polyuria; PD, polydipsia; PP, polyphagia.

- Tabla de AE en perros

TIPO DE CRISIS

Retrospective multicenter evaluation of the "fly-catching syndrome" in 24 dogs: EEG, BAER, MRI, CSF findings and response to antiepileptic and antidepressant treatment

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Seizures
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Obsessive–compulsive disorder

ABSTRACT

The fly-catching syndrome (FCS) is a rare canine condition of sudden, occasional, or constant episodes of biting the air. It may be accompanied by jumping, licking, and swallowing. The etiology of FCS is unknown and controversial. Various explanations for its occurrence have included epileptoid disorders such as visual cortex epileptiform disturbances and simple and complex partial seizures as well as compulsive disorders, hallucinatory behavior, and stereotypy. A retrospective multicenter analysis of 24 dogs with clinical symptoms of FCS is presented. Clinical signs at the time of presentation, the mean age at onset of the disease, the response to treatment, and the clinical outcome were recorded and analyzed in all patients. All dogs underwent clinical, neurological, and otoscopic examinations. Complete blood cell counts (CBCs) and serum chemistry panels were obtained from each dog. Diagnostic testing included MRI and EEG examinations in 21 cases, BAER in 19 cases, and CSF analysis in 20 cases. The EEG revealed spike activity in 8 (38%) of the 21 cases, 7 of which had activity in the occipital lobes. The brainstem auditory evoked response (BAER) revealed three cases of bilateral deafness. The MRI revealed six cases of Chiari malformation (CM), one case of syringohydromyelia (SM), and one case of a falx cerebri meningioma. The dogs were divided into groups according to their treatment protocol. Group A included dogs treated with phenobarbital (PB), and group B consisted of dogs treated with fluoxetine (FLX). Thirty-six percent of the dogs in group A responded to PB, while 100% of the dogs in group B responded to FLX. The results suggest that FCS is more responsive to FLX than PB. However, the etiology of this behavior remains unclear in most cases.

FLUOXETINA MEJOR QUE AE

Levetiracetam in the management of feline audiogenic reflex seizures: a randomised, controlled, open-label study

Journal of Feline Medicine and Surgery 1–7

DOI: 10.1177/1098612X15622806
jfms.com
SAGE

Mark Lowrie[1], Sarah Thomson[1], Claire Bessant[2], Andrew Sparkes[2], Robert J Harvey[3] and Laurent Garosi[1]

Abstract

Objectives Currently, there are no published randomised, controlled veterinary trials evaluating the efficacy of antiepileptic medication in the treatment of myoclonic seizures. Myoclonic seizures are a hallmark of feline audiogenic seizures (FARS).

Methods This prospective, randomised, open-label trial compared the efficacy and tolerability of levetiracetam (20–25 mg/kg q8h) with phenobarbital (3–5 mg/kg q12h) in cats with suspected FARS that experienced myoclonic seizures. Cats were included that had ⩾12 myoclonic seizure days during a prospective 12 week baseline period. This was followed by a 4 week titration phase (until a therapeutic serum concentration of phenobarbital was achieved) and a 12 week treatment phase.

Results Fifty-seven cats completed the study: 28 in the levetiracetam group and 29 in the phenobarbital group. A reduction of ⩾50% in the number of myoclonic seizure days was seen in 100% of patients in the levetiracetam group and in 3% of patients in the phenobarbital group ($P < 0.001$) during the treatment period. Levetiracetam-treated cats had higher freedom from myoclonic seizures (50.0% vs 0%; $P < 0.001$) during the treatment period. The most common adverse events were lethargy, inappetence and ataxia, with no difference in incidence between levetiracetam and phenobarbital. Adverse events were mild and transient with levetiracetam but persistent with phenobarbital.

Conclusions and relevance These results suggest that levetiracetam is an effective and well-tolerated treatment for cats with myoclonic seizures and is more effective than phenobarbital. Whether it will prevent the occurrence of generalised tonic–clonic seizures and other forebrain signs if used early in the course of FARS is not yet clear.

Accepted: 24 November 2015

RAZAS FARMACORESISTENTES

-BORDER COLLIE

-PASTOR ALEMAN

-STAFFORD BULL TERRIER

-RAZAS CRUZADAS

-LABRADOR RETRIEVER

Que antiepileptico usar en primera instancia?

Treatment in canine epilepsy – a systematic review

Marios Charalambous[1*], David Brodbelt[2] and Holger A Volk[1]

Abstract

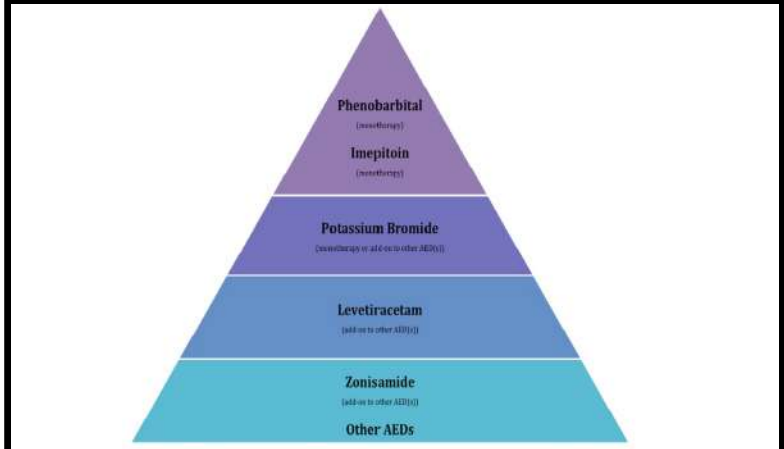
Background: Various antiepileptic drugs (AEDs) are used for the management of canine idiopathic epilepsy (IE). Information on their clinical efficacy remains limited. A systematic review was designed to evaluate existing evidence for the effectiveness of AEDs for presumptive canine IE. Electronic searches of PubMed and CAB Direct were carried out without date or language restrictions. Conference proceedings were also searched. Peer-reviewed full-length studies describing objectively the efficacy of AEDs in dogs with IE were included. Studies were allocated in two groups, i.e. blinded randomized clinical trials (bRCTs), non-blinded randomized clinical trials (nbRCTs) and non-randomized clinical trials (NRCTs) (group A) and uncontrolled clinical trials (UCTs) and case series (group B). Individual studies were evaluated based on the quality of evidence (study design, study group sizes, subject enrolment quality and overall risk of bias) and the outcome measures reported (in particular the proportion of dogs with ≥50% reduction in seizure frequency).

Results: Twenty-six studies, including two conference proceedings, reporting clinical outcomes of AEDs used for management of IE were identified. Heterogeneity of study designs and outcome measures made meta-analysis inappropriate. Only four bRCTs were identified in group A and were considered to offer higher quality of evidence among the studies. A good level of evidence supported the efficacy of oral phenobarbital and imepitoin and fair level of evidence supported the efficacy of oral potassium bromide and levetiracetam. For the remaining AEDs, favorable results were reported in studying their efficacy, but there was insufficient evidence to support their use due to lack of bRCTs.

Conclusions: Oral phenobarbital and imepitoin in particular, as well as potassium bromide and levetiracetam are likely to be effective for the treatment of IE. However, variations in baseline characteristics of the dogs involved, significant differences between study designs and several potential sources of bias preclude definitive recommendations. There is a need for greater numbers of adequately sized bRCTs evaluating the efficacy of AEDs for IE.

Keywords: Systematic review, Epilepsy, Antiepileptic drugs, Treatment, Canine

QUE AE USAR PRIMERO (CANINO)



1 Pyramid of hierarchy describing the recommendation of AEDs based on the assessment of their efficacy and quality of evidence

Systematic review of antiepileptic drugs' safety and effectiveness in feline epilepsy

Marios Charalambous[1*], Akos Pakozdy[2], Sofie F. M. Bhatti[1] and Holger A. Volk[3]

Abstract

Background: Understanding the efficacy and safety profile of antiepileptic drugs (AEDs) in feline epilepsy is a crucial consideration for managing this important brain disease. However, there is a lack of information about the treatment of feline epilepsy and therefore a systematic review was constructed to assess current evidence for the AEDs' efficacy and tolerability in cats. The methods and materials of our former systematic reviews in canine epilepsy were mostly mirrored for the current systematic review in cats. Databases of PubMed, CAB Direct and Google scholar were searched to detect peer-reviewed studies reporting efficacy and/or adverse effects of AEDs in cats. The studies were assessed with regards to their quality of evidence, i.e. study design, study population, diagnostic criteria and overall risk of bias and the outcome measures reported, i.e. prevalence and 95% confidence interval of the successful and affected population in each study and in total.

Results: Forty studies describing clinical outcomes of AEDs' efficacy and safety were included. Only two studies were classified as "blinded randomised controlled trials". The majority of the studies offered high overall risk of bias and described low feline populations with unclear diagnostic criteria and short treatment or follow-up periods. Individual AED assessments of efficacy and safety profile showed that phenobarbital might currently be considered as the first choice AED followed by levetiracetam and imepitoin. Only imepitoin's safety profile was supported by strong level of evidence. Imepitoin's efficacy as well as remaining AEDs' efficacy and safety profile were supported by weak level of evidence.

Conclusions: This systematic review reflects an evidence-based assessment of the published data on the AEDs' efficacy and safety for feline epilepsy. Currently, phenobarbital is likely to be the first-line for feline epileptic patients followed by levetiracetam and imepitoin. It is essential that clinicians evaluate both AEDs' effectiveness and tolerability before tailoring AED to the individual patient. Further studies in feline epilepsy treatment are by far crucial in order to establish definite guidelines for AEDs' efficacy and safety.

Keywords: comprehensive review, epilepsy, feline, antiepileptic drugs, efficacy, adverse effects

Systematic review of antiepileptic drugs' safety and effectiveness in feline epilepsy

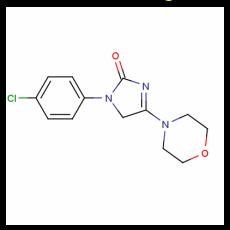
Marios Charalambous[1*], Akos Pakozdy[2], Sofie F. M. Bhatti[1] and Holger A. Volk[3]

Fig. 6 Pyramid of AEDs' safety hierarchy based on the quality of evidence and outcomes assessment

Fig. 5 Pyramid of AEDs' efficacy hierarchy based on the quality of evidence and outcomes assessment

Imepitoina (Pexion)

Tratamiento de primera elección/linea en perros

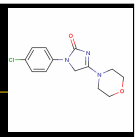


Mecanismo de acción

- Agonista parcial baja afinidad sitio de reconocimiento de benzodiacepinas en receptores GABA.

-Potencia el efecto inhibidor del GABA (supresion impulso nervioso, Cl)

Imepitoina (Pexion)



USO EN EPILEPSIA GENETICA O DE ORIGEN DESCONOCIDO

Dosis inicial (monoterapia) Perros: 10-30 mg/kg/12 horas

Depende de la severidad (niveles 3 dias)

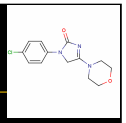
GENERALMENTE COMIENZO A 20 MG/KG/12 HORAS

ESTUDIO 12 PERROS CON EPILEPSIA IDIOPATICA TRATADOS EN MONOTERAPIA

9/12 (75%) de animales disminución en la severidad de crisis epileptiformes con imepitoina.

Estudios con fenobarbital or primidona muestran mas animales libres de crisis (no diferencia Estadisitca) y peores resultados en la disminucion de severidad de crisis.

Imepitoina (Pexion)



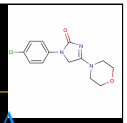
USO DE IMEPITOINA Y FENOBARBITAL EN BITERAPIA

Phenobarbital or potassium bromide as an add-on antiepileptic drug for the management of canine idiopathic epilepsy refractory to imepitoin

E. Royaux [a,*], L. Van Ham [a], B.J.G. Broeckx [b], I. Van Soens [c,d], I. Gielen [e], D. Deforce [b], S.F.M. Bhatti [a]

- Uso de imepitoina en pacintes refractarios con fenobarbital o KBr
- 14 perros grupo fenobarbital y 13 perros grupo con KBr
- Frecuencia de crisis mensuales y frecuencia de crisis diarias por mes disminuye en los dos
- 79% grupo FB y 69 % grupo KBr responden positivamente
- Disminucion en clusters
- **Tolerancia a la medicacion buena y respuesta positiva a maxima dosis de imepitoina**

Imepitoina (Pexion)



USO DE IMEPITOINA Y FENOBARBITAL EN BITERAPIA

Clinical evaluation of a combination therapy of imepitoin with phenobarbital in dogs with refractory idiopathic epilepsy

Jasmin Neßler[1†], Chris Rundfeldt[2,3*†], Wolfgang Löscher[2,4], Draginja Kostic[1,4], Thomas Keefe[5] and Andrea Tipold[1,4]

Abstract

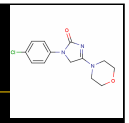
Background: Imepitoin was tested as a combination treatment with phenobarbital in an open-label mono-centre cohort study in dogs with drug-resistant epilepsy. Diagnosis of idiopathic epilepsy was based on clinical findings, magnetic resonance imaging and cerebrospinal fluid analysis. Three cohorts were treated. In cohort A, dogs not responding to phenobarbital with or without established add-on treatment of potassium bromide or levetiracetam were treated add-on with imepitoin, starting at 10 mg/kg BID, with titration allowed to 30 mg/kg BID. In cohort B, the only difference to cohort A was that the starting dose of imepitoin was reduced to 5 mg/kg BID. In cohort C, animals not responding to imepitoin at >20 mg/kg BID were treated with phenobarbital add-on starting at 0.5 mg/kg BID.

Results: The add-on treatment resulted in a reduction in monthly seizure frequency (MSF) in all three cohorts. A reduction of ≥50% was obtained in 36-42% of all animals, without significant difference between cohorts. The lower starting dose of 5 mg/kg BID imepitoin was better tolerated, and an up-titration to on average of 15 mg/kg BID was sufficient in cohort A and B. In cohort C, a mean add-on dose of 1.5 mg/kg BID phenobarbital was sufficient to achieve a clinically meaningful effect. Six dogs developed a clinically meaningful increase in MSF of ≥ 50%, mostly in cohort A. Neither imepitoin nor phenobarbital add-on treatment was capable of suppressing cluster seizure activity, making cluster seizure activity an important predictor for drug-resistance.

Conclusion: A combination treatment of imepitoin and phenobarbital is a useful treatment option for a subpopulation of dogs with drug-resistant epilepsy, a low starting dose with 5 mg/kg BID is recommended.

Keywords: Idiopathic epilepsy, [illegible] treatment, Potassium bromide, Levetiracetam, Phenobarbital, Tonic-clonic seizures

Imepitoina (Pexion)



USO EN GATOS

Imepitoin is well tolerated in healthy and epileptic cats

Odilo Engel[1*], Thilo von Klopmann[2], Arianna Maiolini[3], Jessica Freundt-Revilla[3] and Andrea Tipold[3,4]

Abstract

Background: Epilepsy in the cat is a serious medical condition. To date there are no licensed treatments for feline epilepsy and no well-controlled clinical studies on the efficacy or safety of antiepileptic drugs in cats. The aim of this study was to collect tolerability data and first exploratory efficacy data of imepitoin in both healthy and epileptic cats.

Results: In two tolerability studies, 30 healthy cats received imepition twice daily in doses of 0, 30, 40 or 80 mg/kg bodyweight for 30 days. No serious adverse events were observed in any of the dose groups. In the imepitoin treated groups, emesis was observed in some animals temporarily and intermittently mainly in the second and third weeks of treatment.
In a small, single-arm, open label, uncontrolled clinical trial eight cats suffering from idiopathic epilepsy were treated with imepitoin twice daily at doses of 30 mg/kg bodyweight for 30 days. Four of these cats (50%) achieved seizure freedom for at least 8 weeks under treatment. Adverse events, mostly lethargy, decreased appetite and emesis, were often mild and transient.

Conclusion: In summary, imepitoin was well tolerated in healthy and epileptic cats and showed in a pilot trial indication for efficacy in treating feline epilepsy.

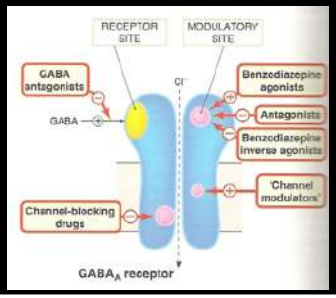
Keywords: Epilepsy, Cat, Imepitoin, Clinical trial

Fenobarbital (FB)

Medicamento primera elección perros y gatos

- Mecanismo de accion

1) Reduce potenciales excitatorios mediados por Glutamato
2) Reduce corriente canales calcicos (block channel)
3) Facilita neurotransmision inhibitoria (GABA), suprime potencial de accion y previene crisis convulsivas.



Fenobarbital (FB)

Medicamento primera eleccion perros y gatos

- Metabolismo hepatico, 25% excretado via renal y ligado a proteinas.
- Dosis inicial:
  - Perro: 3-5 mg/kg/q12h
  - Gato: 1-3 mg/kg/q12h
  - Niveles terapeuticos:
    - 85-150 µmol/ml (20-35 µg/ml)

Concentracion serica estable en;

-Perros 32-90 horas; 10-18 dias

-Gatos 34-43 horas; 10-14 dias

Fenobarbital (FB)

Efectos adversos:

- Reacciones idiosincraticas

- Sedacion, ataxia, hyperexcitabilidad (primeros 10-15d)
- Supresion de la medula osea
- Hepatotoxicidad aguda
- Dermatitis necrolitica superficial
- Prurito facial, edema extremidades and linfoadenopatias (gatos)

- Efetos adversos a largo plazo/transitorios.

- P-P-P, sedacion, ataxia (generalmente transitoria)
- Aumento enzimas hepaticas (autoinduccion citochromo P450), < T4
- HEPATOTOXICIDAD
- Dependencia fisica, perdida de efectividad.

Fenobarbital (FB)

Monitorizacion

Niveles sericos

- Terapia individualizada (cada animal diferente)
- Determinar nivel terapeutico.
- Prevenir efectos toxicos. Hepatotoxicidad.
- 3 semanas tras comenzar tratamiento.

Cada 6meses:

- Niveles sericos FB
- CBC
- Funcionalidad hepatica (enzimas, ac biliares).

Cambios laboratorio

Elevacion ALP, ALT, Colesterol
Depresion albumina serica, T4,fT4, TSH (may estar elevada)

IMEPITOINA /FENOBARBITAL

Epileptic seizure frequency and semiology in dogs with idiopathic epilepsy after initiation of imepitoin or phenobarbital monotherapy

F. Stabile[a,*], J. van Dijk[b], C.R. Barnett[c], L. De Risio[a]

[a] Centre for Small Animal Studies, Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk CB87UU, UK
[b] Centre for Preventive Medicine, Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk CB87UU, UK
[c] A2F Associate, 17 Ferry Bank, Southery, Downham Market, Norfolk PE380PL, UK

- COMPARACION ENTRE FENOBARBITAL Y IMEPITOINA EN PERROS

30 perros con fenobarbital y 31 con imepitoina

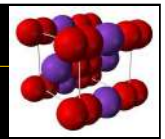
- Perros con fenobarbital mayor reducción en frecuencia de crisis epilépticas

- Perros con imepitoina desarrollaron clusters antes

- Agresividad y discontinuar medicación mas frecuente con imepitoina

FENOBARBITAL MENOS AGRESIVIDAD MENOS CLUSTERS Y MENOS FRECUENTE DISCONTINUAR TRATAMIENTO

Bromuro potasico (KBr)

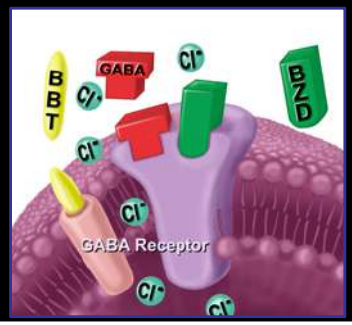


Monoterapia o asociado a FB/imepitoina

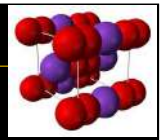
- Epilepsia refractaris
- Enfermedad hepatica
- Efectos adversos severos con FB

Mecanismo de acción

Activa conduccion de Cl, facilita neurotransmision inhibitoria (GABA)

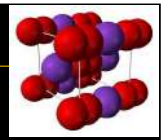


Bromuro potasico (KBr)



- **Excreccion renal.**
- Dietas con alto contenido en sal favorece la eliminación KBr.
- EVITAR EN FALLO RENAL.
- **Effectos secundarios:**
  - Sedacion y dosis dependiente
  - Debilidad
  - Ataxia
  - Irritacion gastrointestinal
  - Pancreatitis
  - Gatos: NO RECOMENDADO (35-42% neumonia-asma)

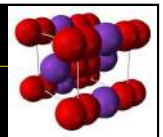
Bromuro potasico (KBr)



- Dosis inicial:
  20-40 mg/kg q24h PO
- Larga eliminacion; vida media (15-20d)
  - Niveles sericos estables 100-120d
  - "Dosis de carga" si necesario

  600 mg/kg/dia (dividido in 4 dias; 150 mg/kg/dia)
- Monitorizar niveles sericos:
  30d, 120, cada 6m
  Rango terapeutico
  Monoterapia: 2-3 mg/ml
  KBr + FB: 1-2 mg/ml

Bromuro potasico (KBr)



Comparison of phenobarbital with bromide as a first-choice antiepileptic drug for treatment of epilepsy in dogs

Dawn Merton Boothe, DVM, PhD, DACVIM, DACVCP; Curtis Dewey, DVM, MS, DACVS, DACVIM; David Mark Carpenter, PhD

Objective—To compare efficacy and safety of treatment with phenobarbital or bromide as the first-choice antiepileptic drug (AED) in dogs.

Design—Double-blinded, randomized, parallel, clinical trial.

Animals—46 AED-naive dogs with naturally occurring epilepsy.

Procedures—Study inclusion was based on age, history, findings on physical and neurologic examinations, and clinicopathologic test results. For either phenobarbital treatment (21 dogs) or bromide treatment (25), a 7-day loading dose period was initiated along with a maintenance dose, which was adjusted on the basis of monthly monitoring. Efficacy and safety outcomes were compared between times (baseline and study end [generally 6 months]) and between drugs.

Results—Phenobarbital treatment resulted in eradication of seizures (17/20 [85%]) significantly more often than did bromide (12/23 [52%]); phenobarbital treatment also resulted in a greater percentage decrease in seizure duration (88 ± 34%), compared with bromide (49 ± 75%). Seizure activity worsened in 3 bromide-treated dogs only. In dogs with seizure eradication, mean ± SD serum phenobarbital concentration was 25 ± 6 µg/mL (phenobarbital dosage, 4.1 ± 1.1 mg/kg [1.9 ± 0.5 mg/lb], PO, q 12 h) and mean serum bromide concentration was 1.8 ± 0.6 mg/mL (bromide dosage, 31 ± 11 mg/kg [14 ± 5 mg/lb], PO, q 12 h). Ataxia, lethargy, and polydipsia were greater at 1 month for phenobarbital-treated dogs; vomiting was greater for bromide-treated dogs at 1 month and study end.

Conclusions and Clinical Relevance—Both phenobarbital and bromide were reasonable first-choice AEDs for dogs, but phenobarbital was more effective and better tolerated during the first 6 months of treatment. (*J Am Vet Med Assoc* 2012;240:1073–1083)

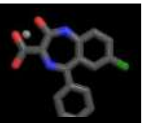
Benzodiacepinas (diazepam, Clorazepato, etc)

Diazepam

- Emergencias (cluster, SE): IV, rectal, intranasal
- Terapia mantenimiento:
  - Perros: NO EFECTIVO (vida media corta (2 hours), tolerancia)
  - Gatos: 0.5-2 mg/kg/d PO div q8-12h (vida media12-14 h)
  - Niveles estables in 3.5-4.5 days
  - Fallo hepatico agudo descrito en gatos

Mecanismo de accion.
Facilita accion inhibitoria del GABA.

Benzodiacepinas (diazepam, Clorazepato, etc)



Clorazepato

- Metabolizado a nordiazepam mejor que diazepam en tratamientos cronicos en perros.
- Tolerancia pero mas despacion que con diazepam.
- 0.5 mg/kg q8-12 hrs
- Al retirarlo posibles crisis convulsivas withdrawal seizure activity

  Util en episodios de clusters

  1 mg/kg/8 hours primeras 24 horas

  Disminuir cada 12 horas durante 24 horas

  Cada 24 horas para prevenir crisis al retirarlo.

AIEs de segunda y tercera generacion.

Segunda-generacion

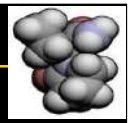
- Levetiracetam (Keppra)
- Gabapentina, Pregabalin
- Zonisamida
- Felbamato
- Topiramato
- Lamotrigina

Epilepsia refractaria ?
Primera opcion?

Tercera-generation

- Lacosamida
- Rufinamida

Levetiracetam (Keppra®)



- Perros, (como primera o segunda opcion)
- **Mecanismo de accion:** Union vesicula sinaptica proteina 2A
- NO metabolismo hepatico
- Dosis: 10-20 mg/kg/q8h PO
- Dosis: 60 mg/kg IV in status epilepticus
- Monoterapia vs asociacion a otro AIE (epilepsia refractaria)
- Muy seguro, efectos adversos minimos
- No necesario monitorizar niveles

Levetiracetam (Keppra®)

Vet Rec. 2017 Oct 14;181(15):401. doi: 10.1136/vr.104190. Epub 2017 Aug 28.

Levetiracetam monotherapy for treatment of structural epilepsy in dogs: 19 cases (2010-2015).

Kelly D[1], Raimondi F[2], Shihab N[3].

Author information

Abstract

To evaluate the efficacy and tolerability of levetiracetam monotherapy in dogs with structural epilepsy. Retrospective case series. Nineteen client-owned dogs with structural epilepsy. Seizure frequencies after initiation of treatment were used to evaluate the efficacy of levetiracetam monotherapy. Seizure control was considered good if no seizures occurred within three months of starting treatment or poor if seizures returned within one month of starting treatment. Tolerability was evaluated by considering the occurrence and severity of any reported side effects. Ten of the 19 dogs were considered to have a good response to treatment with 7 achieving complete seizure freedom. Nine dogs were considered to have poor response to treatment. There was a statistically significant reduction in the percentage of patients experiencing cluster seizures from 68.4% to 15.8% (p=0.002). Side effects were noted in 8 of the 19 dogs but were considered mild in all cases. Follow-up times ranged from 12 days to 426 days. When used in conjunction with other appropriate therapies, levetiracetam may be an efficacious option for monotherapy in dogs with structural epilepsy. Its tolerability makes it a suitable option for use in a wide variety of patients.

Levetiracetam (Keppra®)

J Vet Intern Med 2012;26:341–348

Evaluation of Levetiracetam as Adjunctive Treatment for Refractory Canine Epilepsy: A Randomized, Placebo-Controlled, Crossover Trial

K.R. Muñana, W.B. Thomas, K.D. Inzana, J.A. Nettifee-Osborne, K.J. McLucas, N.J. Olby, C.J. Mariani, and P.J. Early

Background: There is little evidence-based information available to guide treatment of refractory epilepsy in dogs. The antiepileptic drug levetiracetam (LEV) is administered to dogs, although its safety and efficacy are unknown.

Objective: To evaluate the safety and efficacy of LEV as adjunctive therapy for refractory epilepsy in dogs.

Animals: Thirty-four client-owned dogs with idiopathic epilepsy.

Methods: Randomized, blinded trial involving dogs resistant to phenobarbital and bromide. Dogs received LEV (20 mg/kg PO q8h) or placebo for 16 weeks, and after a 4-week washout were crossed over to the alternate treatment for 16 weeks. Owners kept records on seizure frequency and adverse events. Hemogram, chemistry profile, urinalysis, and serum antiepileptic drug concentrations were evaluated at established intervals.

Results: Twenty-two (65%) dogs completed the study. Weekly seizure frequency during the 1st treatment period decreased significantly during LEV administration relative to baseline (1.9 ± 1.9 to 1.1 ± 1.3, $P = .015$). The reduction in seizures with LEV was not significant when compared to placebo (1.1 ± 1.3 versus 1.5 ± 1.7, $P = .310$). The most common adverse event was ataxia, with no difference in incidence between LEV and placebo (45 versus 18%, $P = .090$). No changes in laboratory parameters were identified and owners reported an improved quality of life (QOL) with LEV compared to placebo (QOL score 32.7 ± 4.3 versus 29.4 ± 4.5, $P = .028$).

Conclusions and Clinical Importance: Adjunctive treatment with LEV appears safe in epileptic dogs. Efficacy of LEV over placebo was not demonstrated, although the power of the study was limited. Further evaluation of LEV as treatment for epilepsy in dogs is warranted.

Key words: Clinical pharmacology; CNS disorders; Dog; Epilepsy; Neurology; Seizures.

Levetiracetam (Keppra®)

Pharmacokinetics of rectal levetiracetam as add-on treatment in dogs affected by cluster seizures or status epilepticus

Giulia Cagnotti*, Rosangela Odore, Giulia Gardini, Stefano Amedeo, Iride Bertone, Giulia Guerriero, Laura Lentin Elena Dappiano and Antonio D'Angelo

Abstract

Background: Levetiracetam can be used for seizure control alone or in combination with other antiepileptic medications. A previous study achieved the minimum targeted serum drug concentration after rectal administratio of levetiracetam in healthy dogs. The purpose of the present study was to determine the pharmacokinetics of recta LEV in dogs presented for cluster seizures or status epilepticus and potentially in treatment with other anti-epileptic drugs. Furthermore, preliminary information on response to this treatment as add-on to the standard treatment protocol is reported.

Results: Eight client-owned dogs were enrolled. Plasma levetiracetam concentrations (measured at 0, 30, 60, 90, 120, 180 240, 360, 720, and 1440 min after drug administration) reached the minimum target concentration (5 μg/ml) at 30 min in all but one patient. At T1 (30 min) the mean concentration was 28.2 ± 15.5 μg/ml. Plasma concentrations remained abov the targeted minimum concentration in all patients until 240 min and in 7/8 until 360 min. Six out of eight patients experienced no seizures in the 24-h period after hospitalization and were classified as "responders".

Conclusions: Minimum plasma levetiracetam concentration can be reached after rectal administration of 40 mg/kg in dogs affected by cluster seizures and status epilepticus and concurrently receiving other antiepileptic drugs. These preliminary results may encourage the evaluation of rectal levetiracetam as an additional treatment option for cluster seizures and status epilepticus in a larger number of dogs.

Keywords: Epilepsy, Pharmacokinetics, Neurology, Emergency

Levetiracetam as an adjunct to phenobarbital treatment in cats with suspected idiopathic epilepsy

Kerry Smith Bailey, DVM; Curtis W. Dewey, DVM, MS, DACVIM, DACVS; Dawn M. Boothe, DVM, PhD, DACVIM, DACVCP; Georgina Barone, DVM, DACVIM; Gregg D. Kortz, DVM, DACVIM

Objective—To assess pharmacokinetics, efficacy, and tolerability of oral levetiracetam administered as an adjunct to phenobarbital treatment in cats with poorly controlled suspected idiopathic epilepsy.

Design—Open-label, noncomparative clinical trial.

Animals—12 cats suspected to have idiopathic epilepsy that was poorly controlled with phenobarbital or that had unacceptable adverse effects when treated with phenobarbital.

Procedures—Cats were treated with levetiracetam (20 mg/kg [9.1 mg/lb], PO, q 8 h). After a minimum of 1 week of treatment, serum levetiracetam concentrations were measured before and 2, 4, and 6 hours after drug administration, and maximum and minimum serum concentrations and elimination half-life were calculated. Seizure frequencies before and after initiation of levetiracetam treatment were compared, and adverse effects were recorded.

Results—Median maximum serum levetiracetam concentration was 25.5 μg/mL, median minimum serum levetiracetam concentration was 8.3 μg/mL, and median elimination half-life was 2.9 hours. Median seizure frequency prior to treatment with levetiracetam (2.1 seizures/mo) was significantly higher than median seizure frequency after initiation of levetiracetam treatment (0.42 seizures/mo), and 7 of 10 cats were classified as having responded to levetiracetam treatment (ie, reduction in seizure frequency of ≥ 50%). Two cats had transient lethargy and inappetence.

Conclusions and Clinical Relevance—Results suggested that levetiracetam is well tolerated in cats and may be useful as an adjunct to phenobarbital treatment in cats with idiopathic epilepsy. (*J Am Vet Med Assoc* 2008;232:867–872)

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM Open Access

Serum levetiracetam concentrations and adverse events after multiple dose extended release levetiracetam administration to healthy cats

Heidi Barnes Heller[1] | Martin Granick[1] | Mathew Van Hesteren[1] | Dawn M. Boothe[2]

Pharmacokinetics of Single Oral Dose Extended-Release Levetiracetam in Healthy Cats

L. Barnard, H. Barnes Heller, and D.M. Boothe

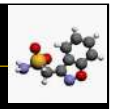
DOSIS DE 500 MG POR GATO, CADA 24 HORAS DURANTE 10 DIAS

NIVELES ACEPTABLES CON POCOS EFECTOS SECUNDARIOS

CADA ANIMAL DIFERENTE, MONITORIZAR

ALTERNATIVA A USAR TRES VECES DIARIAS

Zonisamida (Zonegran®)



- Perros en asociacion a FB vs monotherapia (gatos estudio farmacocin)
- **Mecanismo de accion:**

  Bloqueo de canales de Ca; inhibition excitacion

SHORT COMMUNICATION
Pharmacokinetics and toxicity of zonisamide in cats

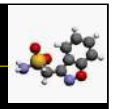
Daisuke Hasegawa DVM, PhD*, **Masanori Kobayashi** DVM, **Takayuki Kuwabara** DVM, **Tomoyuki Ohmura** DVM, **Michio Fujita** DVM, PhD, **Hiromitsu Orima** DVM, PhD

Department of Veterinary Radiology, Nippon Veterinary and Life Science University, 1-7-1 Kyounan-chou, Musashino-shi, Tokyo 180-8602, Japan

With the eventual goal of making zonisamide (ZNS), a relatively new antiepileptic drug, available for the treatment of epilepsy in cats, the pharmacokinetics after a single oral administration at 10 mg/kg and the toxicity after 9-week daily administration of 20 mg/kg/day of ZNS were studied in healthy cats. Pharmacokinetic parameters obtained with a single administration of ZNS at 10 mg/day were as follows: $C_{max} = 13.1$ μg/ml; $T_{max} = 4.0$ h; $T_{1/2} = 33.0$ h; areas under the curves (AUCs) = 720.3 μg/ml h (values represent the medians). The study with daily administrations revealed that the toxicity of ZNS was comparatively low in cats, suggesting that it may be an available drug for cats. However, half of the cats that were administered 20 mg/kg/day daily showed adverse reactions such as anorexia, diarrhoea, vomiting, somnolence and locomotor ataxia.

Date accepted: 30 January 2008

Zonisamida (Zonegran®)



- Perros en asociacion a FB vs monoterapia
- **Mecanismo de accion:**

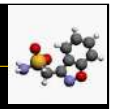
  Bloqueo de canales de Ca y NA, inhibición liberación glutamato y aumento liberación GABA

  Maxima concentración. Plasmatica 2-6 h.
- Metabolismo hepatico
- Dose: 5-10 mg/kg/q12h PO (perros)
- 70% dogs buena respuesta zonisamida en asociacion con FB en epilepsia refractaria.
- Efectos adversos;

  Sedacion transitoria, ataxia, KCS

  Necrosis hepatica, acidosis tubular renal.

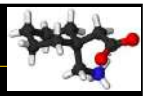
Zonisamida (Zonegran®)



Prospective study of zonisamide therapy for refractory idiopathic epilepsy in dogs

- 11 perros con epilepsia idiopatica refractaria a fenobarbital y BrK.a
- 9/11 responden positivamente con reducción e crisis
- Reducción de crisis 70%.
- Posibilidad de tolerancia en un caso

Gabapentina, pregabalina (Gabapentin®, Lyrica®)



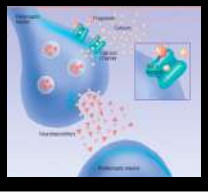
- Dogs en epilepsia refractaria (asociado a FB)
- **Doses:**

  Gabapentina; 10-20 mg/kg/8-12 hours PO

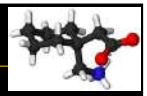
  Pregabalina; 2-4 mg/kg/8-12 hours PO
- **Mecanismo de accion:**

  Union a2-d subunidad pre-sinaptica canales Ca.

  Disminuye liberacion de NT excitatorios



Gabapentina, pregabalina (Gabapentin®, Lyrica®)



- Perros en epilepsia refractaria (asociado a FB)
- **Dosis: GATOS**

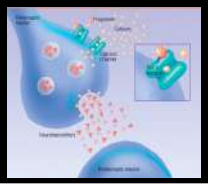
  Gabapentina; 6-10 mg/kg/8-12 hours PO (NO ESTUDIOS)

  Pregabalina; 1-2 mg/kg/8-12 hours PO (recomendado)

- **Mecanismo de accion:**

  Union a2-d subunidad pre-sinaptica canales Ca.

  Disminuye liberacion de NT excitatorios



Gabapentina, pregabalina (Gabapentin®, Lyrica®)

> Vet Rec. 2006 Dec;159(26):881-4.

Treatment with gabapentin of 11 dogs with refractory idiopathic epilepsy

S R Platt [1], V Adams, L S Garosi, C J Abramson, J Penderis, A De Stefani, L Matiasek

Pregabalin as an adjunct to phenobarbital, potassium bromide, or a combination of phenobarbital and potassium bromide for treatment of dogs with suspected idiopathic epilepsy

Curtis W. Dewey, DVM, MS, DACVIM, DACVS; Sofia Cerda-Gonzalez, DVM, DACVIM; Nathan M. Levine, DVM, DACVIM; Britton L. Badgley; Julie M. Ducoté, DVM, DACVIM; Gena M. Silver, DVM, DACVIM; Jocelyn J. Cooper, DVM; Rebecca A. Packer, DVM, MS, DACVIM; James A. Lavely, DVM, DACVIM

MEJORIA EN AMBOS ESTUDIOS EN EPILEPSIA REFRACTARIA

FELBAMATO (Taloxa®)

- Perros en asociacion a otros AE.
- Mecanismo de accion:

  Bloqueo de canales de Ca y canales ionicos NMDA, iy aumento liberación GABA

  Vida media eliminación 5-7 h.
- Metabolismo hepatico
- Dosis: 20 mg/kg/q 8 h PO (perros)
- Analíticas mensuales los primeros 6 meses riesgo hepatopati
- Y anemias en medicina humana.
- Rango terapeutico (humana) 25-100 mg/mL

FELBAMATO (Taloxa®)

Treatment of partial seizures and seizure-like activity with felbamate in six dogs

- Disminución de frecuencia de crisis en todos los perros pocos efectos no deseados.

Felbamate as an oral add-on therapy in six dogs with presumptive idiopathic epilepsy and generalized seizures resistant to drug therapy

Curtis Wells Dewey[1*], Mark Rishniw[2] and Kasie Sakovitch[1]

- Perros con epilepsia refractaria, dosis rango desde 15 a 21 mg/kg/ 8-12 horas
- -83% de casos disminucion mas o igual 50% en crisis, respuesta positiva
- Efectos adversos mínimos.

Topiramato (Topictal, Topamax ®)

- Perros en asociacion a otros AE.
- Mecanismo de accion:

  Bloqueo de canales de Ca y aumento liberación GABA

  Vida media eliminación 2-4 h, 70-80% eliminado por orina.

- Dosis: 2-10 mg/kg/q 8-12 h PO (perros)

FELBAMATO (Taloxa®)

Intravenous Topiramate: Pharmacokinetics in Dogs with Naturally Occurring Epilepsy

Irene Vuu[1,2], Lisa D. Coles[1,2], Patricia Maglalang[1,3], Ilo E. Leppik[2,4], Greg Worrell[5], Daniel Crepeau[5], Usha Mishra[1], James C. Cloyd[1,2] and Edward E. Patterson[6]

Topiramate as an add-on antiepileptic drug in treating refractory canine idiopathic epilepsy

A.-M. Kiviranta, O. Lattinen-Vapaavuori, A. Hielm-Björkman, T. Jokinen

Department of Equine and Small Animal Medicine, Faculty of Veterinary Medicine, University of Helsinki, FI-00014 Helsinki, Finland

- 10 perros con epilepsia refractaria, dosis rango desde 15 a 21 mg/kg/ 8-12 horas

-50 % de casos respondieron positivamente, reducción 66% frecuencia de crisis.

- Efectos adversos mínimos, sedación o ataxia.

EPILEPSIA REFRACTARIA

- TRATAMIENTO SATISFACTORIO SI REDUCION EN FRECUENCIA DE CRISIS EPILEPTICAS > DE 50%
- APROXIMADAMENTE 2/3 DE PERROS CONTINAUAN CON CRISIS EPILEPTICAS
- ENTRE UN 20-30 % DE PERROS REFRACTARIOS AL TRATAMIENT O < 50% REDUCCION DE CRISIS EPILEPTIFORMES
- MUCHOS ESTUDIOS CON FARMACOS DE 2 Y 3 LINEA EN EPILEPSIAREFRACTARIA CON RESULTADOS VARIABLES
- ANIMALES QUE REDUCEN FRECUENCIA PERO CON EFECTOS SECUNDARIOS MARCADOS O INACEPTABLES, REFRACTARIOS

EPILEPSIA REFRACTARIA

Clinical Risk Factors Associated with Anti-Epileptic Dru Responsiveness in Canine Epilepsy

Rowena M. A. Packer[1], Nadia K. Shihab[†1,2], Bruno B. J. Torres[†3], Holger A. Volk[1*]

1 Department of Clinical Science and Services, Royal Veterinary College, Hatfield, Hertfordshire, United Kingdom, **2** Department of Neurology/Neurosurgery, Sou Counties Veterinary Specialists, Ringwood, Hampshire, United Kingdom, **3** Department of Veterinary Medicine and Surgery, Federal University of Minas Gerais, Horizonte, Minas Gerais, Brazil

were in seizure-free remission. Dogs that did not achieve remission were more likely to be male, and to have previously experienced cluster seizures. Seizure frequency or the total number of seizures prior to treatment were not significant predictors of pharmacoresistance, demonstrating that seizure density, that is, the temporal pattern of seizure activity, is a more influential predictor of pharmacoresistance. These results are in line with clinical studies of human epilepsy, and experimental rodent models of epilepsy, that patients experiencing episodes of high seizure density (cluster seizures), not

PERROS QUE NO RESPONDIERON O FARMACO RESISTENTES MAS FRECUENTE MACHOS

Y PERROS QUE TUVIERON CLUSTERS

EPILEPSIA REFRACTARIA

Pregabalin Add-On vs. Dose Increase in Levetiracetam Add-On Treatment: A Real-Life Trial in Dogs With Drug-Resistant Epilepsy

Sandra R. P. Kriechbaumer[1,2], Konrad Jurina[2], Franziska Wielaender[1], Henning C. Schenk[1,3], Tanja A. Steinberg[2], Sven Reese[4], Gesine Buhmann[1], Stefanie Doerfelt[1,2], Heidrun Potschka[5] and Andrea Fischer[1]*

- 26perros con epilepsia idiopatica refractaria
- 14 perros pregabalin 4 mg/kg/12 h y 12 perros levetiracetam (incrementan
dosis).
- Solo 2 perros en grupo pregabalin y 1 en grupo levatiracetam tratamiento c
éxito.
- Necesidad de mejores tratamientos farmacológicos o no farmacológicos

CBD

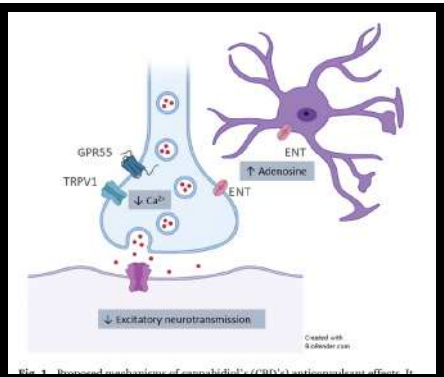
EFECTOS
NEUPROTECTORES
ANSIOLITICOS
ANTIEPILEPTICOS
ANTITUMORALES
ANTIINFLAMATORIOS
OTROS

Do Cannabinoids Confer Neuroprotection Against Epilepsy? An Overview

Anna Capasso*

Cannabidiol in canine epilepsy

Heidrun Potschka[a,*], Sofie F.M. Bhatti[b], Andrea Tipold[c], Stephanie McGrath[d]



MECANISMO PROPUESTO DE ANTICONVULSIVO DISMINUIR

CALCIO INTRACELULAR PRESINAPTICO PREVINIENDO EXCESIVOS

NEUROTRANMISORES EXCITATORIOS

CANABIDIOL

Review

Cannabinoids in treatment-resistant epilepsy: A review

Brooke K. O'Connell [a], David Gloss [b], Orrin Devinsk [a,*]

[a] NYU Epilepsy Center, New York, NY, United States
[b] CAMC, Charleston, WV, United States

Study	Compound	Study Type	N	Efficacy	Toxicity
Oral cannabis extracts					
Gowers [25]	*Cannabis indica* extract, 32 mg/day	Case report of a 40-year-old man with focal epilepsy resistant to bromides	1	Seizure-free for 6 months followed by recurrence with cannabis extract discontinuation. Resumed seizure control with resumption of cannabis use several months	None reported
Porter & Jacobson [32]	CBD/THC extracts of varying composition/dose CBD up to 28 mg/kg/day and THC up to 0.8 mg/kg/day	Survey among participants in a Facebook group for parents of children with TRE	19	16 (84%) reported improvement with CBD/THC, 2 (11%) became seizure-free	Drowsiness, fatigue, decreased appetite
Maa & Figi [33]	Oral cannabis extract, high ratio of CBD:THC	Case report of a 5-year-old girl with DS	1	>90% reduction in generalized tonic-clonic seizure frequency and ability to reduce [illegible] drugs	Somnolence, fatigue
Gedde & Maa [34]	Oral cannabis extract, high ratio of CBD: THC	Survey of parents whose children with TRE used the extract	11	100% had reduction in motor seizure frequency; 8/11 with complete or near [illegible] control	Somnolence, unsteadiness
Press et al. [35]	Oral cannabis extracts	Retrospective case series of children with refractory epilepsy at one center in Colorado	75	25 (33%) reported a >50% reduction in seizure frequency	Somnolence, fatigue, increased seizures. Rare developmental regression, status epilepticus
Tzadok et al. [36]	CBD enriched cannabis extracts	Retrospective case study of children and adolescents with intractable epilepsy at five Israeli pediatric epilepsy centers	74	66 (89%) reported a reduction in seizure frequency; 13 (18%) 75–100% reduction, 25 (34%) 50–75% reduction, 9 (12%) 25–50% reduction, and 19 (26%) <25% reduction	Somnolence, fatigue, gastrointestinal disturbances, irritability 5 patients discontinued use.

REDUCCION DE CRISIS EN LA MAYORIA DE GRUPOS

CANABIDIOL

Randomized blinded controlled clinical trial to assess the effect of oral cannabidiol administration in addition to conventional antiepileptic treatment on seizure frequency in dogs with intractable idiopathic epilepsy

Mismo numero entre grupos respondieron

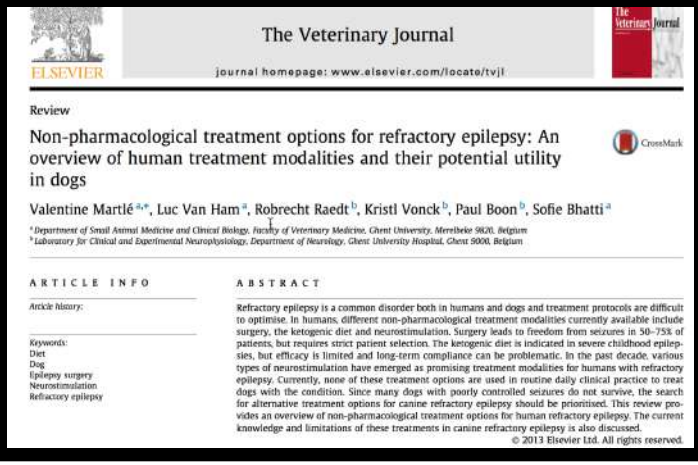
Disminución en frecuencia de crisis en grupo con canabidiol

Dosis de 2.5 mg/kg /12 horas durante 12 semanas

Estudios futuros con mayor dosis de CBD para ver si mayor disminución en frecuencia de crisis

EPILEPSIA REFRACTARIA

TRATAMIENTOS NO FARMACOLOGICOS NUEVOS AVANCES



The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Review

Non-pharmacological treatment options for refractory epilepsy: An overview of human treatment modalities and their potential utility in dogs

Valentine Martlé [a,*], Luc Van Ham [a], Robrecht Raedt [b], Kristl Vonck [b], Paul Boon [b], Sofie Bhatti [a]

[a] Department of Small Animal Medicine and Clinical Biology, Faculty of Veterinary Medicine, Ghent University, Merelbeke 9820, Belgium
[b] Laboratory for Clinical and Experimental Neurophysiology, Department of Neurology, Ghent University Hospital, Ghent 9000, Belgium

ARTICLE INFO

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Refractory epilepsy

ABSTRACT

Refractory epilepsy is a common disorder both in humans and dogs and treatment protocols are difficult to optimise. In humans, different non-pharmacological treatment modalities currently available include surgery, the ketogenic diet and neurostimulation. Surgery leads to freedom from seizures in 50–75% of patients, but requires strict patient selection. The ketogenic diet is indicated in severe childhood epilepsies, but efficacy is limited and long-term compliance can be problematic. In the past decade, various types of neurostimulation have emerged as promising treatment modalities for humans with refractory epilepsy. Currently, none of these treatment options are used in routine daily clinical practice to treat dogs with the condition. Since many dogs with poorly controlled seizures do not survive, the search for alternative treatment options for canine refractory epilepsy should be prioritised. This review provides an overview of non-pharmacological treatment options for human refractory epilepsy. The current knowledge and limitations of these treatments in canine refractory epilepsy is also discussed.

TRATAMIENTOS NO FARMACOLOGICOS NUEVOS AVANCES

TRATAMIENTOS DE DIETA

RESULTS OF A KETOGENIC FOOD TRIAL FOR DOGS WITH IDIOPATH- IC EPILEPSY. Edward (Ned) E. Patterson[1], Karen R. Munana[2], Claudia A. Kirk[3], Steve R. Lowry[4], P. Jane Armstrong[3]. 1. University of Minnesota, St. Paul, MN. 2. North Carolina State University, Raleigh, NC. 3. University of Tennessee, Knoxville TN. 4. Hill's Pet Nutrition Center, Topeka, KS.

GRUPO DE PERROS EPILEPTICOS TRATADOS CON DIETA KETOGENICA Y GRUPO DE PERROS SIN DIETA.

NO HUBO DIFERENCIAS EN EL PATRON DE REDUCCION DE CRISIS EPILEPTICAS

TRATAMIENTOS NO FARMACOLOGICOS NUEVOS AVANCES

Dietary medium chain triglycerides for management of epilepsy: New data from human, dog, and rodent studies

Felicity Y. Han[1] | Lisa Conboy-Schmidt[2] | Galena Rybachuk[3] | Holger A. Volk[4] | Brian Zanghi[2] | Yuanlong Pan[2] | Karin Borges[1]

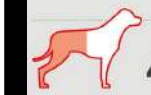
nisms. In conclusion, MCTs are a promising adjunct to standard pharmacologica treatment for both humans and dogs with epilepsy, as they lack central nervous sys tem side effects found with current antiepileptic drugs. There is now a need for large clinical trials in children, adults, and dogs to find the ideal composition and doses o MCTs and the types of epilepsy that respond best.

Resultados prometedores añadido a fármacos antiepieepticos

TRATAMIENTOS NO FARMACOLOGICOS NUEVOS AVANCES

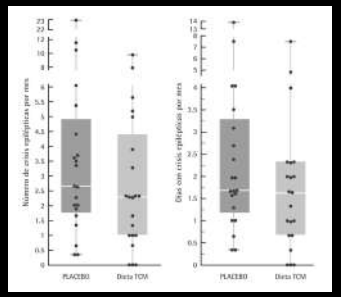
La mayoría de los perros con epilepsia idiopática mostró una reducción de la frecuencia de crisis en 90 días cuando se alimentó con una dieta prueba con TCM como tratamiento veterinario adjunto

71% de los perros experimentó una reducción en la frecuencia de crisis epilépticas



48% de los perros experimentó una reducción superior al 50% en la frecuencia de crisis epilépticas

14% de los perros consiguió permanecer libre de crisis epilépticas



TRATAMIENTOS NO FARMACOLOGICOS NUEVOS AVANCES

Effects of a ketogenic diet on ADHD-like behavior in dogs with idiopathic epilepsy

Rowena M.A. Packer [a,*], Tsz Hong Law [a,b], Emma Davies [a], Brian Zanghi [c], Yuanlong Pan [c], Holger A. Volk [a]

[a] Department of Clinical Science and Services, Royal Veterinary College, Hatfield, Hertfordshire, UK
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Ketogenic
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Anxiolytic

ABSTRACT

Objectives: Epilepsy in humans and rodent models of epilepsy can be associated with behavioral comorbidities including an increased prevalence of attention-deficit/hyperactivity disorder (ADHD). Attention-deficit/hyperactivity disorder symptoms and seizure frequency have been successfully reduced in humans and rodents using a ketogenic diet (KD). The aims of this study were (i) to describe the behavioral profile of dogs with idiopathic epilepsy (IE) while on a standardized nonketogenic placebo diet, to determine whether ADHD-like behaviors are present, and (ii) to examine the effect of a ketogenic medium chain triglyceride diet (MCTD) on the behavioral profile of dogs with idiopathic epilepsy (IE) compared with the standardized placebo control diet, including ADHD-like behaviors.
Methods: A 6-month prospective, randomized, double-blinded, placebo-controlled, crossover dietary trial comparing the effects of the MCTD with a standardized placebo diet on canine behavior was carried out. Dogs diagnosed with IE, with a seizure frequency of at least 3 seizures in the past 3 months (n = 21), were fed the MCTD or placebo diet for 3 months and were then switched to the alternative diet for 3 months. Owners completed a validated behavioral questionnaire to measure 11 defined behavioral factors at the end of each diet period to report their dogs' behavior, with three specific behaviors hypothesized to be related to ADHD: excitability, chasing, and trainability.
Results: The highest scoring behavioral factors in the placebo and MCTD periods were excitability [mean ± SE: 1.910 ± 0.127] and chasing [mean ± SE: 1.824 ± 0.210]. A markedly lower trainability score [mean ± SE: 0.437 ± 0.125] than that of previously studied canine populations was observed. The MCTD resulted in a significant improvement in the ADHD-related behavioral factor chasing and a reduction in stranger-directed fear ($p < 0.05$)

Mejoría en cambios de comportamiento y miedo asociado a epilepsia idiomática

TRATAMIENTOS NO FARMACOLOGICOS NUEVOS AVANCES

CIRUGIA

- **LOBECTOMIA AREA TEMPORAL, (TLE, esclerosis hipocampo) 65% libre de crisis epileptic as.**

- **RESECCIONES EXTRATEMPORALES (Occipital, parietal)**

- **DIVISION CUERPO CALLOSO (Evitar diseminación de crisis de un hemisferio a otro, aproximadamente 35% buena respuesta)**

- **HEMISFERIOTOMIA (Agresiva, pacientes selectos, hasta 70-80% éxito)**

En perros difícil encontrar foco de epilepsia, EEG no rutinaria, examenes de imagen funcionales no hechos.

- **Division de cuerpo calloso hecha en perros con buenos resultados *(Baygley 1995)***

CIRUGIA

Neurosurgery in canine epilepsy

Daisuke Hasegawa [a,b,*], Miyoko Saito [c], Masato Kitagawa [d]

Case Report

Corpus Callosotomy in 3 Cavalier King Charles Spaniel Dogs with Drug-Resistant Epilepsy

Rikako Asada [1], Satoshi Mizuno [1], Yoshihiko Yu [1], Yuji Hamamoto [2], Tetsuya Anazawa [3], Daisuke Ito [4], Masato Kitagawa [4] and Daisuke Hasegawa [1,5,*]

24:122-127, 1995

Clinical Effects of Longitudinal Division of the Corpus Callosum in Normal Dogs

RODNEY S. BAGLEY, DVM, TIMOTHY V. BASZLER, DVM, PhD, MICHAEL L. HARRINGTON, DVM, G. ELIZABETH PLUHAR, DVM, MS, MICHAEL P. MOORE, DVM, MS, ROBERT D. KEEGAN, DVM, and STEPHEN A. GREENE, DVM, MS

TRATAMIENTOS NO FARMACOLOGICOS NUEVOS AVANCES

ESTIMULACION NERVIO VAGO

EN MEDICINA VETERINARIA 10 PERROS NO DIFERENCIAS *Muñana et al*


Feasibility of Non-Invasive Vagus Nerve Stimulation (gammaCore VET™) for the Treatment of Refractory Seizure Activity in Dogs

Kelsey Robinson[1], Simon Platt[1*], Georgina Stewart[2], Lisa Reno[1], Renee Barber[1] and Lindsay Boozer[3]

ESTIMULACION MAGNETICA TRANSCRANEAL

ESTIMULACION CEREBRAL PROFUNDA

NEUROESTIMULACION RESPONSIVA

GRACIAS PREGUNTAS?