

TREATMENT IN CANINE EPILEPSY – A SYSTEMATIC REVIEW

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Background

Various anti-epileptic drugs (AEDs) are used for the management of idiopathic epilepsy (IE) in dogs. Clinical information on the grounds of their efficacy remains, however, quite limited, with most of it derived from non-blinded non-randomized uncontrolled trials and case series.

Aim of the study

This is the first systematic review in veterinary medicine which evaluates studies that describe the efficacy of AEDs used for the management of IE, based on objective criteria.

Material & Methods

- ✓ Electronic searches of PubMed and CAB Direct were carried out (10 August 2014) without date or language restrictions. Proceedings of ECVN/ACVIM annual congresses were searched. Peer-reviewed full-length studies describing objectively the efficacy of AEDs in dogs with IE were included.
- ✓ Studies were selected based on specific inclusion criteria and a two-stage screening process. Final studies were evaluated on the grounds of their overall quality of evidence (figure 1) as well as outcomes measures (table 1).

Figure 1: Criteria for evaluation of the overall quality of evidence for each study

Blinded randomized clinical trials (bRCTs) with large group sizes, clear inclusion criteria and diagnostic investigations that included clinical signs and thorough test results consistent with the diagnosis of IE, describing outcomes specific for IE and low overall risk of bias were considered to provide the highest available quality of evidence.

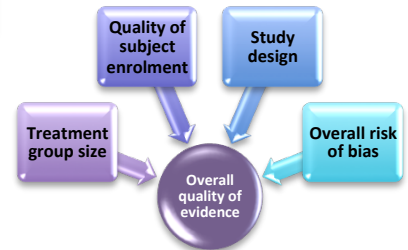


Table 1: Criteria for evaluation of AEDs' efficacy

The overall evidence for/against recommending the use of an AED was allocated according to the system below. The system was based on studies' results as well as the proportion of dogs in the study population that were successfully treated (i.e. 95% confidence interval of dogs with ≥50% reduction in seizure frequency or seizure freedom). The higher the proportion of successfully treated cases was in a bRCT, the strongest the evidence for/against the recommendation for the use of an AED was. If there were not any bRCTs available for an AED, the evidence was characterized as insufficient.

'good' evidence 'for' recommending use of the drug	'fair' evidence 'for' recommending use of the drug	'insufficient' evidence 'for/against' recommending the use of the drug	'fair' evidence 'against' recommending the use of the drug	'good' evidence 'against' recommending the use of the drug	'unclear' evidence
At least one bRCT strongly supported the efficacy of the drug used for IE	At least one bRCT fairly supported the efficacy of the drug used for IE	Studies were supportive (or not) of the use of an AED but bRCTs were not available	At least one bRCT fairly supported the lack of efficacy of the drug used for IE	At least one bRCT strongly supported the lack of efficacy of the drug used for IE	bRCTs presented conflicting results occurred together for the same AED

bRCT(s): blinded randomized clinical trial(s)

Results

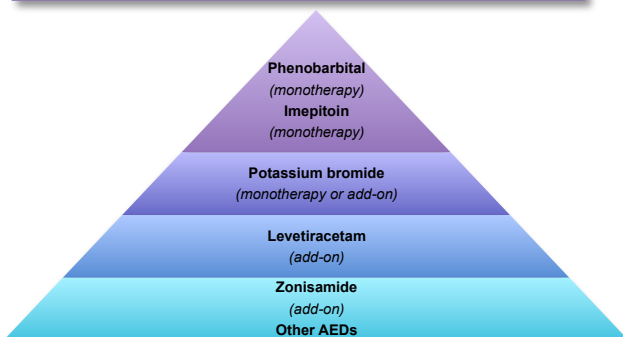
Table 2: Evidence for AEDs' efficacy

Only four bRCTs were detected which were considered to offer the lowest risk of bias and the highest quality of evidence among the 26 final studies. The majority of the studies included small to moderate group numbers of dogs and fairly characterized their inclusion criteria for the diagnosis of IE.

Overall number of studies detected	Total number of studies evaluated after the two-stage screening process	Number of studies with the highest overall quality of evidence	AEDs' efficacy		
			AEDs with good evidence for recommending their use	AEDs with fair evidence for recommending their use	AEDs with insufficient evidence for recommending their use
142	26	4	<ul style="list-style-type: none"> ✓ Phenobarbital (monotherapy) ✓ Imepitoin (monotherapy) 	<ul style="list-style-type: none"> ✓ Potassium bromide (monotherapy) ✓ Levetiracetam (add-on) 	<ul style="list-style-type: none"> ✓ Zonisamide, Gabapentin, Pregabalin, Sodium valproate, Felbamate, Topiramate, Primidone (monotherapy or mainly add-on) ✓ Potassium bromide (add-on), Imepitoin (add-on)

Figure 2: Pyramid of AED hierarchy

Based on the evidence for AEDs' efficacy.



Conclusions & Discussion

- ✓ Oral phenobarbital and imepitoin in particular as well as potassium bromide and levetiracetam are likely to be effective for the treatment of IE in a proportion of dogs.
- ✓ Variations in baseline characteristics of the dogs involved, significant differences between study designs and several potential sources of biases preclude definitive recommendations from the studies evaluated.
- ✓ Only four bRCTs were detected and considered to offer the highest quality of evidence amongst the studies. Thus, there is a need for greater numbers of controlled, adequately sized bRCTs evaluating the efficacy of AEDs for IE.