Epilepsy and movement disorders: new treatments

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The treatment of epilepsy

The barbiturate fenobarbital has been used for many years as an anti-epileptic drug in dogs. Generally spoken, it is effective. Unfortunately, fenobarbital causes quite a number of (unavoidable) side effects. Fenobarbital may cause dullness and somnolence during the first days of treatment. If these side effects do not disappear after a few days, the dose should be reduced. Polyuria and polydipsia are sometimes seen as well as an increased appetite. In a number of animals, the dullness is permanent, and the character of the animal may change. The initial dose of phenobarbital is 2-5 mg/kg bodyweight/per day, divided into 2 to 3 daily doses. The dose can be adjusted after consideration of the clinical effect and the concentration of phenobarbital in blood (20 to 40 mg/litre). Based on several studies investigating the use of the new drug imepitoin the efficacy of fenobarbital is up to 80% (1, 2).
Potassium bromide (it is a salt and not a drug) is probably the oldest anti-epileptic treatment known. The most important advantage of potassium bromide is it effectiveness as an add-on therapy in refractory cases (3-5). Disadvantages are the extremely long t½, and side effect like sedation, dizziness polyuria and polydipsia. However especially in those cases that respond poorly to imepitoin and/or fenobarbital is has proven to be a good add-on (1, 5-7).
As of 2012 imepitoin is also available for veterinary use. It has earned its merits as it has a lower incidence of side-effects compared to fenobarbital (25% versus 40%) but it has a lower efficacy (up to 50%) compared to fenobarbital (up to 80%) (1, 2, 8). Furthermore its use in dogs that cluster may not be prudent as it, according to the author, tends to increase the number of clusters (unpublished data).

For emergency use we tend to use diazepam. The short duration of action makes diazepam an extremely well-suited drug for the treatment of series of seizures (clusters) or status epilepsy. However a recent study revealed that it is not as effective as we think it is and compared to midazolam inferior (9).
There are various other anti-epileptic drugs such as valproin acid, carbamazepine that proofed to be not effective as a monotherapy in dogs because of the very fast resorption and quick elimination of these drugs (3). In a limited number of trials more modern drugs such as zonisamide, levetiracetam, topiramate, gabapentine and pregabalin have been used. In most studies the drugs were used as add-ones and were found to be effective in around 40 to 50% of all treated dogs (10-12).

Of interest are the identification of risk factor for seizures in canine idiopathic epilepsy (13). Some cannot be avoided such as gender (males or young age) but there is proof that oestrus has a disadvantage effect on the number of fits (14). This is not the case for males (15). Having to face a seizure has a dramatic effect on owners (16) with again a negative outcome for the dog. For this reason owners try all kinds of dietary supplements (17) but without any clear indication that they are effective (17). The same applies for the use of essential fatty acids (18) and a ketogenic diet (19, 20) although the latter did improve the behavioral changes that can be observed in dogs with epilepsy (20).

Potential new alternative treatments for canine epilepsy may be the use of cannabidiol although the experience is just anecdotal. However there is a growing number of studies investigating its use is specific types of epilepsies seen in humans (21-23) that merits the investigation of its use in dogs.
Other treatments that are for now unavailable in canine epilepsy are resective surgery as it has turned out to be impossible to properly localise the epileptic focus (24). Promising but again difficult to use and very expensive is deep brain stimulation. Currently both vagal nerve stimulation and transcranial magnetism are being looked at (24).

Movement disorders have a different origin and most likely mode of action and hence other treatments are needed although in some cases dogs with f.i. a PD may respond to anti-epileptics (25). Orthostatic tremor, an action-related postural tremor, may respond to benzodiazepines, fenobarbital or gabapentin (26, 27). The idiopathic head tremor will, in most cases resolve by itself and no treatment has proven to be effective (26). In the case of an action-related kinetic tremor (cerebellar) it is more prudent to find the cause of the tremor than just administer a drug. The same applies for the varies number of peripheral nerve hyperexcitabilities (PNH). Cramps, tetany and tetanus are asking for a proper work-up as they may be metabolic of infectious of origin. Myokymia and neuromyotonia in the JRT has been treated with poor results with sodium-channel blockers (28). Some of the paroxysmal dyskinesia's do respond to treatment with acetozolamide with the CKCS suffering from Episodic Falling as an example (29, 30). However, a recent study of Lowrie and Garosi (2016) clearly demonstrated that PD in both the Labrador and JRT, like EF in the CKCS wears off in time. Furthermore, if the frequency is low it does not merit daily treatment (30).
PD in the Border terrier, most likely a gluten sensitivity, does respond positively to a glutenfree diet (31) which has given rise to social media advertisement of the use of gluten free diets in all kinds of neurological disorders but so far it has only been proven in the Border terrier.

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