CANINE STATUS EPILEPTICUS CARE

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Stefano Cortellini and Luisa de Risio discuss emergency management techniques for a condition that can claim the lives of 25 per cent of afflicted dogs – as the quicker the start of treatment, the better the chances of control

STATUS epilepticus (SE) is a neurological emergency with a mortality of up to 25 per cent in dogs (Bateman, 1999).

SE can be defined as continuous epileptic seizure (ES) activity lasting longer than five minutes, or as two or more ES with incomplete recovery of consciousness interictally.

SE has also been defined as continuous seizure activity lasting for 30 minutes or longer. However, emergency treatment to stop the ES should be administered well before the defined 30-minute time.

The most common type of SE is generalised tonic-clonic status. When this is prolonged, the tonic-clonic clinical manifestations can become subtle, with only small muscle twitching and altered mentation.

This status is called electromechanical dissociation, as continued abnormal electrical activity in the brain persists while the motor manifestations are minimal to absent. In these cases, emergency anti-epileptic treatment is necessary as for tonic-clonic status.

SE can be divided into two stages. The first stage is characterised by generalised tonic-clonic seizures and an increase in autonomic activity that causes tachycardia, hypertension,
hyperglycaemia, hyperthermia and increased cerebral blood flow. The second stage of SE starts after about 30 minutes and is characterised by hypotension, hypoglycaemia, hyperthermia, hypoxia, decreased cerebral blood flow, cerebral oedema and increased intracranial pressure.

Lactic acidosis, hyperkalaemia, hypercarbia and severe myoglobinuria (leading to impaired renal function) can develop secondary to continuous muscle contraction and impaired ventilation.

SE treatment not only requires control of the seizure activity and identification of the underlying aetiology, but secondary systemic effects must also be addressed. Experimental studies suggest that following 15 to 30 minutes of seizure activity, reverberating circuits develop within the brain and ES can become self-sustaining (Manno, 2003). Therefore, the earlier the treatment to stop the seizures is started, the better the chances to control SE and ES in the short and long term.

### Aetiology

SE causes include:

- idiopathic epilepsy (no underlying cause for the ES can be identified and a familial predisposition is presumed);

- symptomatic epilepsy (due to structural forebrain disorders, including brain tumours, infections/inflammations, malformations, trauma and vascular accidents); and

- reactive seizures (“reaction” of the normal forebrain to a systemic insult due to endogenous metabolic causes – such as hypoglycaemia, hypocalcaemia, portosystemic shunt, hepatic/renal diseases or electrolyte imbalances – or exogenous toxic causes, such as metaldehyde, organophosphates, lead and mycotoxins).

In one study (Zimmermann et al, 2009), SE’s prevalence in the veterinary hospital population was 0.7 per cent (114 out of 15,449 dogs), and nearly 30 per cent (114 out of 394) of dogs with ES had SE. The underlying aetiology of SE was idiopathic epilepsy in 37.5 per cent of the dogs, symptomatic epilepsy in 39.8 per cent of the dogs and reactive seizures in 22.7 per cent of the dogs. In this study, dogs with reactive seizures had a significantly higher risk of developing SE as the first manifestation of a seizure disorder than dogs with idiopathic or symptomatic epilepsy.

### Diagnosis

The underlying aetiology of SE should be identified promptly. The history may provide useful information, such as previous diagnosis of idiopathic epilepsy, structural brain disorders, metabolic disorders, suspected toxin intake, ongoing treatment with anti-epileptic drugs (AEDs; such as phenobarbitone – in this case, a blood sample to check phenobarbitone serum concentration should be taken before administering further phenobarbitone) and behavioural, neurologic or other
clinical abnormalities before the onset of SE.

Investigations to reach a definitive diagnosis of the underlying aetiology of SE include haematology and comprehensive serum biochemistry in all dogs. In addition, one or more of the following tests would be appropriate, based on the history and clinical findings: pre and postprandial bile acids, toxicological screening (in dogs with a history of possible toxin exposure), AED serum levels (in dogs on AEDs), serology, coagulation profile, tests for endocrine disorders, urinalysis, abdominal ultrasound, chest radiographs, brain MRI and cerebrospinal fluid (CSF) analysis.

Of course, it is not possible to perform all the above tests in an emergency setting; however, appropriate tests should be performed as soon as possible. The minimum database for the emergency management of dogs with SE includes: glucose, urea, creatinine, packed-cell volume (PCV), total protein (TP) and electrolytes. Samples for toxicological screening (in case of a history of toxin exposure), or AED serum levels (in dogs on AEDs) should be taken. Arterial or venous blood gas will also help to assess and monitor systemic changes caused by the SE.

Emergency treatment

• Stop the seizures

Emergency AED treatment in dogs with SE in which a portosystemic shunt or liver disease is not suspected can include the following approaches.

– Diazepam can be administered IV or per rectum (PR) at 0.5mg/kg to 1.0mg/kg up to three times in 24 hours. The duration of the anti-epileptic effect is about 30 minutes. If the seizures recur, continuous rate infusion (CRI) at 0.5mg/kg/hr to 2mg/kg/hr diluted in five per cent dextrose or 0.9 per cent saline, or a longer-acting AED (such as phenobarbitone) is necessary. An alternative to diazepam is midazolam (0.07mg/ kg to 0.22mg/kg IV or IM) up to three times in 24 hours, and – if seizures persist – as a CRI at 0.3mg/kg/hr to 0.9mg/kg/hr.

– Phenobarbitone at 2mg/kg to 4mg/kg IV may be administered every 20 to 30 minutes to effect (not exceeding 16mg/kg/24hr in dogs already on oral phenobarbitone, and 24mg/kg/24hr in naïve patients). Alternatively, it can be administered at the same dosage IM following the IV diazepam or midazolam.

Phenobarbitone may take up to 30 minutes to reach the brain and exert an anti-epileptic effect. In dogs that appear poorly responsive to benzodiazepine and/or likely to need long-acting AEDs to control the seizure, phenobarbitone 2mg/kg to 4mg/kg IV or IM can be started soon after the first or second administration of diazepam (0.5mg/kg to 1.0mg/kg IV or PR) or midazolam (0.07mg/kg to 0.22mg/kg IV or IM).

If the dog continues to seizure, the following methods can be used.
– Propofol in boluses of 1.0mg/kg to 3mg/kg IV to effect, followed by a CRI at 1.0mg/kg/hr to 3mg/kg/hr to effect. Ventilation needs to be monitored carefully and the clinician should be prepared to intubate and ventilate if needed. The aim of the CRI is to have an awake, seizurefree patient with the minimum dosage of drug infusion. The propofol dose can be decreased by 25 per cent every two hours until the patient is completely weaned and seizure free.

– Inhalant anaesthetic agents such as isoflurane or sevoflurane keep anaesthesia within an adequate plane. The dose of inhalant agent should be reduced by 25 per cent every two hours until the patient wakes up without seizures. Continuous monitoring of cardiovascular and respiratory parameters is mandatory.

For emergency AED treatment in dogs in which portosystemic shunt or liver disease is suspected, use levetiracetam at 60mg/kg slowly IV once in 24 hours (loading dose), or 20mg/kg IV every eight hours. If the dog continues to seizure, levetiracetam can be administered as CRI at 5mg/kg/hr (or higher to effect) IV. Ensure adequate constant monitoring.

• Supportive care

Systemic stabilisation (Table 1) is performed via the following options.

– Airway – check and/or ensure patency, and intubate if necessary.

– Breathing – provide 100 per cent oxygen administration by face mask in conscious dogs that are able to ventilate properly, and by endotracheal tube in unconscious dogs or dogs that severely hypoventilate (PCO$_2$ >55mmHg). Ventilation should be assisted or controlled.

– Circulation – place IV catheter, collect a blood sample and administer IV fluids (such as Hartmann’s solution with 20mmol/L of KCl added). Start IV fluid infusion according to the hydration and volaemic state, and the patient’s predicted losses. Do not use 0.9 per cent NaCl in epileptic dogs on potassium bromide as chloride competes with bromide for renal re-absorption. In dogs with hypovolaemic shock, colloids such as hydroxyethyl starches (5ml/kg IV slowly in 10 minutes, up to three times), can be used. Monitor the response to fluid therapy by clinical evaluation and blood pressure measurements.

– Monitor blood pressure and aim to maintain mean arterial blood pressure at 80mmHg to 100mmHg. This is essential to ensure adequate cerebral blood flow and cerebral perfusion.

– Temperature regulation – if the patient’s temperature is more than 40°C, initiate slow passive cooling (wet towels, fan and/or alcohol sprayed on foot pads or inguinal area), and stop when the body temperature reaches 38.5°C.

• Factors to monitor
– Heart rate, respiration and body temperature.

– Arterial blood gases, SpO\textsubscript{2} and blood pressure.

– Blood glucose, electrolytes, PCV, TP, urea and creatinine.

– AED serum levels in dogs already on AEDs.

– Electrocardiogram (ECG) – myocardial damage can cause arrhythmias up to 72 hours post-stabilisation.

– Urinalysis – monitor urine output and colour (myoglobinuria).

Electrolytes abnormalities should be recognised and treated promptly. Hypocalcaemia should be diagnosed by ionised calcium analysis; this can be measured by most blood gas analysers.

Hypocalcaemia has been defined as calcium plasma levels lower than 5mg/dl (1.25mmol/L), although each analyser has its own range. In critical cases (levels lower than 1.0mmol/L), provide calcium gluconate IV in 20 minutes, at a dose of 0.5ml/kg to 1.5ml/kg. While administering the IV bolus, cardiac activity should be carefully monitored by ECG.

If cardiac toxicity signs are present (bradycardia, widened QRS complexes and widened T waves), the administration of calcium gluconate should be suspended. Calcium plasma levels should be monitored after infusion (q2-4h) or at the reappearance of clinical signs. The underlying disease should be identified and treated (such as eclampsia, renal failure, hypoparathyroidism or ethylene glycol intoxication).

In case of hypoglycaemia (less than 50mg/dl) treatment should be given with dextrose 50 per cent at 1.0ml/kg diluted at least 1:2 in a 10-minute bolus.

Should the patient be unable to maintain adequate glycaemia, start dextrose CRI at 2.5 or five per cent, and check glucose serum levels every one to two hours. An isotonic solution with dextrose 50 per cent should be used.

It is very important to avoid hyperglycaemia, because during decreased cerebral perfusion and O\textsubscript{2} delivery, the increased cellular metabolism and glucose consumption in the brain may lead to lactic acidosis, which worsens neurologic damage. Further diagnostic investigations should be performed to identify the underlying cause of hypoglycaemia (such as insulinoma, paraneoplastic syndrome, infection or hepatic dysfunction).

If clinical signs of intracranial pressure (ICP) are present – such as stupor or coma, abnormal pupil diameter and response to light, or bradycardia with arterial hypertension – administer mannitol
(0.5g/kg to 1.5g/kg IV slowly in 15 to 20 minutes), unless the patient is hypovolaemic or hypernatraemic.

Mannitol has an immediate plasma-expanding effect that reduces blood viscosity and increases cerebral blood flow and oxygen delivery.

This results in cerebral vasoconstriction within a few minutes, causing a rapid decrease in ICP. In addition, the osmotic effect of mannitol reverses the blood-brain barrier osmotic gradient and decreases extracellular fluid volume in the brain parenchyma. Alternatively, in patients that are not treated with potassium bromide, it is possible to use sodium chloride at seven per cent (4ml/kg to 6ml/kg IV in 20 minutes).

However, it is necessary to monitor the electrolytes frequently and continue fluid therapy with isotonic crystalloids.

- Preventing further seizures

Identify the underlying cause for the seizures. If appropriate, start a maintenance AED in a naïve patient (such as phenobarbitone or potassium bromide). In a patient already on AED treatment, adjust this based on serum levels and add in further medications if needed.

References and further reading
