

Guidelines for the management of Seizures

Amalgamation and update of previous policies 7 (Seizure guidelines, ND, 2015) and 9 (Status epilepticus, KJ, 2011)

Seizures can occur in up to 15% of the Palliative Care population. Of these 25-50% will have brain metastases. In the case of patients with primary brain tumours, 30% initially present with a seizure. Seizures are more common in patients with low grade brain tumours and tumours involving the motor cortex and meninges.

Many patients with primary brain tumours or brain metastases may never have a seizure and so the risks of medication for seizure prophylaxis will outweigh any benefits. These guidelines help to address in which patient's seizure prophylaxis should be commenced and which anticonvulsants may be most appropriate.

Aetiology of seizures

In our patients the cause of seizures can be broadly divided into structural and systemic causes.

Structural causes include:	Systemic causes include:
Primary Brain Tumour	Hyponatraemia
Brain Metastases	Uraemia
Brain Abscess	Hypoglycaemia
Bleeding	Hepatic Failure
Radiation Necrosis	Hypoxia
	Medications
	Systemic Infection

Drugs as a cause of seizures

There are a number of ways in which drugs could be implicated in seizure activity. These include;

- Drug withdrawal – including benzodiazepines, alcohol.
- Unable to take usual anticonvulsant – secondary to vomiting, poor swallow, drowsiness.
- New drug interacting with usual anticonvulsant – E. g. dexamethasone and phenytoin.
- New medications in patients without a history of seizures – including antidepressants, antipsychotics (haloperidol, levomepromazine) and tramadol. Also, certain chemotherapy agents including paclitaxel and ifosfamide, can cause seizures

Differential Diagnoses

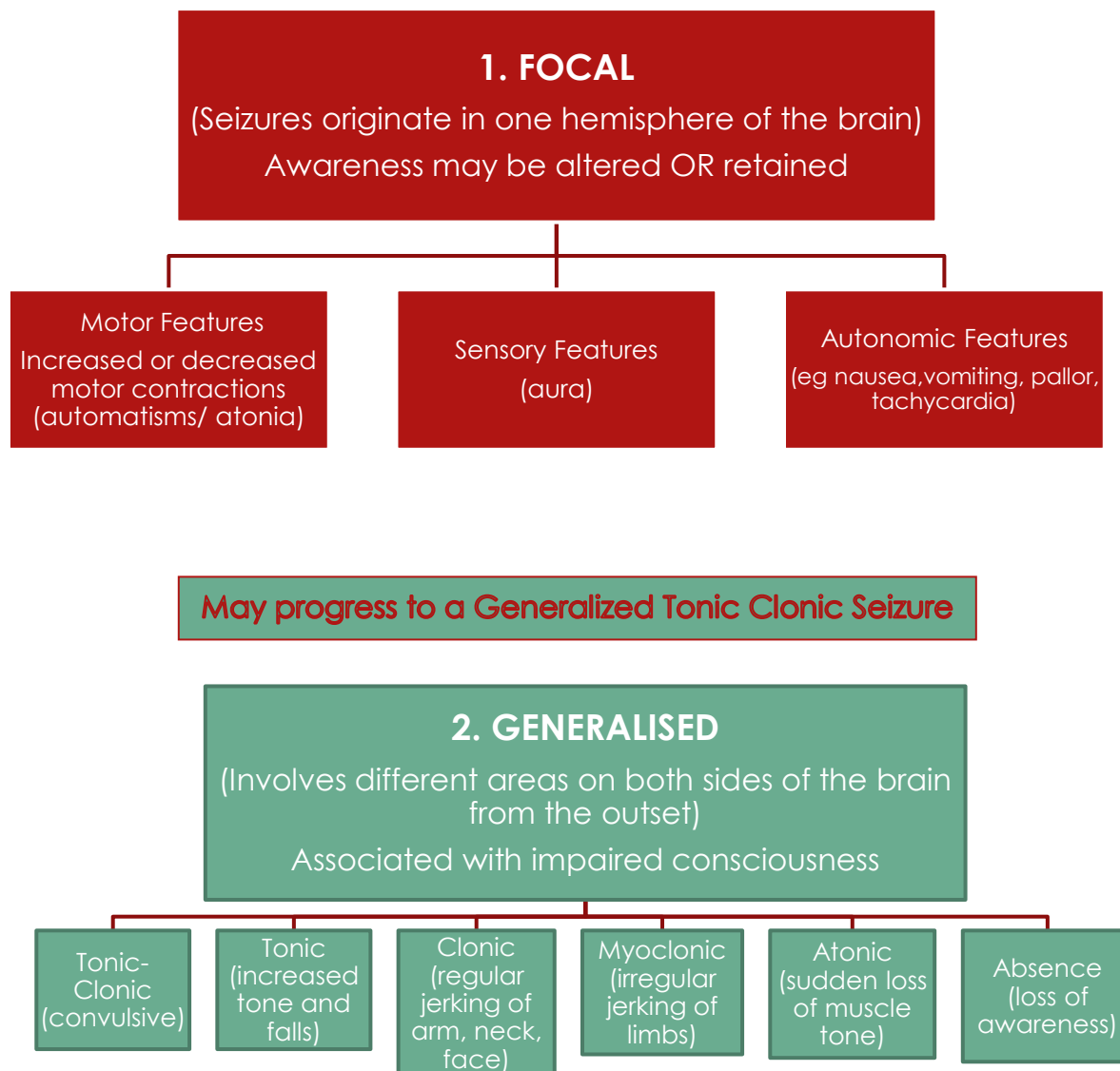
These include post syncope events, rigors, myoclonic jerks (eg from morphine or gabapentin) and tardive dyskinesias.

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Classification of seizures

In recent years the classification system for seizures has been reviewed. This is in part based on neuroimaging findings which may be less relevant to us in palliative care, however it remains important for us to classify seizures in order to aid diagnosis and management.

Seizures are initially classified as focal or generalized, then further classified depending on their clinical features.



Assessment

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Following a seizure, a full history and examination should be performed. Consider checking bloods and transferring for neuroimaging if appropriate.

Patients who have a reversible (non-structural) cause of their seizures should have this treated, therefore anticonvulsant therapy is unlikely to be required.

Initially, high dose dexamethasone and referral for brain radiotherapy should be considered for patients with brain metastases, in addition to an anticonvulsant (see below).

Anticonvulsant Therapy

Patients with a likely irreversible structural cause for their seizures should be commenced on a long-term anticonvulsant following their first seizure, as their risk for a further seizure will persist. There is no evidence for their routine prophylactic use.

By definition, patient's with a structural brain lesion are likely to have focal seizures (but may well progress rapidly to a generalized tonic-clonic seizure) so will respond to broad spectrum anticonvulsants.

Choice of anticonvulsant

This will be an individual decision for each patient dependent on;

- Side effect profile
- Comorbid conditions
- Interactions with other medications

Many anticonvulsants are enzyme inducing drugs. These are best avoided in our patient population because of their interaction with other medications, particularly chemotherapy, benzodiazepines and steroids. Enzyme inducing anticonvulsants include;

- Phenytoin
- Carbamazepine
- Topiramate
- Phenobarbital
- Oxcarbazepine

It is preferable to use monotherapy for control of seizures and to gradually titrate the dose as far as tolerated or until the patient is seizure free. Around 60% of patients will be controlled on the first line anticonvulsant, others may need to try second line medication (there is likely to need to be a cross over period). Seek specialist neurological advice should monotherapy fail.

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Options for first line anticonvulsants

Sodium Valproate

- Indicated for the treatment of focal or generalized seizures.
- Crushable, so may be preferable in patients with a PEG/ RIG.
- Always prescribe the MR form.
- Generally well tolerated and can titrate rapidly.
- Not licensed for SC use however there are reports of using IV Sodium Valproate subcutaneously without ill effects. The ratio PO:SC is 1:1.
- Can also be useful if concurrent neuropathic pain.

Lamotrigine

- Indicated for the treatment of focal or generalized seizures.
- Is usually well tolerated in the elderly as it has a favorable cognitive and behavioral profile.
- However it can worsen myoclonic jerks and cause insomnia.
- The half-life of lamotrigine is prolonged by sodium valproate.

Alternative anticonvulsants

Levetiracetam

- Licensed for the monotherapy of focal seizures.
- Side effects can include low mood or behavioral disturbances.
- Not licensed for SC use but reports do show that it is being used via a syringe driver (or BD boluses), with good effect. The ration PO:SC -1:1 (see acute seizure management guidelines below).

Clobazam

- May be useful to gain control if there are clusters of seizures.

Pregabalin/ Gabapentin

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- Pregabalin is more effective than gabapentin at controlling (focal) seizures.
- Also useful if concurrent neuropathic pain.

Non Pharmacological Considerations

Seizures are frightening and distressing for both patients and their carers.

Treatment should include education of the patient and their family as to the cause and ongoing management of the seizures. Potential problems (eg drug interactions and the risk of seizures if the patient is unable to take oral anticonvulsants) need to also be discussed.

Advance Care Planning discussions should be had with the patient and anticipatory medications be available in the home.

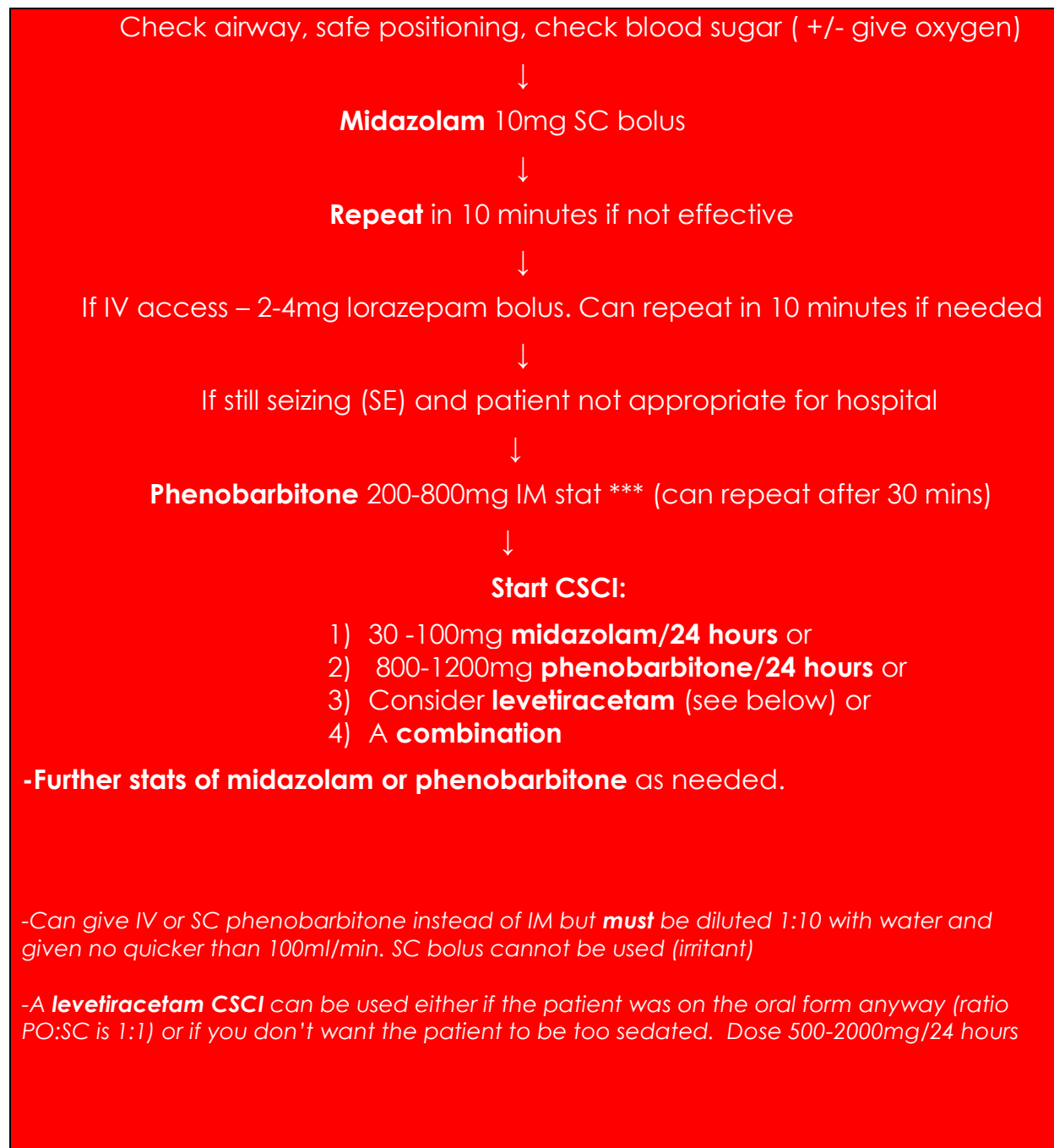
Anticonvulsants in the terminal phase

- Patients should continue oral anticonvulsants as long as they are able to swallow.
- Once they are unable to swallow the regular medication should be substituted with Midazolam 30mg/24 hours CSCI.

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Acute Management of Seizures and Status Epilepticus (SE)

If patient appropriate to transfer to hospital, call 999 and follow steps 1-4



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Once patient more stable:

- 1) consider what the cause might be -investigate and treat as appropriate.
- 2) If brain tumour with oedema, consider increasing/starting dexamethasone (though remember this lowers the plasma concentration of phenytoin).
- 3) Review regular medications, consider checking anti-convulsant levels if appropriate.

Non -Convulsive Status Epilepticus

This is defined as ongoing seizure activity without convulsions for at least 30 minutes, without recovery of consciousness between attacks.

A formal diagnosis requires an EEG however this is unlikely to be appropriate in our patient population.

Clinical features include impairment of consciousness (ranging from mild confusion to coma), aphasia, amnesia, muscle twitching and nystagmus.

If suspected, a trial of treatment with an anticonvulsant, E.g. Sodium Valproate or Midazolam 30mg/24 hours CSCI should be commenced (though no consensus for management at present).

Extra points regarding acute management of seizures

General

- If alcohol or poor nutrition is suspected, consider giving thiamine and vitamin B.
- The clinical signs of seizures can change as they continue -eg reduction in convulsions/ change to non-convulsive status. The later can be difficult to identify. Suspect if jerks stop but patient remains unconscious with hypertonic limbs.

Benzodiazepines

- There is no definite benefit of one benzodiazepine over another, though NICE guidance is as above. Buccal midazolam can be used instead of SC as acts more quickly but not licensed currently for adults.

Phenobarbitone ***

- **The PCF 6 says that the stat IM dose should be 10-15mg/kg. This is a higher initial stat dose than we are used to (100-200mg). The dose to use should therefore depend on the clinical situation. If you think the patient is at high risk of SE, then the PRN dose might need increasing on the drug chart (eg prescribe 200-800mg PRN).**
- The CSCI dosage is 10-15mg/kg (at a rate of no more than 100mg/minute). It is the same protocol as for terminal agitation.
- It cannot be mixed with other medication.

Levetiracetam

- Is less sedating than the benzodiazepines or phenobarbitone. This is being used more often but has not been enough trials and there is no standardised protocol as of yet.

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- It (limited data) can mix with haloperidol, buscopan, midazolam, levomepromazine, methadone, metoclopramide, morphine, oxycodone, ranitidine.
- Consider reducing dose in renal impairment -see PCF 6

References

- BNF and PCF 6
- NICE guidance 2014. Emergency AED therapy for convulsive status
- e ELCA -Management of seizures-update March 2016
- Subcutaneous Keppra for the Management of Seizures at the end of life
Anna Sutherland, BMJ supportive and palliative care-2017
- Seizures in Patients with High Grade Gliomas -a Serious Challenge in the EOL Phase
Sizoo, A short report, BMJ supportive and palliative care, March 14
- Case report -Continuous Subcutaneous Keppra in EOLC. BMJ 2018. Furtado
- SIGN -Diagnosis and Management of epilepsy in adults 2015
- A Rapid Evidence Assessment of the Optimal Phenobarbital Dosage Regime for Management of Intractable Agitation in the Last Days of Life, to Produce a Clinical Guideline. 2018, R Allan et al.
- Guidelines for Seizure Management in Palliative care -Neurologia 2017

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