Anticonvulsants used for Focal Seizures

Focal seizures (now referred to as focal rather than partial) originate in a focal region of the cortex and can be subdivided into those that do not impair consciousness (simple focal) and those that do (focal dyscognitive seizures). Both types of focal seizure can spread rapidly to other cortical areas, resulting in secondary generalised tonic-clonic (GTC) seizures.

Simple focal seizures

- Presentation depends on the site of origin of the discharge - eg, those arising from the motor cortex cause rhythmic movements of the contralateral face, arm or leg (Jacksonian seizures).
- Seizures arising from sensory regions or areas responsible for emotions and memory may produce olfactory, visual or auditory hallucinations, feelings of déjà vu or jamais vu, fear, panic or euphoria.

Focal dyscognitive seizures

- An epileptic seizure that is limited to one cerebral hemisphere and causes impairment of awareness or responsiveness.
- Temporal lobe epilepsy may be simple focal seizures without loss of awareness (with or without aura) or focal dyscognitive seizures (with loss of awareness).

Anti-epileptic drugs used for focal seizures\(^1,^2\)

About two in three adults with new-onset epilepsy will achieve lasting seizure remission on or off anti-epileptic drugs (AEDs), although around half will experience mild to moderately severe adverse effects.\(^3\)

First-line treatment: offer carbamazepine or lamotrigine. Levetiracetam, oxcarbazepine or sodium valproate should be considered if carbamazepine and lamotrigine are unsuitable or not tolerated. If the first AED tried is ineffective, offer an alternative from these five AEDs.

Consider adjunctive treatment if a second well-tolerated AED is ineffective.

Adjunctive treatment: offer carbamazepine, clobazam, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, sodium valproate, perampanel or topiramate as adjunctive treatment if first-line treatments are ineffective or not tolerated.

Other AEDs that may be considered by the tertiary epilepsy specialist are eslicarbazepine acetate, lacosamide, phenobarbital, phenytoin, pregabalin, tiagabine, vigabatrin and zonisamide.

NB: carefully consider the risk:benefit ratio when using vigabatrin because of the risk of an irreversible effect on visual fields.

Interactions\(^4\)

- Interactions between AEDs are complex and may enhance toxicity without a corresponding increase in anti-epileptic effect.
- These interactions are very variable and unpredictable.

Initiation of drug treatment\(^1,^2\)

- AED therapy should only be started once the diagnosis of epilepsy is confirmed, except in exceptional circumstances. AED therapy should be initiated by a specialist.
- Treatment with AED therapy is generally recommended after a second epileptic seizure. AED therapy should be considered and discussed after a first unprovoked seizure if:
  - There is a neurological deficit.
  - The electroencephalograph (EEG) shows unequivocal epileptic activity.
  - The patient considers the risk of having a further seizure unacceptable.
  - Brain imaging shows a structural abnormality.

- The dose of each medication should be titrated slowly to the maximally tolerated dose or the maximum level as recommended in the British National Formulary. The effect may be monitored by patient-recorded seizure frequency.
- Formulations of AEDs are not interchangeable and generic substitution should not be routinely made. Routine switching between different manufacturers of AEDs should be avoided.

Continuation of drug treatment\(^1,^2\)

- Maintain a high level of vigilance for adverse effects of treatment.
- Continuing AED therapy should be planned by a specialist as part of an agreed treatment plan and the needs of the child, young person or adult and their family and/or carers should be taken into account.
If management is straightforward, continuing AED therapy can be prescribed in primary care if local circumstances and/or licensing allow. Adherence to treatment can be optimised with the following:

- Educating children, young people and adults and their families and/or carers in the understanding of their condition and the rationale of treatment.
- Reducing the stigma associated with the condition.
- Using simple medication regimens.
- Positive relationships between healthcare professionals, the child, young person or adult with epilepsy and their family and/or carers.

Regular blood test monitoring is not recommended as routine and should be done only if clinically indicated. Indications for monitoring of AED blood levels are:

- Detection of non-adherence to the prescribed medication.
- Suspected toxicity.
- Adjustment of phenytoin dose.
- Management of pharmacokinetic interactions (e.g., changes in bioavailability, changes in elimination, and co-medication with interacting drugs).
- Specific clinical conditions - e.g., status epilepticus, organ failure and certain situations in pregnancy.

Examples of blood tests include:

- Before surgery - clotting studies in those on sodium valproate.
- FBC, electrolytes, liver enzymes, vitamin D levels and other tests of bone metabolism (e.g., serum calcium and alkaline phosphatase) every 2-5 years for adults taking enzyme-inducing drugs.
- Asymptomatic minor abnormalities in test results are not necessarily an indication for changes in medication.

Management of drug-resistant epilepsy[^1]

- Drug-resistant epilepsy has been defined as failure to achieve sustained seizure freedom after trials of two tolerated and appropriate AED schedules (as monotherapy or in combination). The majority of patients with newly diagnosed epilepsy respond well to AEDs. Failure to do so may be due to:
  - An incorrect diagnosis of epilepsy.
  - An inappropriate choice of AED for the epilepsy syndrome.
  - Failure to take the prescribed AED.
  - An underlying cerebral neoplasm, metabolic condition, or immune process.
  - Concurrent drug or alcohol misuse.

- Given a correct diagnosis of epilepsy, failure to control seizures completely with the first well-tolerated AED is a predictor of drug-resistant epilepsy. Once two AEDs have failed as monotherapy the chance of seizure freedom with further monotherapy is low. Improvement in seizure control may be obtained by combining AEDs.
- A range of different AEDs appropriate to the epilepsy syndrome should be added as necessary in sequence, increasing the dose of each slowly to obtain the best response. It may be worthwhile trying the addition of a small dose of a third AED but it may be necessary to accept the persistence of some seizures.
- Carbamazepine, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, perampanel, pregabalin, topiramate, sodium valproate and zonisamide may be used in the adjunctive treatment of focal epilepsy.
- Failure to respond to appropriate AEDs should prompt a review of the diagnosis of epilepsy and adherence to medication.
- Combination therapy should be considered when treatment with two first-line AEDs has failed or when improved control occurs during the process of phased substitution.

Withdrawal of drug treatment[^1, 2]

- The decision to continue or withdraw medication should be taken after a full discussion of the risks and benefits of continuing or withdrawing AED therapy. Withdrawal of AEDs must be managed by, or be under the guidance of, the specialist.
- The risks and benefits of continuing or withdrawing AED therapy should be discussed when the person with epilepsy has been seizure-free for at least two years.
- Withdrawal of AED treatment should be carried out slowly (at least 2-3 months) and one drug should be withdrawn at a time.
- Particular care should be taken when withdrawing benzodiazepines and barbiturates (may take up to six months or longer) because of the possibility of drug-related withdrawal symptoms and/or seizure recurrence.
- There should be an agreed plan that if seizures recur, the last dose reduction is reversed and medical advice is sought.

Further reading & references

[^1]: Diagnosis and management of epilepsy in adults; Scottish Intercollegiate Guidelines Network - SIGN (2015)
[^2]: Epilepsies: diagnosis and management; NICE Clinical Guideline (January 2012)
[^4]: British National Formulary (BNF); NICE Evidence Services (UK access only)
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