Epilepsy case studies: newer antiepileptics

Trudy Thomas

Epilepsy, the tendency to have recurrent seizures, affects around 600,000 people in the UK. A seizure occurs when there is a sudden burst of intense electrical activity in the brain. Although epilepsy can start at any age, it tends to be more common in those aged under 18 years, when genetic and congenital causes prevail, and in the over-65 age group, when seizures are often a consequence of stroke.

Epilepsy is usually only diagnosed after an individual has had more than one seizure. What happens during a seizure depends on where in the brain the seizure occurs, the function of that part of the brain and how far the seizure activity spreads.

Antiepileptic drugs (AEDs) form the mainstay of the management of seizures. The ultimate aim of AED treatment is seizure freedom with no side effects. Ideally the person’s seizures will be controlled with monotherapy, but dual or polytherapy is sometimes required. It is estimated that 70 per cent of people with epilepsy could be seizure-free if they were able to take their AEDs to maximum effect (currently the figure is probably closer to 50 per cent).

In recent years there has been a significant increase in the number of available AEDs. This article considers some of the newer medicines using a case study approach. Generally these drugs are used as adjunctive therapy in refractory epilepsy where treatment with first-line drugs has failed, or where first-line therapy has resulted in unacceptable adverse drug reactions. These patients require regular specialist review, although pharmacists should not assume that this review is occurring and should ask patients when their specialist appointment is due.

Case study 1

LILY SALTER

AGE: 18 years

PRESCRIPTION: Levetiracetam started four months ago, initially at 250mg daily but gradually increased to 500mg twice daily. Her prescription today is for levetiracetam 500mg at night and lamotrigine 25mg daily, increasing to twice daily after two weeks.

PRESENTATION: Lily has a three-year history of juvenile myoclonic epilepsy (JME). She is currently experiencing an absence seizure every one to two weeks and myoclonic jerks weekly. Her last tonic-clonic seizure was three months ago. The prescription change has been made because Lily has been displaying aggressive behaviour and last week hit her mother. Her mum, Emily, asks if this reduction in dose will stop Lily’s aggression. She also mentions that Lily uses recreational drugs occasionally.
**Discussion points**

JME is an epilepsy syndrome (epilepsy can be classified into syndromes with similar signs and symptoms). JME can occur from the age of eight years, but most commonly arises in the teens or early 20s. People with JME typically experience three seizure types: myoclonic jerks, absences and tonic-clonic seizures. These are all types of generalised epilepsy.

In generalised epilepsy the seizure activity occurs in both sides of the brain at once. The person has no warning and will lose consciousness, albeit in some seizure types, such as absences and myoclonic jerks, for a very brief time. The drug of choice in JME is sodium valproate, however, it would not be used in a person of child-bearing age because of its teratogenic potential (see Keeping risk at bay, p24).

Levetiracetam is a broad spectrum AED that works well in many types of epilepsy. It is currently recommended second line for refractory focal epilepsy. Dosing usually starts at 125mg (half a tablet), although some clinicians will start higher (500mg twice daily) and build up to a maximum of 3,000mg daily if needed.

Levetiracetam is usually well tolerated, however, side effects include anorexia, weight changes, gastrointestinal problems and irritability (often on initiation). Rarely, in some cases this can manifest itself as aggression. The drug benefits from having few interactions in practice and so far appears to have a low rate of teratogenicity compared with other AEDs.

The pharmacist discusses withdrawal of AEDs with Lily and Emily, explaining that lamotrigine is being introduced gradually and the levetiracetam is being slowly reduced to ensure that Lily’s seizures do not worsen. Obviously this means Lily will still have the levetiracetam in her system for some time. The pharmacist also mentions that recreational drugs, particularly stimulants, can trigger seizures and may have contributed to Lily’s aggression. Lily is given a leaflet from one of the main UK charities – Epilepsy Society or Epilepsy Action – which provide more detail and offer advice.

**Case study 2**

**TEGAN MELLORS**

**AGE:** 49 years

**PRESCRIPTION:** Tegretol PR 400mg, two, twice a day; perampanel 4mg daily; clobazam 10mg when required; acetazolamide 250mg one in the morning, one at midday and two at night.

**PRESENTATION:** Tegan has a 20-year history of focal epilepsy in the temporal lobes, which has proved refractory to treatment. She experiences complex focal seizures about three times a week, although her seizure control can be worse around the time of menstruation. She has a body mass index (BMI) of 21 and admits to drinking five to six units of alcohol a day during the week, and more at weekends. Tegan’s consultant has written to her GP suggesting she takes medication for osteoporosis. Tegan enquires whether epilepsy can cause this condition.

**Discussion points**

In focal (also called partial) epilepsy, the person has a small amount of damage (often scarring) in a discrete area of their brain. Where this damage occurs in the brain determines the nature of the seizures that are experienced. This is particularly true of the aura (sensations related to a seizure), which are a feature of this type of epilepsy. Some people with focal seizures remain fully aware during their seizure (sometimes referred to as simple focal epilepsy). Others, while not unconscious, are not aware of what is taking place (sometimes referred to as complex focal seizures).

The Nice guidance recommends carbamazepine or lamotrigine as first line for focal epilepsies. Tegan’s epilepsy is defined as refractory, meaning that treatment is not controlling seizures well or at all. It is likely she will have tried many AEDs over the years. Perampanel is a second line agent, used as an adjunct for focal seizures. Usually given in a dose of 4mg to 12mg once a day, dosing can start at 2mg, increasing by 2mg every two weeks or longer. Side effects include aggression, anxiety, dizziness, sleepiness, changes in appetite, confusion, speech difficulties, balance disorder, blurred or double vision, nausea, back pain, weight gain and risk of falling.

Although an older drug, pharmacists may not be aware of the use of acetazolamide in epilepsy. It is used particularly for epilepsy that is associated with menstruation (catamenial epilepsy), although it can also be used in refractory cases. It must not be used if the person might become pregnant.

Clobazam is used as an adjunct in epilepsy treatment and in refractory epilepsy. It is used in focal epilepsy to ward off a potential seizure if the person is getting sensations indicating that a seizure is imminent. It might also be taken for a number of days around the time of menstruation in catamenial epilepsy.

Some AEDs can lead to thinning of bone. The MHRA has specifically identified carbamazepine, phenytoin, primidone and sodium valproate as being problematic when taken long term. More recent research has shown that levetiracetam can also lower bone mineral density. Women who are at increased risk for other reasons – for example, with a family history or who are underweight – may also require osteoporosis protection.

Tegan’s alcohol consumption may also increase her osteoporosis risk and her risk...
of falling. Drinking more than two units of alcohol in 24 hours can increase the risk of having seizures. Alcohol can interact with some AEDs and may potentiate side effects such as drowsiness and dizziness. The pharmacist tactfully discusses sensible drinking limits with Tegan and the problems associated with drinking and epilepsy. Leaflets are available from both main UK epilepsy charities.

**Case study 3**

**DAVE GREGSON**

**AGE:** 37 years  

**PRESCRIPTION:** Levetiracetam 1,500mg twice daily; Tegretol PR 600mg twice daily; Lacosamide 300mg twice daily.  

**PRESENTATION:** Dave has a five-year history of focal seizures in the frontal lobe following a motor cycle accident. He experiences simple focal seizures once a week, and complex focal seizures every three weeks, which evolve to a tonic-clonic seizure about once every three months. Since starting AEDs, Dave has gained four stone in weight and his BMI is 33. He asks the pharmacist for advice about losing weight and wonders if the 5:2 fasting diet would be suitable. He also asks why his prescription, which used to be for carbamazepine, now says Tegretol.

**Discussion points**

In some people, a focal seizure may sometimes spread to the whole brain, leading to a bilateral generalisation. In some people, a focal seizure may sometimes spread to the whole brain, leading to a bilateral generalisation. In some people, a focal seizure may sometimes spread to the whole brain, leading to a bilateral generalisation. In some people, a focal seizure may sometimes spread to the whole brain, leading to a bilateral generalisation.

Lacosamide is used as adjunctive therapy for focal seizures with and without secondary generalisation. It is usually given in a dose of 200mg to 400mg twice a day. Side effects include nausea, vomiting, constipation, wind, dizziness, headache, impaired co-ordination, drowsiness, tremor, depression, fatigue, abnormal walking, blurred vision, nyctagmus and pruritis.

The MHRA has recently issued guidance on when epilepsy medicines should be prescribed by brand due to issues with variability between manufacturers’ products. Carbamazepine was classified as a category 1, where variability between brands could affect seizure control and so it should be prescribed by brand. Nice guidance recommends that all patients started on carbamazepine should be prescribed the controlled release product.

Some AEDs can promote weight gain. This can be controlled to a degree by diet and exercise and the pharmacist recommends the NHS Live Well website to Dave for advice about this. Some people with epilepsy may experience a seizure if they go without food, so the 5:2 fasting diet (five days eating normally and two days of fasting each week) may be less appropriate. Most people with epilepsy can undertake most types of physical activity, although some types of exercise may not be suitable or require precautions if the person is still having seizures.

**Case study 4**

**GRAEME LEECH**

**AGE:** 24 years  

**PRESCRIPTION:** Retigabine 400mg three times daily, zonisamide 250mg twice daily, sodium valproate 500mg in the morning and 750mg at night.  

**PRESENTATION:** Graeme has experienced focal seizures since infancy. He has been seizure-free for the first time in his life since starting a new agent - retigabine - two years ago, which has resulted in him obtaining his driving licence. Graeme’s consultant would usually like him to stop using retigabine, but Graeme is reluctant to do so as he has tried so many drugs over the years and they make either no difference to his seizures or give him unpleasant side effects. He asks the pharmacist about the risks associated with retigabine. He has also had an itchy skin rash for a few weeks, but his GP said retigabine did not usually cause rashes. Graeme smokes 20 to 30 cigarettes a day and would like to give up and asks about using nicotine replacement therapy (NRT).

**Discussion points**

Retigabine is used as an adjunct to treatment of focal seizures. It has been found to colour skin, lips and nails and can also lead to retinal pigmentation, which may reduce visual acuity. It is not known if this effect is reversible. For this reason, it is recommended only as adjunctive treatment for drug-resistant focal onset seizures with or without secondary generalisation in adults, where other appropriate drug combinations have proved inadequate or have not been tolerated.

A comprehensive ophthalmic examination should be done at the start of treatment and at least every six months thereafter while treatment is ongoing. The pharmacist should confirm that Graeme has this appointment. Retigabine has also been associated with arrhythmias and psychosis. Skin rash is rarer but is a recognised side effect of retigabine.

Zonisamide is another drug used for focal seizures either as monotherapy or in combination with other drugs, with and without secondary generalisation. Skin rash is an indication for withdrawal of zonisamide, and the pharmacist advises Graeme to contact his consultant immediately.

Giving up smoking can be stressful and it would seem sensible to do this when seizures are under control or, in Graeme’s case, once the situation with his skin is sorted. Anecdotally some people with epilepsy report loss of seizure control when stopping smoking suddenly, so a controlled reduction over time may be beneficial. Bupropion is known to cause seizures in approximately one out of every 1,000 people taking it, and the BNF suggests it should be prescribed only if benefit clearly outweighs risk. NRT is considered suitable for people with epilepsy.

**Further information**

- Epilepsy Action: epilepsy.org.uk  
- Epilepsy Society: epilepsysociety.org.uk

**References**

- MHRA. Retigabine (Trobalt): indication restricted to last-line use, and new monitoring requirements after reports of pigment changes in ocular tissue, skin, lips, or nails. 2013. Available online at: www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON296401 (Accessed 04.03.14)
CPD Zone Update

/one.pnum_onum. Around nine people in the UK are affected by epilepsy.

/true or false. The drug of choice for treating juvenile myoclonic epilepsy (JME) is lacosamide.

/true or false. Anorexia, weight changes, gastrointestinal problems and irritability are all side effects of levetiracetam.

/true or false. Perampanel is mainly used for epilepsy associated with menstruation.

/true or false. Long-term use of carbamazepine, phenytoin, primidone and sodium valproate has been associated with osteoporosis.

/true or false. Drinking more than two units of alcohol in four hours can increase the risk of having seizures.

/true or false. Nice recommends that all patients started on carbamazepine should be prescribed a controlled release formulation.

/true or false. Side effects of retigabine include arrhythmias and psychosis.

/true or false. Zonisamide has been found to cause skin, lips and nails.

/true or false. Nicotine replacement therapy is contraindicated in patients taking AEDs.

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Take the 5 Minute Test

1. Around 900,000 people in the UK are affected by epilepsy.
   True or false?
2. The drug of choice for treating juvenile myoclonic epilepsy (JME) is lacosamide.
   True or false?
3. Anorexia, weight changes, gastrointestinal problems and irritability are all side effects of levetiracetam.
   True or false?
4. Perampanel is mainly used for epilepsy associated with menstruation.
   True or false?
5. Long-term use of carbamazepine, phenytoin, primidone and sodium valproate has been associated with osteoporosis.
   True or false?
6. Drinking more than two units of alcohol in 24 hours can increase the risk of having seizures.
   True or false?
7. Nice recommends that all patients started on carbamazepine should be prescribed a controlled release formulation.
   True or false?
8. Side effects of retigabine include arrhythmias and psychosis.
   True or false?
9. Zonisamide has been found to cause skin, lips and nails.
   True or false?
10. Nicotine replacement therapy is contraindicated in patients taking AEDs.
    True or false?

Tips for your CPD entry on epilepsy

Reflect Which type of epilepsy is acetazolamide used to treat? What are the side effects of lacosamide? Which aids for stopping smoking are most suitable for patients taking antiepileptic drugs?

Plan This article discusses some of the newer antiepileptic drugs available using a case study approach. It includes information about different types of epilepsy, the side effects and monitoring required of newer drugs and advice that pharmacists can give about weight loss, exercise and stopping smoking for those taking antiepileptic medication.

Act Read the Update article and the suggested reading (below), then take the 5 Minute Test (above). Update and Update Plus subscribers can then access their answers and a pre-filled CPD logsheet at chemistanddruggist.co.uk/mycpd.

Find out more about epilepsy from the NHS Choices website tinyurl.com/newaeds1

Revise your knowledge of the medicines used to treat epilepsy from the BNF section 4.8 Antiepileptic drugs

Read the MUR tips for epilepsy on the C+D website tinyurl.com/newaeds2

Read the advice for patients with epilepsy about sport participation on the Epilepsy Research website and drinking alcohol on the Epilepsy Action website tinyurl.com/newaeds3 tinyurl.com/newaeds4

Find out about charities that provide help and useful information for patients with epilepsy and their carers.

Evaluate Are you now confident in your knowledge of the newer drugs available for treating epilepsy? Could you give lifestyle advice to patients taking antiepileptic medicines?

ASK THE EXPERT

April is neurology month and our expert is on hand to answer your queries. From neuropathic pain to Alzheimer’s disease, submit your questions by email: pooja.sisodia@ubm.com

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