Modern management of epilepsy

JP Leach, consultant neurologist and honorary associate clinical professor; H Abassi, SpR in neurology Southern General Hospital, Glasqow G51 4TF

Introduction

Epilepsy is one of the most common neurological conditions, affecting around 0.5–1% of any given population. It accounts for 2–3% of admissions to acute general medical services. The outlook for newly diagnosed epilepsy remains good for most people. Around 65–70% of patients will attain longterm seizure freedom with the first or second antiepileptic drug (AED) tried.¹

The past 20 years have seen marked changes in epilepsy management. Publications from the Scottish Intercollegiate Guidelines Network (SIGN) and the National Institute for Health and Clinical Excellence (NICE) have provided clear guidance on many aspects of epilepsy care. These have proved powerful in driving changes in the infrastructure for managing epilepsy at all stages across the UK, albeit patchily in some areas.

Diagnosis

Epilepsy is defined as a disorder in which there is a tendency to have unprovoked seizures. The cornerstone of the diagnosis is a history from the patient and witnesses.

In the past, a lack of neurologists and epileptologists in the UK was associated with the misdiagnosis and mistreatment of epilepsy in many patients.² The 1990s saw a rapid expansion in the number of neurologists in the UK, many of whom had specific training in epilepsy, and this led to the evolution of epilepsy-specific clinics. In keeping with SIGN3 and NICE (2004 and 2012)4 guidance, a dedicated First Seizure Clinic allows for better diagnosis of epilepsy, more accurate classification, and differentiation from mimics such as cardiac arrhythmias, syncope and pseudoseizures. Such clinics can also provide appropriate counselling and investigation of patients sustaining a single seizure. They should be rapidly accessible, ideally within two weeks of the episode.

The terminology of epilepsy has changed slightly in recent years,⁵ and it is hoped that the next few years will finally see the end of terms such as 'grand mal' and 'petit mal' for description or classification of seizures. Seizure nomenclature should reflect clinical features and the underlying pathology. This aids communication between clinicians and allows better monitoring of changes in individual seizure patterns. Seizures and

epilepsy may be best considered to be 'focal' where the origin is a localised disturbance, or 'generalised' where the underlying problem is a widespread change, eg genetic syndromes such as juvenile myoclonic epilepsy. Such classification may not be apparent or available at the first visit and may require the passage of time or some further investigation.

Investigation

First seizure

Anyone who experiences a loss of consciousness should undergo ECG. Where seizure is suspected, cranial imaging should be carried out. MRI achieves the best pickup rates, but CT will exclude an intracranial space-occupying lesion. The guidelines state that EEG should only be carried out where there is no doubt that there has been an unprovoked seizure:3,4 this tool should not be used to exclude seizure as it is insufficiently sensitive or specific. Where there are recurrent episodes of dubious origin (eg myoclonus or 'blank spells') then capturing EEG during these can be of diagnostic value. This may require ambulatory or video EEG. Where there has been a definite seizure, EEG can help to provide prognostic information; where EEG shows epileptiform activity, this may signify higher risk of recurrence in that individual and may increase the use of AED treatment following a first seizure.

Table 1. Information needs for people with epilepsy.

General information What epilepsy is, cause, explain investigations, seizure

classification, syndrome, epidemiology, prognosis, genetics and sudden unexplained death in epilepsy

(SUDEP)

Anti-epileptic drugs Choice of drug, efficacy, side effects, adherence,

interactions, free prescriptions

Seizure triggers Sleep, alcohol, drugs, stress, lights

First aid General guidelines, status

Issues for women Oral contraceptive pill, pre-conception, pregnancy and

breastfeeding, menopause

Lifestyle Driving, employment, education, leisure, relationships,

safety in the home

Possible psychological

consequences

Stigma, memory loss, depression, anxiety, maintaining

well being, self-esteem, sexual difficulties

Support organisations

New epilepsy

All patients who have had two or more unprovoked seizures should have an ECG at time of diagnosis. The guidelines promote imaging in all adults with new-onset epilepsy, but children should also be imaged if their seizures are focal. The role of the EEG in established epilepsy is to provide classification information, which informs treatment choice. It is highly unlikely that epilepsy beginning after the age of 35 will be of generalised type, so EEG should be reserved for patients whose seizures began before their mid-thirties.

Modern digital recording techniques allow prolonged EEG recordings, often with accompanying video that may improve diagnostic yield. Use of ambulatory EEG, home video EEG or video telemetry can be helpful in obtaining certainty about the nature and origin of the events.

Established epilepsy

Once the patient has been fully controlled for 12–18 months, they can be referred back to their GP for continuing care. Of course, re-referral should occur if there are breakthrough seizures, concerns about adverse effects, possibility of planned pregnancy or a question of AED withdrawal.

If the patient is refractory to treatment, it is important to review the diagnosis and classification of epilepsy.6 There are a number of reasons why patients with epilepsy might not respond to drugs, including misdiagnosis and misclassification with resultant use of the wrong AED. Further investigation (repeat imaging using highdefinition MRI and/or capturing an event on EEG) might allow treatment and outcomes to be improved. For other patients, poor AED compliance and lifestyle issues such as exposure to alcohol or drugs can contribute to incomplete response. The risk of harm, including death, as the result of seizures should ensure that patients are referred for specialist care if their seizures are a threat to life or quality of life.

Treatment

The number of AEDs has increased markedly in the past 20 years. In fact, the list has become bewildering and complex for the non-specialist. Treatment is usually recommended only after there have been two or more unprovoked seizures within a period of about 12 months or so, and should only be commenced if there is certainty about the diagnosis. There is little to be gained from hasty initiation of treatment or a 'trial of treatment', and the passage of time will allow both the patient and their doctor to review clearly the need for treatment.

Most patients will become seizure free on the first or second monotherapy.¹ The initial drug choice should be made with regard to seizure classification, possibility of interactions, possibility of future pregnancy, adverse effect profile, and rapidity of action. The choice of AED should be made

Key points

Diagnosis of epilepsy should be done in specialist clinic

EEG is only useful for classification

Around two-thirds of patients with epilepsy become seizure free with their first or second anti-epileptic drug

Status epilepticus has significant mortality and requires rapid intervention

Management of epilepsy requires a multidisciplinary approach

KEY WORDS: epilepsy, classification, diagnosis, treatment

in an appropriate specialist setting; there is no role for phenytoin in outpatient management of newly diagnosed epilepsy.^{3,4} The newer drugs have similar efficacy to their older counterparts, but have fewer pharmacokinetic, and tolerability problems, making them more attractive and useful in the long term.^{3,4}

The SANAD study suggested that for patients with focal epilepsies, lamotrigine is the best tolerated AED.⁷ For those with generalised epilepsies, valproate might offer the best efficacy, although there are caveats about its use in women who might become pregnant.⁸ The SANAD II study is due to start imminently and will investigate levetiracetam for both focal and generalised onset of epilepsy.

Information

Many aspects of life are affected by a diagnosis of epilepsy (Table 1). The guidelines provide a wide array of information domains and their discussion with patients takes time, experience and tact. A consultation with an epilepsy nurse might be required to cover all of these issues in enough depth. Space will not permit us to look at all these areas here, but a comprehensive list is provided in SIGN guideline number 70.³ Patients should be given an idea of future prognosis that will allow informed future treatment choices.

Follow up

The effects of epilepsy and its treatment mean that anyone with ongoing refractory epilepsy merits follow up at a clinic run by someone with expertise in epilepsy^{3,4} and anticipation of future pharmacodynamic or pharmacokinetic interactions.

Acute management

Despite the burgeoning number of AEDs, the drug treatment of acute seizures has remained largely unchanged (Fig 1). The vast majority of seizures will not last more than 2 minutes. Seizure activity that is sustained for 15 minutes or more satisfies the definition of status epilepticus and should be managed aggressively to avoid further complications.^{3,4} Benzodiazepine treatment should be used in the first instance, but intravenous preparations of AED should be administered if the effect is not immediate or sustained. Management in an intensive therapy unit (ITU) should be an early resort where the seizures continue or where there is respiratory or metabolic compromise.

In patients with a previously treated epilepsy, it is important to try to ascertain whether there has been a primary cause of the exacerbation, such as intercurrent infection, a drop in AED levels, or exposure to alcohol or illicit drugs. Replacement of usual AEDs, provision of thiamine and treatment of any infection will be needed by such patients. In severe cases, electrolyte disturbance might also need to be corrected.

Summary

The expected quality of care for epilepsy has increased sharply in the last two decades, informed and directed by published guidance. Meeting these demands has become possible only by providing adequate numbers of consultants and nurses with the relevant expertise, alongside improvements in investigative facilities. The increasing choice of AEDs has been helpful in improving treatment options. Both primary and secondary care have an important role to play in easing diagnosis of new cases and highlighting cases where improvement in control are needed.

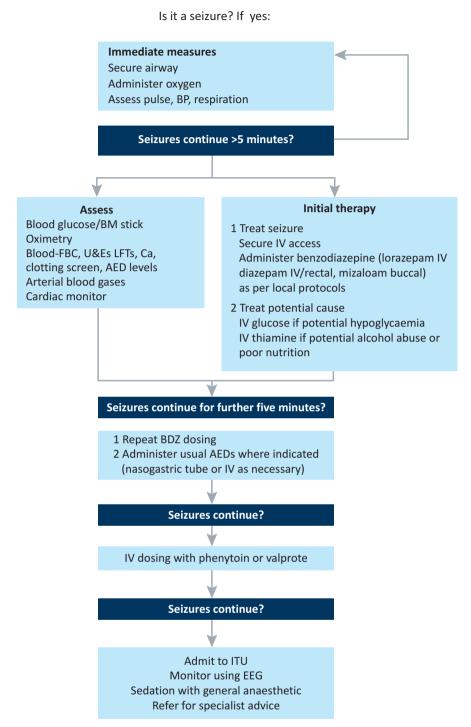


Fig 1. Management of status epilepticus. BDZ = benzodiazepine; Ca = calcium concentration; FBC = full blood count; IV = intravenous; LFT = liver function test; U&Es = urea and electrolytes.

References

- Kwan P, Brodie MJ. Early identification of refractory epilepsy. New Engl J Med 2000;342:314–9.
- 2 Smith DF, Defalla BA, Chadwick DW. The misdiagnosis of epilepsy and the management of refractory epilepsy in a specialist clinic. QJM 1999;92:15–23.
- 3 Scottish Intercollegiate Guidelines Network. Diagnosis and management of epilepsy in adults. SIGN guideline no. 70, 2003, updated 2005. www.sign.ac.uk/guidelines/fulltext/70/index.html [Accessed 10 January 2013].
- 4 National Institute for Health and Clinical Excellence. *The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care.*NICE clinical guideline 137. London: NICE, 2012. http://publications.nice.org.uk/theepilepsies-the-diagnosis-and-management-of-the-epilepsies-in-adults-and-children-in-primary-and-cg137 [Accessed 10 January 2013].
- 5 Berg AT, Berkovic SF, Brodie MJ et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 2010;51:676–85.
- 6 Leach *JP*. When the antiepileptic drugs are not working. *Pract Neurol* 2009;9:27–32.
- Marson AG, Al-Kharusi AM, Alwaidh M et al. The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblinded randomised controlled trial. *Lancet* 2007;369:1000–15.
- 8 Marson AG, Al-Kharusi AM, Alwaidh M et al. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. Lancet 2007;369:1016–26.

Address for correspondence: Prof JP Leach, Institute of Neuroscience, Southern General Hospital, Glasgow G51 4TF. Email: johnpaul.leach@ggc.scot.nhs.uk