Managing mood problems in elderly patients with epilepsy

Epilepsy is more common in elderly people than it is in younger age groups. Yet, its recognition in older people is hampered by atypical presentation and non-specific symptoms. Mood problems frequently occur in elderly patients in relation to epilepsy, especially depression and anxiety. Treatment of these symptoms may have a greater impact on quality of life than reducing seizure frequency.

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Epilepsy is common in old age with a prevalence of 1.5% in those over 65 years, and the incidence continues to rise with age. Because new-onset epilepsy in old age is more likely to involve focal seizures symptoms can easily be mistaken for those of syncope, transient ischaemic attacks (TIAs), or acute confusional states. Epilepsy in old age is more likely to be secondary to other brain related disorders (symptomatic epilepsy).

The commonest cause of symptomatic epilepsy in this age group is stroke, either acute or chronic, due to haemorrhage or infarction. Other causes are metabolic (hypo- or hyperglycaemia, hypo- or hypernatraemia, hypocalcaemia, uraemia, or liver failure), brain trauma, sepsis, alcohol withdrawal, and space occupying lesion. Alzheimer’s disease also seems to be associated with epilepsy, particularly in early onset Alzheimer’s and in those six years or more from diagnosis of Alzheimer’s. Clearly many of these conditions predisposing to epilepsy can cause can cause cognitive impairment.

New-onset epilepsy in this age group often responds well to treatment, with around 70% of patients becoming seizure free on mono or dual therapy. Neuropsychiatric complications of epilepsy are common, and evidence suggests that addressing them is more important to health related quality of life than reducing seizure frequency or severity unless full seizure remission could be achieved. Hence early recognition and treatment of conditions such as anxiety or depression in people with epilepsy may contribute to improved quality of life. Furthermore it may reduce frequency of use of healthcare facilities and could have an impact on the up to 32-fold increase in risk of suicide in patients with epilepsy and depression compared with non-epileptic controls. Older patients with epilepsy may be subject to an even greater risk of suicide as the incidence of suicide generally increases with age. The most common neuropsychiatric complications of epilepsy are depression (20% in a community sample, 30% in a primary care sample and 50% in tertiary care sample) and anxiety (10% in community and 40% in a sample of patients with refractory epilepsy). Other common neuropsychiatric problems associated with epilepsy in elderly include psychosis, cognitive problems, personality changes and non-epileptic attacks. Non-epileptic attacks resemble seizures but they are not caused by epileptiform activity in the brain. Some may have a physical cause, but this is frequently not the case and they are thought to be due to psychological factors. In this paper, we will focus on affective disorders, including depression and anxiety.

Depression

Depressive episodes in patients with epilepsy sometimes have a temporal relationship with the patient’s seizures. They may occur over a few days or hours preceding...
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a seizure (pre-ictal), during a seizure (ictal), or in the seven or so days following a seizure (post-ictal). Patients with epilepsy can also have depressive episodes that do not have a temporal relationship with seizures (interictal).

Patients with epilepsy often do not fit ICD-10 or DSM-IV criteria for depressive disorder neatly and may have more atypical symptoms. For example, pre-ictal depression may take the form of irritability rather than low mood; and in ictal depression, which is a manifestation of seizure activity, symptoms such as anhedonia, feelings of guilt and suicidal ideation are common. Suicidal ideation will generally be brief, stereotypical and occur in the absence of the full syndrome of depression.

Interictal depression may take the form of a dysphoric syndrome with irritability, anhedonia, hopelessness, fear and anxiety, agitation, impulsive self-harm, and psychotic phenomena occurring more frequently than in depression in people without epilepsy. Blumer has described brief periods of subclinical dysthymia-like episodes occurring in inter-ictal phases, which tend to respond to antidepressant medications. He calls this condition “interictal dysphoric disorder”.

The features of depression may be either masked or mimicked by the effects of epilepsy or antiepileptic drugs. Somatic symptoms of depression, such as sleep disturbance, appetite, concentration and changes in levels of energy, may be less helpful in diagnosing depression because of the overlap with the common side effects of antiepileptic drugs (AEDs) and symptoms of epilepsy. Psychological features such as lack of interest, anhedonia and depressive cognitions may be more helpful pointers towards depression because they are unlikely to be due to side effects of medication or epilepsy. Screening instruments may help with early detection and referral for management. Specifically validated tools such as the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) for screening depression in epilepsy may help with diagnosis.

Box 1: A case study

Over the past few months, a 66-year-old woman with a long-standing history of epilepsy has started to have more frequent seizures. She has presented to A&E departments on a few occasions and was recently admitted to the neurology ward following a cluster of seizures. She has been feeling constantly “low and tearful” for the last three months, with her low mood becoming worse after her favourite nephew moved abroad. She avoids any communication with her remaining family and has become socially withdrawn. She complains of difficulties with her memory, which fluctuate in intensity but are persistent. As a consequence, she has not been able to do usual daily tasks.

She showed evidence of intermittent bursts of spikes and slow waves on ECG between seizures. A MRI brain scan was normal with no white matter changes that are consistent with cerebrovascular disease or evidence of atrophy. Blood tests, including FBC, U&E, liver function tests, thyroid function tests, serum glucose and B12 and folate, were normal. Neuropsychological assessment confirmed impairment in the domains of working memory, speed of information processing and visual and verbal memory, but no other impairment of higher brain functions. Additionally, she showed evidence of sustained depressed affect with loss of interest, anhedonia, reduced socialisation and depressive cognitions (such as hopelessness and death wishes).

The patient’s cognitive impairment may have been caused by a combination of interictal bursts of epileptiform discharges, depression, and the impact of antiepileptic drugs. A number of factors contributed to her low mood including the deterioration in her health, a sense of loss of control due to the unpredictable nature of her seizures, and the departure of her nephew. During the recent neurology admission, the dose of sodium valproate (which she was already receiving) was increased and she was given clobazam (Frisium). Her seizures responded well to this treatment.

She was also treated successfully with sertraline 100mg once daily. Her mood lifted further when she noticed improvements in her memory.

Although this case report is based on clinical experience and reflects common scenarios encountered, the patient described above is fictitious.
Ictal depression, being a manifestation of the seizure, should be treated by optimising seizure control. Pre- and post-ictal depressive symptoms are usually self-limiting and in our opinion, optimising seizure control may be beneficial as there is no evidence that antidepressants are effective in these conditions. The only exception would be when post-ictal depression appears to be lowering the seizure threshold or it is rather prolonged and distressing; in which case, the addition of a low dose of antidepressant might be appropriate (based on clinical experience).

Treatment of interictal depression should follow the biopsychosocial approach used in non-epileptic patients (ie, explored, social and biological factors should be explored and addressed simultaneously). Psychosocial issues specific to this patient group might be family history of depression, stigma associated with having epilepsy, learned helplessness, and lack of social support. Patients with frequent seizures and prominent memory problems may not be suitable for cognitive behavioural therapy (CBT) as CBT requires an ability to recall and re-examine thoughts, feelings and behaviours to challenge automatic negative responses.

Before commencing treatment, potential biological causes of depression should be ruled out as should iatrogenic causes, such as antiepileptic drugs (AEDs). In particular, phenobarbital, primidone, topiramate and tiagabine have been reported to lower mood and folate depletion. Once potentially reversible causes have been addressed, it may be possible to choose an AED with mood stabilising qualities, such as sodium valproate, carbamazepine, or lamotrigine. However where a patient is stable on medication, it may be preferable to add in an antidepressant rather than risk a change in AED.

Generally, doctors have been reluctant in the past to prescribe antidepressants in epilepsy due to fear of lowering the seizure threshold and thereby increasing seizure frequency. Certainly drugs such as clomipramine, amitriptyline, dosulepin, maprotiline and bupropion, which significantly lower seizure threshold, should be avoided. However, newer antidepressants, such as SSRIs, have been shown to have a very low risk of lowering seizure threshold (0.1–1%) and this risk should be balanced against the risk of depression lowering the seizure threshold, the effect of the depressive episodes on patients’ quality of life and the significantly increased risk of suicide in patients with epilepsy and depression.
One study showed sertraline to be both effective and safe up to a daily dose of 200mg. Another study found mirtazepine, citalopram and reboxetine to be safe and effective. Although moclobamide does not increase the risk of seizure, it is used less frequently due to the necessary restrictions on co-prescribing and diet. Venlafaxine may have a slightly higher risk of lowering seizure threshold and should be avoided as a first-line treatment.

In addition to concerns about pro-convulsive effects of antidepressants, there is the possibility of pharmacodynamic interactions with AEDs: some antidepressants affect the activity of the P450 isoenzymes involved in metabolising AEDs. Fluoxetine, fluvoxamine and sertraline may decrease the metabolism of phenytoin and carbamazepine. Paroxetine may also reduce the metabolism of phenytoin.

In the case of sertraline, this is dose related. As a consequence, it may be advisable to monitor AED levels while introducing an antidepressant. The AEDs phenytoin, carbamazepine, phenobarbital and primidone are known to induce cytochrome P450 isoenzymes, which may cause a reduction in imipramine and clomipramine levels.

One should also be aware that sedation and cognitive impairment, as side effects from antidepressants and AEDs, can be additive. These may also need to be taken into consideration when choosing medication.

### Anxiety

Anxiety in patients with epilepsy may occur on its own or in conjunction with depressive symptoms. Up to three quarters of epilepsy patients with depression also meet criteria for an anxiety disorder. As with depression, anxiety can more difficult to identify in patients with epilepsy. More discriminating symptoms might be altered sleep pattern, a feeling of tension, subjectively impaired intellectual function and physical symptoms, such as palpitations and urinary frequency. Panic attacks are common, perhaps as prevalent as 21%, and can be hard to distinguish from ictal fear, which is experienced as the sudden onset of fear with no precipitant cause and is a manifestation of partial seizure activity. It, however, is usually brief (less than 30 seconds) and there may be other indications of seizure activity, such as a coincident brief period of confusion or automatisms. In contrast, a panic attack might last as long as 20 minutes and there would generally be autonomic features such as sweating, palpitations and shortness of breath.

Between seizures, patients may exhibit phobic anxiety, particularly for places where attacks have occurred in the past, or they may be agoraphobic with an underlying fear of having a seizure in public. All these conditions can have a profound impact on a patient’s ability to live a normal life.

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**Table 1: Differentiating between panic attacks and temporal lobe seizures**

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<thead>
<tr>
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<th>Panic attack</th>
<th>Temporal lobe seizure</th>
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<tbody>
<tr>
<td>Alertness</td>
<td>Usually alert</td>
<td>May diminish with evolution of seizure</td>
</tr>
<tr>
<td>Length of attack</td>
<td>5–20 minutes</td>
<td>Less than 120 seconds</td>
</tr>
<tr>
<td>Déjà vu, olfactory hallucinations</td>
<td>Very rare</td>
<td>More than 5%</td>
</tr>
<tr>
<td>Autonomic symptoms</td>
<td>Rare</td>
<td>Common with evolution of seizure</td>
</tr>
<tr>
<td>Changes on sleep-deprived inter-ictal EEG</td>
<td>Unusual</td>
<td>Often</td>
</tr>
<tr>
<td>Changes to temporal lobe on MRI</td>
<td>Rare</td>
<td>Often</td>
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Adapted from Handal et al.10
Treatmet

Ictal anxiety, like ictal depression, is part of the seizure semiology or aura. Its treatment is optimisation of seizure control.

Inter-ictal anxiety disorders, such as panic disorder and phobias, should be managed as in non-epileptic patients. Non-pharmacological management such as anxiety management, relaxation techniques and CBT should be considered the first-line treatment. Pharmacological options include use of antidepressants such as SSRIs particularly sertraline, for which there is good evidence of efficacy in anxiety disorder, or use of drugs, such as pregabalin or clobazam. Neurologists may be more familiar with and hence be more comfortable with using pregabalin or clobazam, particularly if these drugs may help optimise seizure control.

Because of the risk of dependence and withdrawal seizures, benzodiazepines should generally be avoided except for clobazam, which is commonly used for seizures and has a positive effect on anxiety symptoms.

Conclusion

Epilepsy is common in older patients, though due to the frequency of atypical presentations with multiple problems it can be difficult to diagnose. The identification and treatment of mood problems is an important part of management and may have a more significant impact on quality of life than a sole focus on reducing seizure frequency. Psychotropic medications can and should be used in these patients where necessary, but care must be taken when choosing which one due to the potential for lowering seizure threshold, pharmacodynamic interactions with AEDs and the possibility of additive side effects, especially sedation and cognitive impairment. According to the 2004 NICE guidelines for epilepsy, all new-onset epilepsy patients should be seen by a specialist, irrespective of age, as a matter of urgency. Many patients with mild-to-moderate depression or anxiety with epilepsy could be treated in primary care or by neurologists. Patients with more complicated presentations such as those with multiple neuropsychiatric comorbidities should be reviewed by specialists (neuropsychiatrists or old age psychiatrists) who are best placed to advise about management and who can provide access to other multidisciplinary team members.

References

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