tolerated, although it occasionally causes irritability. In a study of 34 older patients with poststroke epilepsy, levetiracetam rendered 82% seizure free, whereas 20% had side effects.[10] Oxcarbazepine is related to carbamazepine and is likely to replace it in the future because it does not require serum level monitoring or surveillance blood work; however, it can cause hyponatremia. It has some mood-stabilizing properties that can be advantageous and was moderately well tolerated in a prospective open-label study of a small subgroup of elderly patients.[11]

Although they did not investigate efficacy in the elderly, there are a few comparative efficacy studies in the adult population that help select among AEDs. The seminal Veteran's Administration Cooperative Study[12] found carbamazepine and phenytoin to be better tolerated and generally more effective for partial seizures than phenobarbital and primidone (a drug rarely used now). While it is unlikely that one of these AEDs would be selected as a first choice today, it substantiates the contemporary wisdom that phenobarbital is less well tolerated. The Standard and New Antiepileptic Drugs (SANAD) study is the only large prospective study of multiple AEDs for treatment of partial seizures, although it is an open-label study.[13] Lamotrigine was generally the most efficacious with regard to time to treatment failure (defined as time to switching drugs for side effects or ineffectiveness) compared to carbamazepine, gabapentin, oxcarbazepine, and topiramate, but carbamazepine had the shortest time to a 1-year remission. This is generally interpreted to suggest that lamotrigine is the most efficacious drug. An alternative interpretation is that it might be logical to start with carbamazepine because those who tolerate it have the shortest time to remission; however, this requires great vigilance for side effects and, if present, to quickly move to lamotrigine. A complementary SANAD study of valproate, lamotrigine, or topiramate for generalized or unclassified seizures found valproate had a better time to treatment failure than topiramate, and shorter time to 1-year remission than lamotrigine, thus concluding that valproate is generally preferable for generalized seizures.[14] The SANAD studies have several limitations but these are somewhat ameliorated by the large number of patients in each trial; 1,721 patients in the partial seizure study and 716 in the generalized seizure study.

Summary

Treating seizures and epilepsy seems more intimidating today because there are so many AEDs to choose from. However, most second-generation AEDs are well tolerated, have few drug interactions, and are seemingly nearly equally efficacious, thereby making it more difficult to choose the wrong AED. Knowing a few principles of AED treatment will allow clinicians to select the appropriate AED based on a few comparative effectiveness studies, and the knowledge of unique properties of AEDs, which suggest certain specific AEDs are better in patients with specific characteristics, especially based on age, comorbid depression, migraine, chronic pain, and obesity. A logical next step in management of the current case is to reduce lamotrigine to a tolerated dose. If seizures do recur, select another agent from among those previously reviewed.

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QUESTION-AND-ANSWER SESSION

Q: Would it make sense in this case to simply substitute an extended-release lamotrigine preparation rather than moving on to an alternative drug given that the toxicity described is clearly a peak level effect?

Dr. Fountain: Switching to an extended-release preparation of lamotrigine would be a logical strategy, although I suspect the patient is very close to the maximum tolerated dose of lamotrigine because "encephalopathy" for 90 minutes is a somewhat severe degree of side effect.

Q: Is there any evidence for choosing between gabapentin and pregabalin?

Dr. Fountain: Some patients in efficacy trials of pregabalin responded to pregabalin but had not previously responded to gabapentin, so pregabalin was more effective for these patients.[1] However, there are no head-to-head comparisons, and it is likely the reverse would be true for some patients. Gabapentin is also less expensive, and affordability may be a concern for some patients.

Q: Are there circumstances in which you add a second medication and achieve seizure control, but then leave the first medication in place rather than withdrawing it?

Dr. Fountain: Patient preference certainly plays a role in this. Seizures are sometimes so persistent that once control is achieved it is reasonable to continue on two medications because the risk for side effects is less than the risk from recurrent seizures.

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