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Treating epilepsy in the elderly: More art than science

AS DRs. GHOSH AND JEHI discuss in this issue of the *Journal*,¹ physicians face many challenges when caring for elderly patients who have epileptic seizures.

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Owing to the graying of America and higher rates of incidence and prevalence of epilepsy in older patients than in younger ones, the number of patients with epilepsy will climb steeply in the coming years. Among patients in nursing homes, the numbers are much higher (an incidence of up to 16 per 1,000 per year and a prevalence of 60 per 1,000) than in community-dwelling elderly.^{2,3}

■ DOES THE PATIENT HAVE EPILEPSY?

The first concern is to make the correct diagnosis. Epilepsy is defined as a condition of the central nervous system predisposing to seizures. Younger patients need to have two unprovoked seizures for epilepsy to be diagnosed. However, a recent modification in the definition allows epilepsy to be diagnosed after a single seizure in a person who has a condition of the central nervous system known to significantly increase the risk of additional seizures.⁴

■ CONSIDERATIONS IN TREATMENT

When treating any patient, one size does not fit all, and this is especially true with elderly patients, in whom treatment should be based on health status. Many elderly patients with epilepsy have age-related comorbidities, and one would treat epilepsy differently in patients who are otherwise healthy than in those who are frail or have multiple comorbidities.⁵

Elderly people who live in their own homes have different needs from those who reside in a nursing home.

These patients have social and psychological problems as well as medical ones. For example, the loss of driving privileges can be a major concern with epilepsy patients; it is often emotionally devastating, in addition to greatly limiting independence.

Comorbidities, seizures, and treatment share a complex and tangled relationship. To decide on the appropriate therapy, a physician needs to evaluate the effects that antiepileptic drugs and central nervous system disorders can have on mood, cognition, and neurologic function. In addition, it is imperative to consider the possible pharmacokinetic and pharmacodynamic interactions of antiepileptic drugs with the many drugs used to treat other conditions.

Should treatment be started?

Antiepileptic drugs can cause side effects, and an elderly person who has had a single seizure may never have another one. On the other hand, given that seizures can pose higher risks to the elderly and lead to injuries that can be more devastating than in the young, preventing recurrent seizures may be very appropriate. Lack of studies of this issue means that there is no evidence to support either decision.

Which antiepileptic drug should be used?

Things to consider when selecting an antiepileptic drug include efficacy, tolerability, pharmacokinetic properties, adverse effects, use of other drugs that interact with these drugs, and compliance.

Pharmacokinetics can be affected by age-related changes in the function of the gastro-

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intestinal tract, kidneys, and liver and in protein binding. However, contrary to common perception, hepatic metabolism in healthy elderly people may not change significantly with advancing age. Ahn et al⁶ gave radiolabeled phenytoin (Dilantin) intravenously to patients with epilepsy and found that its clearance changed only slightly with age.

Antiepileptic drugs can interact with other drugs, herbal remedies, and food. Physicians need to know about the metabolic pathways of these drugs and other substances to make appropriate decisions about treatment. Interactions between antipsychotic and antiepileptic drugs are particularly worrisome because they involve both pharmacokinetic and pharmacodynamic mechanisms. Certain antiepileptic drugs can also induce (ie, increase) the hepatic metabolism of certain other drugs. Other drugs may lower the threshold for seizures.

Is the patient's drug level stable?

We assume that if a drug is taken on a regular schedule at the same dose, its serum concentration will remain relatively stable (at a "steady state"). And in younger adults, antiepileptic drug concentrations vary relatively little over time, by about 20% in compliant patients.⁷ This was assumed to be true for elderly patients as well.

However, Birnbaum et al⁸ found that phenytoin levels fluctuated as much as two- to threefold in serial measurements in nursing home residents, even though the dose or for-

mulation had not been changed and the patients were not taking any interfering medication. Yet some of the patients had very stable levels. The authors observed similar variations in levels of carbamazepine (Tegretol) and valproic acid (Depakote).⁹

The reasons for this variability are not known but may involve age-related changes in the gut.

RESEARCH NEEDED

Epilepsy is increasing in elderly people. Yet little basic or clinical research has been done to clarify the mechanisms or to determine the best treatment in terms of quality of life. Lacking appropriate animal models, basic research has been slow. For example, we do not know if the mechanisms leading to seizures after strokes differ from those leading to seizures in people with Alzheimer disease. Thus, it is not possible to choose an antiepileptic drug on the basis of its mechanism of action.

Many elderly patients who have epilepsy also have conditions that may alter the pharmacokinetic and pharmacodynamic properties of antiepileptic drugs, and data from younger people may be misleading.

Given the magnitude of the problem, we need to make a concerted effort to answer these questions with additional research.¹⁰ Meanwhile, the treatment of elderly patients with epilepsy is more of an art than a science. ■

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Little research has been done to elucidate mechanisms or determine the best treatment