Older Antiepileptics and Polytherapy Are Linked to an Increase in Adverse Effects

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MADRID — Adverse events are more common in patients who take older antiepileptic drugs or who take more than one antiepileptic, compared with patients on monotherapy or newer agents.

“The adverse effect profiles of antiepileptic drugs are often determining factors in drug selection, and yet adverse effects may be overlooked in everyday clinical practice,” Joyce A. Cramer wrote in a poster presented at the annual congress of the European Federation of Neurological Societies.

Ms. Cramer, a research scientist at Yale University, New Haven, Conn., conducted a population surveillance study to evaluate the adverse effects of both newer and older antiepileptic drugs (AEDs). The cross-sectional study was conducted in six European countries and consisted of a single clinical examination and structured interview.

The study population comprised 1,019 patients (mean age, 31 years) who had been on a stable dosing regimen for a median of 13 months. Of those, 57% were on monotherapy, and 43% were on polytherapy.

Most of the patients (71%) were taking at least one older AED (carbamazepine, clobazam, clonazepam, phenobarbital, phenytoin, or valproate). The rest were taking at least one newer AED (gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, tiagabine, topiramate, and zonisamide).

At least one adverse effect occurred in 68% of the patients. Newer AEDs were associated with fewer reports of adverse effects than were older drugs (61%, compared with 71%, respectively), and monotherapy was associated with fewer reports of adverse effects than was polytherapy (66%, compared with 71%).

Neurologic adverse effects were more common in those taking older AEDs than in those taking newer AEDs (60% vs. 54%, respectively), as were systemic adverse effects (42%, compared with 33%).

Neurologic adverse effects were also more common in patients on polytherapy than in those on monotherapy (64% vs. 53%), although the percentage of patients reporting systemic adverse effects was equal in these two groups (40%).

Adverse effects that were significantly more common in those taking the older drugs, compared with the newer drugs, were cognitive slowing (30% vs. 22%), sedation (30% vs. 23%), and tremor (18% vs. 10%).

Adverse effects that were significantly more common in those taking polytherapy, compared with those taking the newer drugs, were cognitive slowing (36% vs. 22%), psychological problems (31% vs. 22%), tremor (21% vs. 11%), and gait disturbances (12% vs. 7%).

A logistic regression analysis concluded that patients on newer AEDs were 36% less likely than those on the older drugs to report at least one adverse effect. Treatment modifications were 52% more likely in those reporting adverse effects; at the study visit, 23% of patients changed therapy, mostly because of an adverse effect.

Ms. Cramer noted that patients who were taking levetiracetam were 67% less likely to report an adverse effect than were those who were not taking the drug, and those taking lamotrigine were 49% less likely to report an adverse effect than were those not taking lamotrigine.

The study was sponsored by UCB Pharma Inc., the company that manufactures levetiracetam. Ms. Cramer is a consultant for the company.

Neurologic adverse events were significantly more common in patients taking older AEDs who were taking levetiracetam, carbamazepine, clobazam, clonazepam, phenobarbital, phenytoin, or valproate.

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