Study Links Four Anticonvulsants to Suicide Risk

BY MARY ANN MOON

The link between anticonvulsant agents and suicidal acts or violent death—first revealed in a Food and Drug Administration meta-analysis in 2008—appears to have been confirmed for four of the drugs: gabapentin, lamotrigine, oxcarbazepine, and tiagabine, investigators reported.

In what they described as the first study to directly compare suicide risks with different anticonvulsants given in routine care, the investigators reported finding "increased risk for suicidal acts beginning within the first 14 days of treatment initiation." The finding opens the possibility that anticonvulsants "could induce [adverse] behavioral effects prior to the achievement of their full therapeutic effectiveness," reported Dr. Elisabetta Patorno of Brigham and Women's Hospital, Boston, and her associates (JAMA 2010;303:1401-9).

In the FDA meta-analysis, the number of events was small and largely confined to cases of suicidal ideation only. This "prevented definitive conclusions about the safety of individual agents," the investigators said. In addition, the anticonvulsant agents were used as adjunctive treatment in many of the studies included in the meta-analysis, "further complicating the assessment of their individual effect. Thus, the FDA meta-analysis could not provide patients or clinicians with clear guidelines on risk for specific agents or patient subgroups," Dr. Patorno and her colleagues noted.

They addressed these issues by conducting a cohort study using a database that included 297,620 new prescriptions for anticonvulsant drugs in 17 states between 2001 and 2006. The risk of attempted or completed suicidal acts or violent deaths was compared between patients aged 15 and older who had initiated treatment with one of two reference anticonvulsants (topiramate or carbamazepine) and patients who had initiated treatment with any of 13 other anticonvulsants. The study subjects were to be followed for 180 days or until they discontinued or switched medications, had a study outcome, or discontinued the study for other reasons. The mean follow-up turned out to be 91 days.

There were 801 attempted suicides, 26 completed suicides, and 41 violent deaths within 180 days of initiating anticonvulsant therapy.

Compared with subjects initiating use of topiramate or carbamazepine, those starting on gabapentin, lamotrigine, oxcarbazepine, and tiagabine were at significantly increased risk for these events, the investigators said.

A further analysis of the data showed that new users of gabapentin had an excess of 5.6 cases of attempted or completed suicide per 1,000 person-years, new users of oxcarbazepine had an excess of 10 cases per 1,000 person-years, and new users of tiagabine had an excess of 14.1 cases per 1,000 person-years, compared with new users of topiramate.

"These findings are compatible with the results of the FDA meta-analysis, which found similarly increased risks of suicidal behavior or ideation for all anticonvulsant drugs compared with placebo," Dr. Patorno and her associates said.

They cautioned that their study was exploratory in nature, and so could only suggest rather than definitively establish a causal relationship between these drugs and suicidal behavior. "There is no clear understanding of a possible mechanism of action that could lead to suicidal behavior in patients taking these medications," the researchers added.

Gabapentin and lamotrigine have been linked to behavioral problems such as aggression and hyperactivity, particularly in children and adults who have learning disabilities or cognitive impairment. Tiagabine has been reported to cause nervousness and depressive mood in some patients. And oxcarbazepine is thought to have a stimulant effect on psychomotor functioning in some, they said. ■

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