Four Anticonvulsants' Link to Suicide Supported

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, according to a report in JAMA.

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

The investigators noted that 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."

In addition, in many of the studies included in the meta-analysis, the anticonvulsant agents were used as adjunctive treatment, "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 were 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. 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 (JAMA 2010;303:1401-9).

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.

This study was funded by the HealthCore Fellowship in Pharmacoepidemiology and the Pharmacoepidemiology Research and Training Fund of the Harvard School of Public Health. Dr. Patorno reported no financial conflicts of interest. ■

FDA Approves Harder-to-Abuse Formulation of OxyContin

BY MARKETTE SMITH

A new formulation of the potent pain-relief drug, OxyContin, has been approved by the Food and Drug Administration in an effort to curb abuse and misuse of the widely prescribed opioid medication.

OxyContin will be reformulated into tablets that are harder to cut, crush, break, chew, or dissolve, the FDA said.

The new formulation will not affect the drug's intended purpose as a 12-hour controlled-release medication to alleviate moderate to severe chronic pain, noted the FDA.

Known on the street as "OxyCotton" for the euphoric highs it triggers when improperly used, abusers commonly break down the pills and release higher amounts of the active ingredient oxycodone. The drug is then snorted or injected into the bloodstream, the FDA explained in a written statement. The reformulation was approved April 5.

The new formulation maintains OxyContin's controlled-release properties but is specifically "intended to prevent immediate access to the full dose of the drug. "Attempts to dissolve the tablets in liquid result in a gummy substance that cannot be drawn up into a syringe or injected," the FDA said.

While the change will result in a pill that is harder to crack, officials at the FDA acknowledge that the move is not a complete solution to the problem of OxyContin abuse in the United States.

"Prescribers and patients need to know that its tamper-resistant properties are limited and need to carefully weigh the benefits and risks of using this medication to treat pain," said Dr. Bob Rappaport, director of the Division of Anesthesia and Analgesia Products in the FDA's Center for Drug Evaluation and Research.

The FDA says accidental overdoses have been reported after health care practitioners have crushed OxyContin tablets to give to patients who could not swallow them.

About 4.7 million Americans misuse and abuse prescription drugs for nonmedical purposes, according to a 2002 study by the National Institute on Drug Abuse. ■

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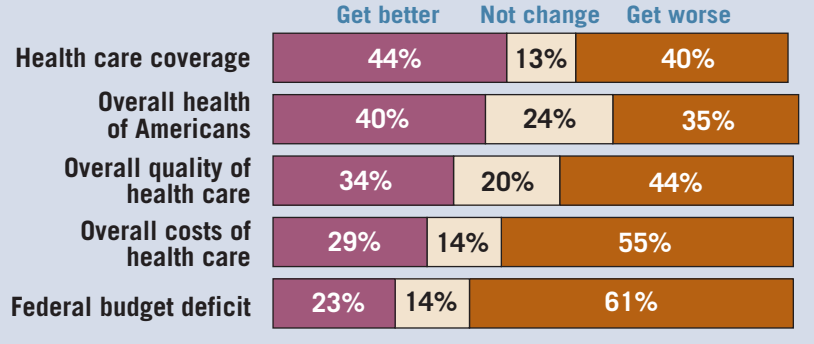
VITAL SIGNS

Concerns Remain After Health Care Reform Passage

Will each of the following get better, not change, or get worse than if no health care bill passed?



Notes: Based on a USA Today/Gallup poll of 1,033 adults conducted March 26-28. Don't know/refused responses not shown.

Source: Gallup Inc.