Lacking Alternatives, MDs Stick With Atypicals

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MADRID — Prescriptions for atypical antipsychotics have not decreased significantly among elderly patients with dementia, despite the black box warning of an increased risk of death associated with the drugs, according to Henry Riordan, Ph.D., speaking at the 10th International Conference for Alzheimer's Disease and Related Disorders.

Overall, prescribing has declined only 2.4%, even though the number of new prescriptions issued has decreased by 37%, Dr. Riordan said at the meeting presented by the Alzheimer's Association.

This pattern probably reflects physicians' perceptions that the clinical benefits of the drugs outweigh their well-documented risks for older dementia patients with serious behavioral issues.

More than 80% of Alzheimer's patients will eventually develop psychotic symptoms, said Dr. Riordan, vice president and global head of medical and scientific affairs for I3 Research in Basking Ridge, N.J. "These are the issues that typically result in institutionalization and take a big chunk out of these patients' quality of life," he said in an interview.

The problem lands patients, families, and physicians on the horns of a very sharp dilemma. "Withholding the drugs is dangerous, especially when you are dealing with behavior that can be either self-injurious or harmful to caregivers," Dr. Riordan said, but the risks of atypical antipsychotics were well documented years before the Food and Drug Administration's warning.

Fifteen of the 17 randomized atypical antipsychotic trials the FDA reviewed found a significantly increased risk of death—usually cardiovascular or infectious—among elderly, demented patients taking the drugs, compared with placebo. The resultant black box warning highlighted the danger and reiterated that the drugs are not approved for the treatment of patients with dementia-related psychosis.

To estimate the impact of the black box warning on prescribing patterns, Dr. Riordan examined claims data from a large U.S. health plan, for 10 months before and 10 months after the 2005 warning was issued. The database included 900,000 people older than 65 years of age; 20,515 had a diagnosis of dementia. Of those, 5,000 were taking at least one atypical antipsychotic before the black box warning.

Physicians responded to the black box warning by taking patients younger than 81 years off atypical antipsychotics while leaving older patients on.

Ten months after the warning, 4,883 people were still taking the drugs. New prescriptions had decreased significantly, however, declining from 3,423 to 2,148. "This probably tells us that if you were on the drug, you stayed on it, but that physicians might have been looking at something else for patients with new symptoms."

A supporting pattern emerged when Dr. Riordan broke down the data by age: Prescriptions decreased more among patients younger than 81 (5%) than they did among older patients (0.73%). "Here we're probably seeing a risk-benefit ratio that's perceived as different for older people," Dr. Riordan said.

"If someone has been on it with good efficacy, it would probably just be continued. But the physician's thought process might be very different for someone younger, in the earlier stages of the disease," according to Dr. Riordan.

Among the six drugs included in the study (aripiprazole, clozapine, ziprasidone, risperidone, quetiapine, and olanzapine), only two showed significant pre- and post-warning prescribing changes. Prescriptions for quetiapine increased significantly, while those for olanzapine decreased significantly.

"It could be that quetiapine is being used more now for its sedative effect in sleep difficulty, and clozapine less due to its issues with increasing cardiovascular risk factors."

Dr. Riordan now is investigating whether the decrease in new prescriptions caused any similar increases in prescriptions for alternative treatments, like mood stabilizers or antianxiolytics. ■