Dementia Risk Associated With Anxiety and Sleep Disorder Drug

Posted on October 30, 2012 by AmenClinics

Benzodiazepines possess sedative, hypnotic, and amnesic actions which are why they are sometimes used to treat anxiety and sleep disorders for short periods of time. Their use is becoming increasingly common for people age 65 years and older and in many cases is use becoming chronic.

The danger in chronic use is that the long-term adverse effects of benzodiazepines are not clearly understood, especially in relation to risk for dementia. Recognizing this growing cause for concern, a group of researchers at the University of Bordeaux Segalen in France set out to evaluate the association between use of benzodiazepines and incident dementia.

After a 15-year large population-based study, French researchers found older adults who use benzodiazepines have about a 50% greater chance of developing dementia than their peers who don’t use benzodiazepines. When you add these results to the existing research that shows benzodiazepine use increases the risk for falls and fractures in elderly, health providers should be especially careful to assess expected benefits versus potential risks, and to limit prescriptions to a few weeks.

Lead author of the study Dr. Billioti de Gage urged patients should be informed of the potential adverse effects of these drugs, including long-term risk when initiating benzodiazepines and about the necessity of gradual discontinuation when stopping the treatment.

The analysis included 1063 men and women (average age of 78.2 years) from the PAQUID (Personnes Âgées Quid) project, a prospective, population-based study of cognitive aging and dementia involving a total of 3777 participants from France. The study started in 1987 and follow-up lasted 20 years, with clinic visits every 2 to 3 years.

All participants in the current analysis were free of dementia at the beginning of the study and did not start taking benzodiazepines until at least the third year of follow-ups. Ninety-five (8.9%) reported benzodiazepine use at the 5-year visit, indicating new use between years 3 and 5. Year 5 was baseline for the analysis.

During the 15-year follow-up period, 253 (23.8%) cases of dementia were confirmed: 30 (32%) in benzodiazepine users and 223 (23.0%) in nonusers.

The PAQUID investigators say their findings are consistent with 3 recent case-control studies that found an increased risk for dementia in benzodiazepine users. Two of the studies from Taiwan used health insurance data and showed an increased risk for dementia in long-term users and current users. The third study, a nested case-control study among French people, found an increased risk for dementia in former users. Other studies, however, have not found an increased risk for dementia among elderly people using benzodiazepines.

Greg A. Sachs, MD, who was not involved with the study but reviewed it for Medscape Medical News, said it is “yet another study that suggests that benzodiazepines are bad drugs for older adults.” Dr. Sachs is chief of the Division of General Internal Medicine and Geriatrics, Indiana University School of Medicine, and investigator at the IU Center for Aging Research, Regenstrief Institute, Indianapolis.

“Many of these drugs,” Dr. Sachs said, “are on ‘Do Not Prescribe’ lists for older adults. If used at all, they should be used for short periods of time (10 days or less) and in the lowest dose possible to achieve benefit for the target symptom.” Benzodiazepines “should not be used long term for either
sleep or anxiety; safer alternatives exist.”

Dr. Sachs said there are several “positive distinguishing factors about this study.” It was large; it followed patients over many years with little dropout; it was prospective and longitudinal rather than cross-sectional; the diagnosis of dementia involved both neuropsychological testing and examination by a neurologist; and the researches had excellent information about drug use from patients, he explained.

The exclusion of people who were already receiving benzodiazepines at time of study entry and for a period of a few years “run in” is another key strength, he said.

“This is important regarding the notion of ‘reverse causation’ — that people could end up taking benzodiazepines because of symptoms of depression or anxiety that are early symptoms relating to a developing dementia. Without doing that, it could bias the study toward people with dementia already brewing getting benzodiazepines at a higher rate, instead of the notion that it is contributing to dementia development,” Dr. Sachs said.

“The analyses were “carefully done” and the findings were “explored and confirmed using more than one approach. The PAQUID study is one of the higher quality cohort studies examining dementia,” he added.

Dr. Billioti de Gage told Medscape Medical News that “contrary to most of the previous study on the topic, our study is based on a long period of follow-up (up to 15 years) and was carried out in a large representative cohort of elderly participants. This allows to take into account the somewhat long prodromal period of dementia and to generalize the conclusions.”

She and her colleagues say further study is needed to determine whether long-term use of benzodiazepines in people younger than age 65 years is also associated with an increased risk for dementia and uncover possible correlations between dosage or cumulative length of exposure and dementia.

Dr. Sachs agrees. The analysis “cannot tell us anything about long versus short acting meds, specific meds, dose, or duration of therapy,” he told Medscape Medical News. Also, the small numbers of people on benzodiazepines in the study is a limitation, he added.

Another limitation, he said, is that the analysis is primarily focused on “ever use” of benzodiazepines, “and that means we do not have information here on whether stopping the meds would help prevent dementia. In fact, because of the ‘ever use’ approach to analysis, I’d be concerned that someone misinterpret this and think ‘why bother stopping’ once someone has been exposed.”

Dr. Sachs also noted that “far greater numbers of people who developed dementia had not been exposed to benzodiazepines than those who had; so while it increases relative risk, how much it contributes to development of dementia should not be overplayed; this still was an observational study, so assigning causation is hard to do no matter how well the study is done.”