Risperidone Eases Some Symptoms of Dementia

Dose of about 1 mg per day brings improvements, but risk of cerebrovascular events rises threefold.

BY JEFF EVANS
Senior Writer

STOCKHOLM — Off-label use of low-dose risperidone is effective in treating the behavioral and psychological symptoms of patients with dementia, but clinicians must balance the drug's usefulness with its increased risk of cerebrovascular events, Peter P. De Deyn, M.D., said at the 12th Congress of the International Psychogeriatric Association.

Most of the available data on the treatment of the behavioral and psychological symptoms of dementia (BPSD) with atypical antipsychotics relates to risperidone, said Dr. De Deyn of the department of neurology at the University of Antwerp (Belgium).

BPSD include verbal and physical aggression, psychotic symptoms, agitation, anxiety, and depression.

Risperidone is approved to treat schizophrenia and bipolar mania associated with bipolar disorder. In May, the Food and Drug Administration opted not to approve risperidone for psychosis of Alzheimer's disease (AD).

In an analysis of pooled data from 1,150 patients in three double-blind, randomized, placebo-controlled trials, Dr. De Deyn and his associates found that 722 patients who had received risperidone had significantly greater improvement from baseline on the Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) and the Cohen-Mansfield Agitation Inventory (CMAI) at week 4 through the end of treatment at week 12 than did 428 patients who received placebo (Clin. Neurol. Neurosurg. 2005;107:497-508).

Risperidone patients received a mean dose of 1 mg per day in each trial, said Dr. De Deyn, a speaker and consultant for Janssen Pharmaceutica, which markets risperidone as Risperdal.

In the pooled data set, investigators and caregivers similarly judged risperidone patients as having significantly greater improvement on the Clinical Global Impressions scale than did placebo patients.

At a dose of about 1 mg per day, risperidone also has significantly greater efficacy than haloperidol (Haldol) as shown by results of BEHAVE-AD and CMAI—beginning around week 4-6 of treatment—in two trials of treatment for agitation and aggression in patients with dementia (Neurology 1999;53:946-55; Am. J. Geriatr. Psychiatry 2004;12:509-16).

Psychotic symptoms in patients with psychosis at baseline improved significantly more with risperidone than with placebo in an analysis from one of the trials in the pooled data set that used patients' last available scores as the end point.

In all trials, risperidone did not increase extrapyramidal symptomatology more than placebo. But in trials involving doses of 1 mg of haloperidol per day, the conventional antipsychotic significantly increased the rate of such symptoms.

Risperidone has a statistically significant threefold increase in the relative risk of cerebrovascular adverse events in elderly patients with dementia, including transient ischemic attacks and incapacitating strokes.

The risk appears to be a drug-class phenomenon, since other atypical antipsychotics such as olanzapine (Zyprexa) and aripiprazole (Abilify) also have an increased risk of such events, he said. Risperidone has a warning on its label about the risk of cerebrovascular events in elderly patients with dementia.

A Food and Drug Administration analysis of 17 placebo-controlled trials of atypical antipsychotics in patients with dementia-related psychosis concluded that the drugs were associated with a 60%-70% increase in all-cause mortality, most of which was attributable to infections and cardiovascular disease. But in an analysis of all-cause mortality and risperidone in particular, treatment with risperidone did not contribute to a statistically significant increase in mortality within 30 days of ending treatment, Dr. De Deyn said.

All atypical antipsychotics, including risperidone, have a warning about an increased risk of mortality in elderly patients with dementia.

In a separate poster session, Dr. De Deyn presented a metaanalysis of four double-blind, randomized, controlled trials that examined the effects of risperidone in patients with psychosis of AD.

The metaanalysis included patients from the three trials he pooled to analyze the effects of risperidone on BPSD.

These three 12-week trials indicated that treatment with risperidone significantly improved psychosis subscale scores on the BEHAVE-AD from week 8 onward and on the Clinical Global Impressions scales for severity of illness and change beginning at week 2, compared with placebo (Neurology 1999;53:946-55; J. Clin. Psychiatry 1999;60:107-15; J. Clin. Psychiatry 2003;64:134-43).

But a fourth study included in the meta-analysis showed that risperidone did not prove to be better than placebo after 8 weeks of treating psychosis of AD. Patients in this trial—the results of which are slated to be published in the American Journal of Geriatric Psychiatry—had an average Mini-Mental State Examination score of 13, while in other trials the average was between 6 and 8.

The psychotic symptoms of patients in this 8-week trial were also less pronounced than those of patients in the three other trials, Dr. De Deyn said. ■

Most Clinicians Opt Not to Disclose Dementia Diagnosis

BY JEFF EVANS
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STOCKHOLM — Clinicians shy away from disclosing a diagnosis of mild cognitive impairment and its potential to convert to Alzheimer's disease.

They also differ in how they word the disclosure when they opt to share the diagnosis and prognosis with the patient and relatives. For their part, families may not want patients to know when they have been diagnosed with Alzheimer's disease, according to reports presented at the 12th Congress of the International Psychogeriatric Association.

"In dementia, disclosure is not common clinical practice"—only about 15% of professionals disclose the diagnosis to patients—"but there seems to be a trend toward more openness about the diagnosis," said Els Derksen, R.N., a researcher at the Alzheimer's center at St. Radboud University Medical Center, Nijmegen, the Netherlands. But in contrast to several studies of disclosing a diagnosis of dementia, no studies have been published about disclosing a diagnosis of mild cognitive impairment (MCI).

Ms. Derksen discussed the responses of physicians who completed an optional appendix to a questionnaire that was a part of the European DESCRIPA (Development of Screening Guidelines and Diagnostic Criteria for Predementia Alzheimer's Disease) multicenter study. The study included patients with suspected MCI.

In discussions with 101 patients with MCI or possible early dementia, physicians told 28% that they had MCI, 62% that they had abnormal memory or cognitive problems, 4% that they had worrisome symptoms or depression plus memory problems, 3% that they had normal memory problems or forgetfulness, 2% that they had amnestic symptoms, and 1% that they had mixed and vascular dementia.

In discussions with 101 patients with mild cognitive impairment (MCI) or possible early dementia, physicians told 28% that they had MCI.

Among 100 patients who received information about their prognosis, physicians told 4% nothing, 18% that the prognosis was unknown or uncertain, 20% that the condition probably would remain stable, 10% that it probably would progress, and 66% that follow-up would be indicated. (The percentages do not add to 100% because follow-up was included with other information for some patients.)

When physicians were asked to describe their use of the term Alzheimer's disease in their interactions with a total of 80 patients, they reported that they did not use the term at all in 23%. Physicians told 72% that they could possibly convert to Alzheimer's disease. They told 4% of the patients that they had Alzheimer's disease or predementia, and 1% that Alzheimer's was not present or detected.

In nearly all instances, the same information about diagnosis, prognosis, and specific use of the term Alzheimer's disease was given to patients' families.

Alzheimer's disease in its predementia stage was suspected in 77 of 101 patients. A physician's decision to inform a patient of the diagnosis was most often guided by the patient's wish to know, a belief in shared decision making between physician and patient, and initiation of medication.

A qualitative analysis of 41 patients found that there was a difference between some centers in using the terms MCI or more descriptive language such as "memory problems or worrisome symptoms," which suggests that "some centers are more hesitant than others in disclosure of their suspicions," Ms. Derksen said.

"I think that further research is needed on how to inform patients about MCI," she added.

In a separate study, family members of patients with Alzheimer's disease indicated that they did not wish to reveal the diagnosis to the patient primarily because of a concern for causing anxiety and depression in the patient.

Filip Bouckaert, M.D., of the department of old age psychiatry at University Centre St. Jozef, Kortenberg, Belgium, interviewed 50 family members of outpatients with Alzheimer's disease and 50 family members of inpatients with the disease.

Their results, reported during a poster session at the congress, showed that 57% did not want the patient to be told the diagnosis; this included 42% of family members of outpatients and 72% of family members of inpatients.

Half of family members who did not want the patients to know about the diagnosis cited the possibility of causing anxiety or depression as the main reason not to tell. Similarly, half of the family members who thought the patient should be told said that his or her right to know was the primary reason to tell the patient the diagnosis.

More family members approved of the disclosure of diagnosis in patients with mild dementia (86%) than in those with moderate (39%) or severe (31%) dementia.

Despite the wish by most family members not to disclose the diagnosis to their affected relatives, 90% of family members wanted to be told their diagnosis if they developed Alzheimer's disease.

A similar study in Ireland found that 83% of family members said that patients with Alzheimer's disease should not be told the diagnosis (BMJ 1996;313:529-30). ■