Dementia Guidelines Issued for Primary Care

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Cholinesterase inhibitors and memantine are not one-size-fits-all drugs that can be prescribed to every patient with dementia and should only be employed after assessing each drug's risk/benefit profile in light of an individual patient's needs, according to a new set of clinical guidelines.

"The most important thing to keep in mind is that there is no cure for dementia," said Dr. Amir Qaseem, author of the guidelines and a member of the Joint American College of Physicians/American Academy of Family Physicians Panel on Dementia.

"These drugs can only alleviate symptoms and may slightly delay progression. But they should not be prescribed to every dementia patient because the benefits are very modest and some patients may not show benefit at all, and all the drugs carry potential harms."

Although many patients do show statistically significant improvements while taking the drugs, most of those changes are small and not clinically meaningful, according to the guidelines (Ann. Intern. Med. 2008;148:370-8).

The panel also concluded that there is insufficient evidence to recommended one drug over another for the treatment of dementia. Instead, "the choice of therapy should be based on an evaluation of adverse events, tolerability, and cost, because there is no evidence that one treatment is more effective than another," Dr. Qaseem said in an interview.

The recommendations are particularly important for primary care physicians, who care for most patients with dementia, said Dr. William Thies, vice president of medical and scientific affairs for the Alzheimer's Association.

"[Most] dementia patients are being managed by primary care physicians, and this is going to increase," he said in an interview. "As these guidelines point out, the emphasis when treating these patients should be that the physician, patient, and family work as a unit to decide the best use of a medication and the best time to stop."

The guidelines panel mined data from 59 studies that examined any of the five drugs approved for dementia treatment in the United States (donepezil, rivastigmine, galantamine, tacrine, and memantine). Drugs were assessed for their effects on symptoms (cognition, function, and behavior), quality of life, and their adverse event profile. The results of this evidence review accompany the guidelines (Ann. Int. Med. 2008;148:379-97).

The largest body of high-quality evidence was seen for donepezil: Twenty-four studies compared it with either placebo or vitamin E. Most showed statistically significant effects in favor of the drug for at least one measure of cognition. Improvements in function also were reported. Nine studies also showed that these improvements were clinically meaningful. "These findings are important because although the average improvement in cognition … did not reach statistical significance, a subset of patients may have clinical improvement," the panel noted. Up to 57% of patients discontinued their donepezil because of adverse events; the most commonly reported were gastrointestinal upset and muscle cramps.

Ten studies examined the use of galantamine. It was associated with statistically significant, but not clinically important, improvements in cognition and behavior. Withdrawal because of adverse events ranged from 8% to 57%, with the most common being gastrointestinal symptoms, eating disorders, weight loss, and dizziness.

Rivastigmine was assessed in nine placebo-controlled studies. Overall, there was significant but very inconsistent cognitive benefit, and no significant benefits on behavior or quality of life. Up to 29% of patients withdrew because of adverse events, including dizziness, nausea and vomiting, diarrhea, weight loss, and headache.

Eight studies examined the use of tacrine; seven were placebo-controlled and one compared tacrine with idebenone. One trial showed a significant cognitive benefit and three showed significant benefit in function; there were no effects on behavior or quality of life. Up to 55% of patients discontinued the drug, which was associated with serious adverse events, including hepatic abnormalities and abnormal liver enzymes. The panel concluded that there was insufficient evidence to substantiate any benefit of tacrine on cognition or behavior.

Memantine, the only neuropeptide-modifying agent available in the United States, was assessed in five studies, all of which compared the drug with placebo. Three trials showed significant, but not clinically important, improvements in cognition. One study showed significant improvements in behavior, and three showed significant quality of life benefits. The withdrawal rate varied from 9% to 12%. Adverse events included nausea, dizziness, diarrhea, and agitation.

The panel found only three high-quality head-to-head trials. Two pitted donepezil against galantamine. A 52-week study showed no significant difference in the primary outcome of function. An 8-week trial, favored galantamine for cognition.

The third trial compared donepezil with rivastigmine over 2 years. Patients taking rivastigmine fared significantly better in function and some measures of behavior, but experienced more adverse events than did those receiving donepezil.

The guideline writing panel attempted to address the appropriate duration of therapy; however the response to pharmacotherapy varies so widely. Generally, the beneficial effect from any of the drugs—disease stabilization or symptom improvement—will be apparent within 3 months of initiating treatment but will be temporary. When slowing decline is no longer a therapeutic goal, "treatment with a cholinesterase inhibitor or memantine is no longer appropriate."

Honest communication at the time of diagnosis is the best way to optimize medical therapy, said Dr. David A. Smith, a professor of family medicine at Texas A&M University, College Station. When families and patients understand up front that the benefit from these drugs will be modest and temporary, they are more likely to stick with the treatment plan, squeezing every possible benefit from it.

"A lot of people do get started on these drugs, but the dropout rate is huge, because there is [an] expectation of large benefit," he said. "It's important to remember that even small changes in cognition and behavior can roll into bigger changes over time, like in the rate of institutionalization."

Dr. Thies agreed. Despite their limitations, "These drugs are the best that we have at this point, and you don't want patients to throw away the only opportunity that we do have. You want the patient and family to go into therapy with a rational view of what is going to happen. The more they know about what to expect, the better they will do."

Early diagnosis is key to getting everyone on the same page about expectations. "If someone with Alzheimer's is to get into this discussion in a rational fashion, early diagnosis is critical. That way, patients can be involved in determining not only the course of therapy, but [also] can express their opinions on placement and end-of-life care. These questions become much easier if the patient is involved, rather than having the family guess about his wishes at a later point." ■

Psychiatric Diagnoses Common in Chronic Idiopathic Urticaria

BY ROBERT FINN
San Francisco Bureau

Nearly half of all patients with chronic idiopathic urticaria have Axis I psychiatric diagnoses and 45% have Axis II diagnoses, a new study shows..

Obsessive-compulsive disorder (OCD) and major depression were the most common Axis I diagnoses among 89 consecutive patients with chronic idiopathic urticaria (CIU), and both psychiatric illnesses were significantly more common in the patients than in a control group.

Among the patients, 26% had OCD, compared with 2% of the controls, and 13% had major depression, compared with 3% of the controls, reported Dr. Faruk Uguz and his colleagues at Selcuk University, Konya, Turkey (J. Psychosom. Res. 2008;64:225-9).

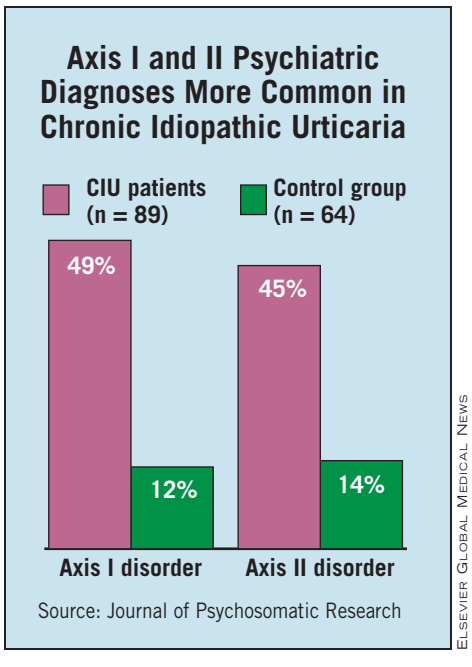
Obsessive-compulsive personality disorder and avoidant personality disorder were the most common Axis II diagnoses among the CIU patients, and both were significantly more prevalent in the patients than in the controls. Thirty percent of the patients had obsessive-compulsive personality disorder, compared with 3% of the controls, and 18% of the patients had avoidant personality disorder, compared with 5% of the controls.

Characterized by the rapid appearance of itchy wheals, urticaria is considered chronic when it is recurrent for at least 6 weeks. Few chronic urticaria cases have identifiable physical causes, such as infections, reactions to drugs or foods, or vasculitic diseases. But 75% of all cases have no known cause, and these are referred to as chronic idiopathic urticaria.

The study involved 89 consecutive patients with CIU who were seen at an outpatient clinic in Turkey and a control group of 64 hospital employees and their relatives who were matched to the patients' sociodemographic characteristics. The investigators excluded from both groups individuals who were illiterate, and those who had accompanying severe medical illnesses, or had used corticosteroid or psychotropic medications within the prior 4 weeks.

Psychiatrists made Axis I diagnoses using the Structured Clinical Interview for DSM-IV and the Structured Clinical Interview for DSM, Revised Third Edition, Personality Disorders.

In all, 44 of the CIU patients (49%) and 8 of the individuals in the control group (12%) had an Axis I disorder. Forty of the CIU patients (45%) and nine of the controls (14%) had Axis II disorders. Both differences were statistically significant.



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The investigators acknowledged that their study could not establish a causal relationship between psychiatric disorders and CIU because of its cross-sectional design. Psychiatric disorders could either be a cause or a consequence of CIU.

"We think that obsessive-compulsive and avoidant personality disorders may constitute a predisposition for occurrence of both urticarial symptoms and Axis I psychiatric disorders, negatively impacting patients' coping mechanisms with stressful life events or leading to cognitive misinterpretations of various life events, which are actually not stressful," the authors wrote.

They concluded that all patients with CIU should be screened for Axis I psychiatric disorders, particularly patients with OCD. ■