Caution Needed in Treating Bipolar Disorder in Elderly

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Psychiatrists treating elderly patients with bipolar disorder face a minefield of risks and potential complications and a paucity of clinical evidence and guidelines. Because of a lack of definitive guidelines and clinical evidence, elderly patients with bipolar disorder pose particular challenges in terms of appropriate pharmacotherapy. Psychiatrists must consider the unique response of elderly individuals to each drug and monitor these patients more closely than is typically required for younger adults. So explained experts at a session titled “Without a Map: Treating Geriatric Bipolar Disorder in the Absence of Guidelines” at the annual meeting of the American Association for Geriatric Psychiatry (AAGP) in March.

Challenges in Diagnosis

Kenneth Shulman, M.D., a professor of psychiatry at Sunnybrook Health Sciences Centre at the University of Toronto and an expert in geriatric psychiatry, discussed the diversity of underlying etiologies and manifestations in older patients. In addition to those who have had bipolar disorder from a young age, symptoms of mania and cycling mood may emerge later in life as a result of vascular or neurological disorders. Stroke and brain lesions have been linked to late-life bipolar disorder in past research. Diagnosis is further complicated by presentations that mimic certain types of dementia such as disinhibition syndrome and impaired cognitive functions.

Shulman cited data indicating that mania is associated with higher mortality risk than is unipolar depression in the elderly. “Late-life bipolar disorder causes a heavy burden on health care services,” he commented. Comorbidities, both nonpsychiatric and psychiatric, are common in elderly patients and lead to worse outcomes and more complications. Shulman recommended that clinicians conduct thorough assessments in older patients who present symptoms of depression and mania, including neurological and neuroimaging exams, cognitive function tests, cardiovascular disorder screening, history of mood disorders earlier in life, or other comorbidities.

Little Systematic Evidence

“Pharmacotherapy is a cornerstone of treatment of geriatric bipolar disorder,” said Robert Young, M.D., a professor of psychiatry at the Institute of Geriatric Psychiatry at Weill Cornell Medical College. Psychotherapy interventions, including individual, group, and family therapies, are also applied in the clinical setting. He reminded clinicians not to dismiss electroconvulsive therapy, which has been shown to be highly effective and may work fairly rapidly in elderly patients.
The biggest difficulty facing clinicians is the lack of prospective, randomized, controlled clinical trials in this patient population. Neither the efficacy nor the minimum and maximum dosages have been clearly established for lithium, valproate, carbamazepine, and other anticonvulsants.

Data on second-generation antipsychotics such as quetiapine and aripiprazole suggest some efficacy in bipolar depression, but these data were extracted from a small number of elderly patients in clinical trials who were above age 60 but less than age 80 and were generally healthy and with few comorbidities. “There are no available data regarding the efficacy of atypical antipsychotic medication in the very old,” Young said.

Evidence of the efficacy and safety of long-term maintenance treatment with lithium and other agents is equally limited and generally based on retrospective analyses.

Young is the principal investigator of the ongoing multisite Acute Pharmacotherapy of Late-Life Mania (GERI-BD) study funded by the National Institute of Mental Health. It is a nine-week, randomized, double-blind, concentration-controlled, parallel-group clinical trial of bipolar patients over 60 years old. The study is expected to provide much-needed clinical evidence for rational treatment.

Dementia Complicates Treatment

“We have seen a growth in the use of atypical antipsychotic drugs as the first-line treatment for mania in the past few years,” said Martha Sajatovic, M.D., a professor of psychiatry at Case Western Reserve University School of Medicine and director of Geropsychiatry at University Hospitals of Cleveland.

Although a number of antipsychotic drugs have been approved by the Food and Drug Administration (FDA) for the treatment of mania in adults, their safety profile in frail elderly patients remains unclear. In 2005 the FDA issued warnings on the use of second-generation antipsychotics for the treatment of behavioral disorders in elderly patients with dementia because of increased risk of death. Whether similar concerns apply to elderly bipolar patients without dementia is unclear, Sajatovic noted.

Drug concentrations in plasma are affected by age, sex, genetic differences, comorbid diseases, physiological variations, and drug-drug interactions. For older patients, polypharmacy and multiple comorbidities are two of the most prominent considerations in choosing the right drug and dosage by the clinician. Sajatovic cited data showing that individuals with bipolar disorder may develop dementia at a greater rate than others at the same age without the disorder and that adverse drug reactions increase dramatically with advancing age.

The pharmacokinetic and pharmacodynamic changes associated with aging means that the dosage guidelines derived from clinical trials in younger adults cannot be automatically extrapolated to older adults, both Sajatovic and Young pointed out.

For example, decreased cardiac, renal, and liver functions common in the elderly can reduce the clearance rate of most mood-stabilizing agents. Certain drugs frequently used by the elderly, such as diuretics, angiotensin-converting enzyme inhibitors, and nonsteroidal anti-inflammatory drugs, can interact with lithium and put patients at risk for serious toxicity. Both valproate and carbamazepine significantly inhibit or induce the liver enzymes responsible for the metabolism of various concomitant drugs including antidepressants and antipsychotics.
Sajatovic urged psychiatrists to consider comorbid medical conditions carefully and obtain a complete medication history before and during a patient’s pharmacologic treatment for bipolar disorder.

“Primary care providers may change non-psychiatric drugs without the knowledge of psychiatric specialists,” she said. “Ask your patients to bring all of their pill bottles.”

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