23 The Elderly

Essential Concepts

- Antidepressants with few drug interactions are best tolerated, such as citalopram, bupropion, or sertraline.
- For the elderly, lithium should be dosed at half the level used in the nonelderly. A level of 0.4 ng/dL can be therapeutic in the elderly patient with bipolar disorder.
- Valproate is better tolerated than lithium for bipolar disorder in the elderly.
- Among antipsychotics, ziprasidone and aripiprazole are overall best tolerated.

UNIPOLAR DEPRESSION

Depression is very common in the elderly. First-episode depression can occur in persons older than age 60 years, representing a second peak of incidence (the first occurring around age 30 years). It used to be thought that any mood episodes occurring for the first time after age 40 are mainly secondary to underlying medical illness. It is true that such a course should engender careful examination of potential medical etiologies. In the pre-managed-care era, some centers used to test all new mood disorder patients of any age with magnetic resonance imaging (MRI) of the head, a sleep-deprived electroencephalogram (EEG), and neuropsychological testing. While managed care has led to less testing in younger patients who develop primary mood disorders in their 20s and 30s, it is still reasonable to conduct such testing where feasible, especially in new-onset mood disorders after age 40.

Nonetheless, it is being recognized increasingly that many persons with new-onset depression after age 60 do not demonstrate clear secondary medical etiologies. It is often thought that such depressive episodes may accompany the losses of aging associated with grief for the deaths of family and friends, physical impairment in daily activities, loss of work-related satisfactions, and isolation. Concurrent medical

illnesses, especially neurologic, cardiac, and oncologic diseases, are also highly associated with major depression. It is not definitively clear that antidepressant treatment improves psychological and medical outcomes in such persons, but it is likely that continued depression produces worse outcomes. Psychotherapy and antidepressant medication treatment probably are commonsensical in such circumstances.

In the elderly, special attention should be given to the medical side effects of many antidepressant medications that, though highly tolerated in younger adults, can produce significant problems in the elderly. Since most elderly persons take medications for other medical illnesses, it is prudent to avoid antidepressants with many drug interactions, such as fluoxetine, fluvoxamine, or nefazodone. Further, sedating antidepressants [such as venlafaxine, mirtazapine, and the tricyclic antidepressants (TCAs)] generally are best avoided owing to their marked cognitive effects in the elderly. TCAs generally should be avoided owing to their cardiac risks. Paroxetine usually is better avoided owing to its anticholinergic effects. All these agents are useful in some patients but likely are not ideal first choices.

TIP

The agents with likely the least side effects are citalopram, sertraline, and bupropion SR, all of which have been shown to be effective in elderly depression.

BIPOLAR DISORDER

Usually, mania in the elderly occurs in persons with long-standing bipolar disorder (although sometimes not previously diagnosed or misdiagnosed in the past as unipolar depression). Sometimes, new manic episodes in the elderly occur secondary to underlying etiologies such as thalamic stroke or white matter infarcts. Whatever the etiology, as with younger persons, the treatment of bipolar disorder, especially type I, generally should include a standard proven mood stabilizer, such as lithium, divalproex, carbamazepine, or lamotrigine.

Special care should be taken in the use of lithium in the elderly. The blood-brain barrier becomes more porous with aging, and renal function declines gradually. As a result, the

elderly patient requires much lower serum lithium levels in the blood to achieve the same central nervous system (CNS) lithium levels that are obtained only with higher serum lithium levels in younger persons. There is also decreased renal clearance of lithium with age. In other words, a serum lithium level of 0.8 ng/dL in a nonelderly adult is needed to obtain a CNS lithium level of 0.4 ng/dL to 0.8 ng/dL, which seems to be the effective range, with 0.8 ng/dL being considered as high as would be acceptable. In an elderly adult, a serum lithium level of 0.4 ng/dL translates into a CNS lithium level of about the same level. In other words, a serum lithium level of 0.4 ng/dL in an elderly person is basically therapeutic and similar in effect to a serum lithium level of 0.8 ng/dL in a nonelderly adult. As a corollary, a serum lithium level of 0.8 ng/dL in an elderly adult can be toxic, equivalent to almost twice that level in a nonelderly adult. Unfortunately, many clinicians are fooled by standardized laboratory ranges that report "therapeutic" levels often in the 0.6 ng/dL to 1.2 ng/dL range, which is incorrect for the elderly. If lithium is used in the elderly, it usually should be used at "low" levels, which are, in fact, therapeutic levels.

TIP

Lithium is difficult to use in the elderly owing to a notable risk of toxicity with dehydration. If lithium is used, therapeutic levels should be about half those used in nonelderly adults. A level of 0.8 ng/dL can be toxic.

In contrast, divalproex levels appear to be largely the same in the elderly as in younger adults. Divalproex is in some ways safer as a result, with its wider therapeutic dose range leading to fewer medical complications in the elderly than often occurs with lithium. Carbamazepine usually is not helpful owing to its many drug interactions, given the need for polypharmacy for multiple medical conditions in most elderly persons. Oxcarbazepine might be a viable alternative if needed, although equivalent efficacy for bipolar disorder with this agent compared with carbamazepine has not been demonstrated, and risks of hyponatremia still need to be monitored. If drug allergies are not present and rash risks are understood, lamotrigine also can have a role in some elderly persons with bipolar depressive symptoms.

If atypical neuroleptic agents are used, the less anticholinergic and less antiadrenergic ones are generally to be preferred.

Certain specific cautions are in order. Risperidone has been associated with a possible increased risk of stroke in the elderly, with a Food and Drug Administration (FDA) black box warning to that effect; it is unclear to what extent this association is causal. Otherwise, low-dose risperidone is often well tolerated for agitation in the elderly. Quetiapine has notable antiadrenergic effects, which can lead to notable sedation and orthostatic hypotension, especially in the elderly. Given the major mortality risks associated with falls in the elderly, this risk of orthostasis needs to be considered and monitored carefully. Increased age is also a risk factor for parkinsonism, thus perhaps leading to some relative advantage to quetiapine and clozapine on this issue, although clozapine also is quite risky medically in the elderly, given its increased risk of seizures, marked sedation, and risk of agranulocytosis. Low doses of aripiprazole or ziprasidone may be well tolerated. Intramuscular ziprasidone in particular is becoming common for the management of agitation in the elderly. The lack of metabolic effects (increasing diabetes and cardiovascular risks) with ziprasidone and aripiprazole in particular may make them useful in the elderly. Although olanzapine may be useful both for mania and agitation, its metabolic risks, as with clozapine, may limit its long-term utility in elderly persons. As with younger adults, my view is that antipsychotics generally should not be used alone as mood stabilizers, where, in my reading of this literature, the evidence is equivocal, but mainly as adjuncts to standard mood stabilizers if needed.

KEY POINT

Among atypical neuroleptics, seek to use those with the least anticholinergic and antiadrenergic effects while keeping in mind that the elderly also are more sensitive to extrapyramidal symptoms. The newest agents, aripiprazole and ziprasidone, may be the best tolerated.

If antidepressants are used in the elderly for bipolar depression, special attention should be given to the medical side effects of many antidepressant medications that, although highly tolerated in younger adults, can produce significant problems in the elderly. Since most elderly persons take medications for other medical illnesses, it is likely prudent to avoid antidepressants with many drug interactions, such as

TABLE 23.1. Management of Bipolar Disorder in the Elderly

Agent	*Advantages*	*Disadvantages*	*Comments*
Mood stabilizers	Mainstay of long-term treatment	Lithium toxicity more common; drug interactions with carbamazepine problematic	Divalproex and lamotrigine probably most tolerable; oxcarbazepine may be alternative
Antipsychotics	Useful for management of acute mania and agitation	Probably not effective long-term in monotherapy; clozapine and olanzapine have metabolic risks; quetiapine associated with notable sedation and risk of falls; risperidone associated with possible stroke; more extrapyramidal symptoms in the elderly	Aripiprazole and ziprasidone probably best tolerated
Antidepressants	May be helpful for acute depressive symptoms	Not effective in long-term prevention of depression in bipolar disorder; many agents have drug interactions	Bupropion, sertraline, and citalpram are probably best tolerated

fluoxetine, fluvoxamine, or nefazodone. Further, sedating antidepressants (such as venlafaxine, mirtazapine, and TCAs) generally are best avoided owing to their marked cognitive effects in the elderly; TCAs generally should be avoided owing to their cardiac risks and risks of induction of mania. Paroxetine, although documented as having a low mania induction risk, can tend to have bothersome anticholinergic effects in the elderly, including confusion. All these agents are useful in some patients but likely are not the ideal first choices. The agents with likely the least side effects are citalopram, sertraline, and bupropion SR, all of which have been shown to be effective in elderly depression and are associated with relatively low risks of mania in studies of bipolar depression. As with younger patients, I would strongly advocate for mostly short-term use of antidepressants in most patients with bipolar disorder (during the acute phase) but discontinuation of antidepressants after recovery from the acute phase (owing to lack of maintenance efficacy in randomized trials and some evidence of potential long-term worsening of the course of illness through mood destabilization; see Table 23.1).

In summary, the elderly with bipolar disorder should be treated with standard mood stabilizers, as is the case in younger adults. However, lithium is more difficult to use in the elderly, perhaps providing for more of a role for divalproex or possibly lamotrigine. Among antidepressants, agents with the least drug interactions, such as bupropion, sertraline, and citalopram, may be useful. And among antipsychotics, low doses of agents with the least metabolic risks, such as ziprasidone and aripiprazole, seem best tolerated, although sometimes other agents may be needed to control unresponsive agitation.