Treating Psychotic Symptoms in Elderly Patients

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Research has shown that elderly patients are especially at risk for the development of psychotic symptoms. A combination of factors contributes to the increased risk for psychosis in this patient population. Various DSM-IV diagnostic categories including delirium, schizophrenia, delusional disorder, mood disorders, dementia, substance abuse, and medical-neurologic conditions can be associated with psychotic symptoms. In general, medications are prescribed for specific target symptoms, started at low doses, and titrated gradually. Although buspirone, trazodone, valproic acid, and carbamazepine have been used with some success, antipsychotic medications have been the primary treatment of psychosis in the elderly. Because the atypical antipsychotics offer effective management of psychotic symptoms combined with low liability of extrapyramidal symptoms, these agents may be the current treatment of choice for psychotic symptoms in the elderly when used cautiously.

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It is well established that elderly patients are at increased risk for the development of psychotic symptoms.[1,2] Community surveys reveal mental and behavioral disturbances in many elderly residents. The Epidemiologic Catchment Area (ECA) survey reported a range of psychoses from 16% to 23% in an older population.[3] Christensen and Blazer[4] identified paranoid symptoms in 4% of 997 older adults in their community survey. A recent survey of over 5000 elderly residents (over age 65 years) in Utah identified behavioral disturbances in 61% of the patients with dementia (4 times greater than in age-matched, nondemented community residents).[5] In one survey of a long-term care facility, 91% of 80 subjects had at least 1 psychiatric diagnosis, and 50% had 4 or more behavioral problems.[6]

Many factors, in combination, contribute to the increased risk for psychosis in the elderly.[7] Age-related deterioration of cortical areas such as the temporal or frontal lobes, as well as neurochemical changes common in aging, may be involved in the increased incidence of psychosis. Further, a combination of comorbid physical illnesses, social isolation, sensory deficits (such as hearing loss), cognitive changes, and polypharmacy that is frequently seen in elderly patients adds to the vulnerability for psychosis as well as complicates the treatment of these symptoms. Age-related pharmacokinetic and pharmacodynamic changes in the elderly affect drug response and increase the risk for delirium.

As reflected in the DSM-IV, many diagnostic categories including delirium, dementia, schizophrenia, delusional disorder, mood disorders, substance abuse, and a range of medical-neurologic conditions (e.g., brain tumors, Parkinson's disease, metabolic encephalopathies) can be associated with psychotic symptoms (Table 1).[8] More than 50% of patients with senile dementia of the Alzheimer's type manifest psychotic symptoms during the course of this progressive illness, and some authors have reported rates of behavioral disturbance up to 70%.[1,2,5] In addition, several commonly prescribed medications can also produce psychotic symptoms in elderly patients.

The frequent coexistence of psychotic symptoms occurring in patients with moderate-to-severe memory disorder who may have other medical problems and can be taking several medications complicates an already fragile treatment situation in an older patient. This article reviews psychopharmacologic treatment strategies for managing psychotic symptoms in elderly patients.

DIFFERENTIAL DIAGNOSIS OF PSYCHOSES IN THE ELDERLY

The identification of psychotic symptoms in the elderly may be obscured by the presence of multiple medical illnesses and medications. It may be best to extend a broader definition of psychosis as an impairment of reality testing that causes cognitive and/or behavioral disturbances and that is often manifested as delusions and/or hallucinations. Agitation and aggressiveness are also associated with psychosis in the elderly and are frequently the precipitating reason for psychiatric consultation.

The presenting symptoms of psychosis may differ in quality and intensity in older patients compared with

Table 1. DSM-IV Diagnoses Associated With Psychoses in the Elderly

Delirium
Schizophrenia
Delusional disorder
Mood disorder
Dementia (every type)
Substance abuse
Metabolic disturbances
Chronic medical conditions
Neurologic conditions
Drug-induced psychosis

younger psychotic patients. For instance, somatic and visual hallucinations may be more common in elderly than in younger patients, particularly when the psychosis is secondary to a medical condition (e.g., Parkinson's disease). Further, there may be a genuine organic basis for these symptoms that must be ruled out. Visual hallucinations must be differentiated from illusions due to poor vision, and auditory hallucinations must be distinguished from carotid bruits or tinnitus in the elderly. Similarly, delusions (fixed false beliefs) must be differentiated from misperceptions due to sensory deficits or cognitive impairment. The misperception of theft due to a misplaced object may be incorrectly described as delusion. Alternatively, the assertion of theft by an older patient may at first seem plausible enough and actually delay recognition of a genuine psychotic symptom.[2] Hence, the identification of the underlying cause of the symptoms must precede treatment interventions.

The clinician must consider psychotic symptoms within the context of the underlying etiology of these symptoms. Psychotic symptoms can be manifested among a spectrum of disorders that must be considered in the differential diagnosis prior to any pharmacologic treatment intervention.

Delirium

Delirium is an acute, reversible state of confusion characterized by changes in cognition and consciousness that is frequently unrecognized or misdiagnosed in an elderly population.[9] These patients present with disorientation, an inability to focus or sustain attention, impaired memory, perceptual disturbances (delusions and hallucinations), psychomotor changes of hypoactivity or hyperactivity, labile mood, anxiety, impaired speech, sleep/wake impairment, and disruptive behavior. The prevalence of delirium is reported to be 11% to 24% in elderly patients at the time of hospital admission, although it has been reported in a much higher percentage of postsurgical patients.[10] Delirium may be superimposed on other neuropsychiatric conditions such as schizophrenia, depression, or dementia, which can obscure its identification. However, the key distinguishing feature of delirium is reduced alertness (clouded consciousness) in which it is difficult for the patient to sustain attention. In elderly patients, the symptoms

may become most pronounced in the evening, yielding a "sundowning" syndrome characterized by incoherence and confused, illogical behaviors, which can lead to injury.

Early recognition of incipient delirium is important because its persistence can contribute to increased morbidity and mortality. Personality changes, irritability, distractibility, and loosening of associations may precede the changes in consciousness that tend to characterize delirious patients. Unfortunately, delirium is often not recognized in the early stages. Farrell and Ganzini[11] reported that more than 40% of elderly patients evaluated for depressive disorder in a Veterans Affairs (VA) hospital setting actually had delirium. Further, Cameron and colleagues[12] reported that only 1 in 20 cases of delirium was actually recorded as such by the attending physician.

Delirium is generally the manifestation of an underlying medical illness or drug toxicity that disrupts cerebral metabolism and neurotransmission, particularly of dopamine and γ-aminobutyric acid.[13] Infections such as pneumonia, hypoxic conditions such as chronic obstructive pulmonary disease, intoxication, and medication withdrawal are the most common causes of delirium in the elderly. Some drugs (e.g., conventional antipsychotics, anticholinergic drugs, and long-acting benzodiazepines) or toxins can also act to cause delirium. The underlying disease or causative agent affects both the course and resolution of delirium.[14] Although the onset is usually abrupt, the symptoms may fluctuate and persist for days to weeks.[7,11] Elderly hospitalized patients with delirium are at high risk for death, and the presence of delirium may serve as an indicator of a poor prognosis. Although treatment can often reverse the initial presentation of the condition, some studies have shown a persistence of symptoms in the majority of these patients.[14–16] Levkoff and coworkers[16] reported that fewer than 20% of delirious patients had achieved full resolution of symptoms 6 months after hospital discharge. In some instances, persistent cognitive deficits may also reflect a concurrent dementing illness that was unmasked by the state of delirium.

The management of delirium requires that the underlying causative factors be identified and treated, if possible. Although it is preferable not to add medications during delirium since it might further complicate the clinical picture, some reports[9,17] have shown that low doses of atypical antipsychotics can be helpful in regaining behavioral control and reducing agitation. However, there is no consensus on the pharmacologic treatment of delirium. It is important to monitor the ongoing clinical status of the patient with delirium. Brief neuropsychological assessment tools may facilitate the serial monitoring of delirious patients.

Schizophrenia

Most first episodes of schizophrenia occur in young adults, and symptoms generally continue to be manifest throughout life. However, it has been shown that 10% of

first-episode cases of schizophrenia do occur in patients who are older than 45 years.[1,7] Although schizophrenia continues into old age, the symptoms may become less severe and may not require ongoing antipsychotic medications.[18] Strauss and Carpenter[19] evaluated the progression of schizophrenia over time and found that most symptoms improve in 20% of patients, remain unchanged in 60%, and worsen in only 20% of patients. Ciompi[20] suggested that advancing age might mitigate the intensity of schizophrenic illness, allowing more patients to live as outpatients with residual states.

Schizophrenic patients may develop dementia in later life. In one study, Davidson and colleagues[21] reported that two thirds of a chronically institutionalized group of schizophrenic patients had cognitive impairment consistent with dementia. Elderly patients with comorbid schizophrenia and dementia may present with a complex clinical picture of confusion and psychosis. The evolving dementia in a schizophrenic patient may go unrecognized in a long-term care setting. The comorbid dementia may benefit from cholinesterase inhibitor drugs, whereas anticholinergic drugs could exacerbate the confusion. Elderly schizophrenic patients are very susceptible to extrapyramidal symptoms (EPS) when treated with conventional neuroleptic drugs, and women in particular are most at risk for the development of tardive dyskinesia.[22] Tardive dyskinesia was identified in 26% of elderly psychotic patients after exposure to conventional antipsychotic medications for 1 year, and in 60% after 3 years.[23] Atypical antipsychotics herald a new era in the treatment of older schizophrenic patients because they convey much less risk for EPS and tardive dyskinesia.

Delusional Disorder

The symptom of paranoia extends beyond the single diagnostic category of delusional disorder and has been noted in many elderly patients with other underlying disorders.[24] The discrete illness of delusional disorder (coded as 297.10 in the DSM-IV) refers to patients who reveal persistent delusions without prominent hallucinations in the absence of dementia, schizophrenia, or mood disorders.[8] The delusions of these patients are usually nonbizarre in nature, well circumscribed, and may include beliefs about somatic illnesses, jealousy, persecutions, theft, marital infidelity, and mistaken identity.

Generally, delusional disorders appear in men between the ages of 40 and 49 years, and in women, between the ages of 60 and 69 years.[1,24,25] Certain premorbid personality disorders (schizotypal, paranoid) and early life traumas (sexual or physical abuse) have been associated with delusional disorder.[1,7,8,25]

Patients with delusional disorder are characteristically reluctant to seek treatment and resistant to accept it when they finally come to medical attention. Frequently, the paranoid ideas and behaviors are more distressing to family members or neighbors than they are to the patient, who may deny that the problem exists at all. Antipsychotic medications are sometimes helpful in reducing the delusional beliefs when combined with behavioral and supportive therapy.

Mood Disorders With Psychosis

Depression is the most common psychiatric disorder in older patients. The ECA community survey identified symptoms of depression in 27% of the elderly.[3] Retirement, relocation, loss of social support, bereavement, financial problems, and chronic medical illnesses contribute to the increased risk for depression in the elderly.[7,26] Psychotic symptoms are often associated with depression in elderly patients. Nelson and colleagues[25] observed delusions in 39 of 109 patients over 60 years of age being treated for depression. Similarly, Mayers and Greenberg[27] reported that approximately 45% of elderly depressed patients had delusions. The delusions usually include persecutory beliefs, guilt, suspiciousness, and sin. Hallucinations may also occur and can sometimes include commands pertaining to suicide.[2] In contrast to nonpsychotic depression, psychotic depression in the elderly is associated with increased risk for relapse, more persistent symptoms over 1 year, more suicide attempts, more hospitalizations, comorbidity, and financial dependency.[1,28] The cognitive status of the elderly depressed patient may also be compromised and influence the course of the illness.

Elderly patients with psychotic depression respond poorly to antidepressants alone and frequently require the addition of antipsychotic medication. Depressed patients are highly susceptible to the neuromuscular side effects of conventional antipsychotic medications, particularly tardive dyskinesia.[22] Electroconvulsive therapy is often effective in elderly depressed patients with psychosis and may be a reasonable alternative treatment intervention for some patients.[28]

Mania can also present in elderly patients.[7,29] Elderly manic patients are rarely euphoric and more commonly present with irritability, paranoia, and mild confusion.[29] The safe use of drugs like lithium or valproic acid requires consideration of comorbid medical illnesses and concomitant medications that might affect the metabolism and blood levels of these agents.[30]

Dementia With Psychosis

Elderly patients with dementia are at high risk for the development of psychotic symptoms and behavioral disturbance during the course of this illness. More than 50% of Alzheimer's patients manifest psychotic symptoms during the course of this progressive illness, and some authors have reported rates of behavioral disturbance up to 70%.[1,7,31] Tariot[31] surveyed the Alzheimer's disease literature and reported median values of 28% for occurrence of hallucinations, 44% for agitation, 24% for verbal

aggression, 34% for disturbed ideation (delusions), and 18% for wandering. Cummings et al.[32] found persecutory delusions in 30% of patients with Alzheimer's disease and in 40% of patients with multi-infarct (vascular) dementia.

Typically, patients with dementia will report simple paranoid beliefs and frequently describe visual and auditory hallucinations. Tariot[31] has emphasized the importance of differentiating these true psychotic symptoms from misperceptions, which result from a patient's compromised capacity to organize perceptual information. Initially, efforts to adjust the environment, optimize sensory input, and provide supportive reality orientation may ameliorate the symptoms. Mild delusions or hallucinations may be tolerated in a safe environment. Global agitation or aggressiveness, however, may be harder to manage safely and may necessitate pharmacologic intervention. The decision to introduce psychotropic medication must be examined within the context of the total medical presentation of the patient, including comorbid medical illnesses and concomitant medications. It has also been suggested that cholinesterase inhibitor drugs may have antipsychotic effects as well.[33,34]

Another dementia syndrome that has been given increased attention is dementia with Lewy bodies (DLB).[35] Lewy bodies are inclusion bodies immunoreactive to ubiquitin that have been described in patients with Parkinson's disease and Alzheimer's disease. Demented patients with Lewy bodies may represent the second largest group of patients with dementia. DLB was found in 19% of demented elderly patients in a British community survey.[35,36] It is a form of dementia in which fluctuations in cognition and alertness (attention) are prominent findings in conjunction with behavioral disturbance, visual hallucinations, and motor features of parkinsonism.[35] Often, these patients have histories of falls and/or syncope related to transient loss of consciousness. It has been suggested that demented patients with Lewy bodies may be particularly responsive to cholinesterase inhibitor drugs.[37] Patients with Lewy body disease, however, are extremely sensitive to conventional neuroleptic medication and have frequent adverse reactions including persistence of motor symptoms after drug withdrawal.[36]

Substance Abuse and Psychosis

Substance abuse because of loneliness or boredom or overuse of prescription drugs (such as barbiturates) is a common problem in elderly patients. Consequently, acute and chronic substance abuse can be a factor in the development of psychosis in this population. Acute alcohol withdrawal can elicit delirium complete with vivid hallucinations and delusions.

Elderly patients may not report alcohol or substance abuse. A drug screen is useful when the etiology of psychotic symptoms is unknown, particularly if the patient's medication use has not been supervised. The risk of seizures due to abrupt withdrawal must be considered when recent medication use is not completely known. It is also important to exclude thiamine deficiency in these patients who may have poor nutrition and may suffer from Korsakoff's psychosis or Wernicke's encephalopathy.

Psychotic Disorders Due to Medical or Neurologic Conditions

Medical disorders may predispose elderly patients to develop psychotic symptoms. Common disorders including thyroid disease, diabetes, vitamin B_{12} and folate deficiency, sodium-potassium imbalance, sleep deprivation, and dehydration, as well as chronic illnesses have been associated with psychosis in the elderly.[16,38] Presenting symptoms can include delusions and/or hallucinations and often meet criteria for delirium.[8] Vivid visual hallucinations and confusion are particularly common when the etiology of the psychosis is related to an underlying metabolic disturbance. Structural brain lesions or subtle seizure disorders must be ruled out as well.

Behavioral disturbances are common in elderly patients who develop neurologic disorders. Parkinson's disease, Huntington's disease, multiple sclerosis, and amyotrophic lateral sclerosis can all lead to the development of psychotic symptoms.[17]

There is a complex relationship between dementia, depression, and the dopaminergic medications (L-dopa or carbidopa) used to treat patients with Parkinson's disease. Psychotic symptoms may result from the disease process, emerging dementia, or depression or the dopaminergic drugs used to treat the disease. Consequently, up to 40% of Parkinson's disease patients develop psychotic symptoms and the incidence increases with age.[7,39] Amantadine, anticholinergic drugs, and dopaminergic drugs can elicit psychotic symptoms in patients with Parkinson's disease. Well-formed visual hallucinations (often of people or animals) occur in over 20% of patients receiving dopaminergic agents and appear to be dose related.[39] Patients are often very frightened by these hallucinations and may become agitated, particularly if they have an associated Parkinson's dementia. Conventional antipsychotic drugs like haloperidol tend to exacerbate the neuromuscular dysfunction of these patients, increase the tremor, and worsen their overall psychomotor retardation. Alternatively, atypical antipsychotics like clozapine, quetiapine, and olanzapine can effectively treat Parkinson's psychosis because of their low liability for the development of EPS.[40–42]

Drug-Induced Psychosis

Elderly patients are often receiving multiple medications when they present with psychotic symptoms. Table 2 lists a group of commonly used drugs that can produce psychotic symptoms in elderly patients.[43] Drug interactions and dosage must be considered when evaluating drugs as causative agents of psychotic symptoms.

Table 2. Medications Associated With Psychotic Symptoms in the Elderly[a]

Antiparkinsonian drugs and related compounds
  Levodopa or carbidopa
  Amantadine
  Bromocriptine
Anticholinergics and antihistamines
  Diphenhydramine
  Hydroxyzine
  Cimetidine
Antidepressants
  Tricyclic antidepressants
    Amitriptyline
    Imipramine
    Doxepin
  Selective serotonin reuptake inhibitors
    Fluoxetine
    Sertraline
    Paroxetine
  Bupropion
  Venlafaxine
Conventional antipsychotics
  Chlorpromazine
  Thioridazine
  Haloperidol
Benzodiazepines[b]
Alcohol (ethanol)[b]
Stimulants
  Methylphenidate
  Amphetamine
  Ephedrine
Analgesics and anti-inflammatory drugs
  Indomethacin
  Aspirin (acetylsalicylic acid)
Antineoplastic drugs
Anticonvulsants
  Phenytoin
  Primidone
  Carbamazepine
Prednisone
Antidysrhythmics
  Digoxin
  Quinidine
  Procainamide
  Propranolol

[a]Adapted with permission from Targum and Abbott[7] and Wood et al.[43]
[b]Including withdrawal from these agents.

PHARMACOLOGIC TREATMENT OF PSYCHOSES IN THE ELDERLY

Elderly patients presenting with psychotic symptoms require social, behavioral, and environmental interventions that are necessary for their safety and reorientation. Given the likelihood of comorbid medical disorders and concomitant medications, the mere presence of delusions or hallucinations is not always an indication for additional medications. However, some patients may need pharmacologic intervention in order to manage the behavioral disturbance that often results from the psychotic symptoms. A careful assessment of underlying medical conditions and concomitant medications that might contribute to the psychotic symptoms is essential prior to the initiation of pharmacotherapy. A psychiatric history may reveal earlier episodes of psychosis or depression that may pre-

dispose elderly patients to psychotic symptoms. There may be more than one causal factor contributing to the emergence of psychotic symptoms. For instance, psychiatric disorders like schizophrenia or depression may coexist with organic illness like dementia and/or toxic causes of psychosis (like medication-induced delirium). The possibility of treating or reducing predisposing factors must be considered prior to pharmacologic intervention.

Psychotropic drugs are often used to manage the behavioral disturbances as well as the overt psychotic symptoms (hallucinations and delusions) that present in elderly psychotic patients. In demented patients who present with a complex array of problems, Tariot[31] has compiled a list of specific symptoms and disturbed behaviors into a "psychobehavioral metaphor" that may approximate drug responsive syndromes and guide the appropriate selection of pharmacotherapy. The clinician identifies and treats the "target" symptoms that require intervention, regardless of the putative diagnosis. The assessment may reveal that depressive symptoms are the dominant presenting problem. In this type of case, a trial of antidepressants may precede the introduction of antipsychotic medications in psychotic elderly patients.

Generally, medications are prescribed for specific target symptoms, started at low doses, and gradually titrated until there is clinical benefit. If there is clinical benefit, it is prudent to continue the treatment at the same effective dose for at least 2 to 4 months prior to gradually tapering the dose and discontinuing it. The optimal duration of treatment with any psychotropic agent is not known and depends upon the residual clinical picture and psychosocial context of the patient. It may be possible, however, to completely withdraw medication in some patients after sustained behavioral control has been achieved. In a nursing home study, long-term maintenance antipsychotic medication was withdrawn from stable demented patients who had no current behavioral symptoms. Approximately 50% of these patients experienced recurrent psychotic symptoms within 6 months, but the others remained stable without medication.[44]

Choices for pharmacologic intervention for psychotic symptoms generally include anxiolytics, antidepressants, anticonvulsants, and antipsychotic medications.[30,45]

Anxiolytic and Antidepressant Medications

Anxiolytic medications, such as lorazepam or oxazepam, are often used for the management of agitation in demented elderly patients. However, benzodiazepine use is limited by virtue of side effects such as further cognitive impairment, drowsiness that can lead to physical injury from falls, paradoxical increases in anxiety in some patients, as well as tolerance and withdrawal syndromes. Benzodiazepines have also been associated with disinhibition in some cases. Other than for short-term use to treat acutely anxious or agitated patients, benzodiazepines

have a limited long-term benefit in the treatment of psychotic symptoms.

Buspirone, a novel serotonergic 5-HT$_1$ agonist drug with anxiolytic properties, has also been used in the management of agitation in psychotic elderly patients.[45,46] The side effects of buspirone are fewer than with the benzodiazepines and are generally limited to headaches and/or dizziness in the elderly. One double-blind study comparing buspirone with haloperidol failed to show improvement, but the doses of both drugs may have been too low.[46] Divided doses of buspirone of 30 to 40 mg/day may be effective to manage the anxiety or agitation associated with psychotic symptoms in some elderly patients.

Antidepressants have also been evaluated for managing the agitation and aggressive behavior associated with psychosis in the elderly. These drugs may have added usefulness in elderly patients who are also depressed. Trazodone, a serotonergic antidepressant with 5-HT$_2$ and α-adrenergic blocking activity, has been used effectively in treating the agitation seen in elderly psychotic patients.[47] In one double-blind study, trazodone (mean dose = 218 mg/day) was equal in efficacy to haloperidol (1 to 5 mg/day).[47] Other antidepressants including citalopram, sertraline, and fluoxetine have been reported to be effective in some anecdotal reports. Antidepressants may alleviate the emotional bluntness as well as the anxiety, irritability, and restlessness seen in psychotic patients. However, it must be noted that the side effects of the commonly used selective serotonin reuptake inhibitors can include restlessness, agitation, and gastrointestinal problems as well as sleep disturbances. Other antidepressants, such as bupropion and venlafaxine, have dopaminergic properties that might exacerbate psychotic symptoms in some elderly patients. Furthermore, delusions or hallucinations are unlikely to benefit from antidepressants and may in some cases be exacerbated by these drugs. Consequently, agitation or aggressive behaviors resulting from delusional beliefs or responses to hallucinations would be less likely to benefit from antidepressant medications.

Anticonvulsant Medications

Carbamazepine and valproic acid are often used in the management of behavioral disturbances in elderly demented patients, particularly for emotional lability, impulsivity, and agitation.[48,49] One recent survey of a large long-term care facility found that 10% of all residents were receiving an anticonvulsant medication for behavioral problems.[50]

Numerous case reports have suggested that carbamazepine may be effective in the treatment of agitated behaviors in the elderly psychotic patient. Two double-blind, placebo-controlled trials conducted in nursing homes revealed that carbamazepine was significantly more effective than placebo in reducing agitation in demented elderly patients.[49,51] The average dose of carbamazepine used was 300 mg/day.[49] The side effects of carbamazepine can include rashes, sedation, ataxia, and hepatic and hematologic abnormalities that necessitate careful monitoring for long-term use.

Divalproex sodium (the enteric-coated derivative of valproic acid) may be better tolerated than carbamazepine and equally effective in managing agitation and aggressive behaviors in elderly psychotic patients.[48] Although divalproex sodium is generally well tolerated, its side effects may include sedation, weight gain, thrombocytopenia, and hepatic abnormalities.

Although not in common practice as yet, the newer anticonvulsant medications such as lamotrigine, gabapentin, and topiramate may also have a role in the treatment of elderly psychotic patients.

Antipsychotic Medications

Although drugs like buspirone, trazodone, valproic acid, and carbamazepine have been used with some success, the primary treatment of psychoses in the elderly has been with antipsychotic medications.[17,45,51] Antipsychotic medications are divided into conventional and atypical groups based on their pharmacologic profile and liability to produce EPS.

In a review of 34 published studies, Sunderland and Silver[52] noted positive clinical responses in 60% of elderly patients receiving conventional antipsychotic medications for psychotic symptoms. Generally, low doses of haloperidol (up to 2 mg/day) or thioridazine (up to 75 mg/day) are effective. However, the usefulness of these conventional antipsychotic agents is limited by virtue of undesirable side effects (orthostasis, sedation, anticholinergic symptoms, and EPS) and the risk of tardive dyskinesia. Specifically, the extrapyramidal symptoms of dystonia, dyskinesia, bradykinesia, and akathisia contribute to gait disturbances (with increased risk of falls and fractures), irritability, and restlessness that further complicate the management of psychotic symptoms.[52,53] Further, the risk of developing tardive dyskinesia increases dramatically in elderly patients. Jeste and colleagues[23] reported that tardive dyskinesia was identified in 26% of elderly patients (mean age = 66 years) within 1 year of exposure to conventional antipsychotics in contrast to 4% in younger patients. Consequently, when conventional antipsychotics are prescribed, the practice has been to limit their use to brief periods and attempt to taper their use, if possible.

Atypical antipsychotic drugs like olanzapine and quetiapine (which have lower liability for EPS and tardive dyskinesia and have better overall safety profiles) provide a new therapeutic approach for the treatment of psychotic symptoms in elderly patients and may eventually replace conventional antipsychotics in these elderly patients. The atypical antipsychotics differ slightly in their pharmaco-

logic profile, and risperidone and olanzapine do have some risk for the development of EPS at increasing dosage levels.

Clozapine was the first atypical antipsychotic medication approved for use in the United States.[51] In addition to blocking dopamine activity (D_2 antagonism) common to the conventional antipsychotics, clozapine has serotonergic blocking activity (5-HT_2 antagonism) that appears to blunt the nigrostriatal dopamine blocking effect and thereby minimize the development of EPS or tardive dyskinesia.[51,53] Doses less than 100 mg/day are usually effective in managing psychotic symptoms in elderly patients. However, the side effects of clozapine require very cautious use in elderly patients. In addition to orthostasis, impaired glucose utilization, and sedation, clozapine can induce agranulocytosis in 1% to 2% of patients and can have cardiac effects as well.[51] Patients must be monitored weekly with blood work to rule out leukopenia. The other atypical antipsychotic medications do not have this hematologic risk and do not require weekly blood monitoring. Consequently, clozapine should be reserved for use only after other antipsychotic agents have failed.

Risperidone is effective in reducing aggressive behavior as well as paranoia and delusions in elderly psychotic patients.[51,53,54] In a study of 12,000 long-term care residents, risperidone was equivalent to both haloperidol and thioridazine but had fewer side effects.[54] In another nursing home study of 456 Alzheimer's patients, risperidone in doses of 0.5 to 2 mg/day was significantly better than placebo in this 12-week double-blind study.[55] In this study, EPS was reported in 7% of patients receiving 0.5 mg of risperidone and 21% of patients receiving 2 mg of risperidone.[55] Beyond the emergence of EPS with increasing doses of risperidone, orthostasis and sedation are safety concerns as with other antipsychotic medications.

Olanzapine was significantly better than placebo in double-blind nursing home studies of psychotic, demented elderly patients.[56] After starting treatment at doses of 2.5 mg/day, final titrated doses between 5 and 10 mg/day are usually effective in managing delusions, hallucinations, and aggression. Although the emergence of significant EPS was not reported in the nursing home study, it has been reported that EPS is exacerbated when olanzapine is given to Parkinson's disease patients.[17,40] Other side effects include orthostasis and sedation, abnormal gait, and recent concerns about impaired glucose utilization.[57]

Quetiapine was effective in a 52-week open-label treatment study of psychotic elderly patients.[51,58] Side effects of quetiapine include sedation, orthostasis, and dizziness. Unlike risperidone or olanzapine, quetiapine has had no reports of increased incidence of EPS with rising doses in younger schizophrenic patients or in Parkinson's disease patients. The starting dose of 25 mg/day can be effective in some patients, although the mean dose in elderly patients is about 125 mg/day.[58]

Ziprasidone is the most recent atypical antipsychotic to be approved for use in the United States. Consequently, it has not as yet had wide use in treating psychotic symptoms in elderly patients. The pharmacologic profile of ziprasidone suggests that it will also be effective in treating psychosis in the elderly and have similar side effects of sedation and orthostasis but limited EPS in this population. A safety concern regarding ziprasidone has been a prolongation of the QTc interval that could have implications for patients on multiple medications or with cardiac conditions.

Cholinergic Drugs

Some studies have suggested that the cholinergic drugs used to treat patients with Alzheimer's disease may also affect behavior in these patients. Tacrine, physostigmine, and xanomeline (all cholinesterase inhibitor drugs) have been shown to yield a greater reduction in delusions, suspiciousness, hallucinations, and agitation than placebo.[32,33,45] Although cholinergic drugs are not a primary treatment for psychotic symptoms in dementia, these findings reflect the interrelationship between cognitive difficulties and disruptive behavior.

SUMMARY

Psychosis in the elderly is often accompanied by behavioral disturbances including agitation and uncooperative behavior. The early recognition of emerging psychotic symptoms, interpretation of underlying etiologies, and initiation of appropriate treatment interventions will reduce morbidity and improve the quality of life for these patients. The relatively recent introduction of atypical antipsychotic medications (clozapine, quetiapine, olanzapine, risperidone, ziprasidone) offers a group of drugs that are very effective in managing psychotic symptoms, yet have a low liability for the development of extrapyramidal symptoms. Cautious use of these atypical antipsychotic drugs (i.e., watching for orthostasis, dizziness, and sedation) may offer the best available pharmacologic treatment for psychotic symptoms in elderly patients at the present time.

Drug names: amantadine (Symmetrel and others), amitriptyline (Elavil and others), amphetamine (Adderall), bupropion (Wellbutrin and others), carbamazepine (Tegretol and others), carbidopa-levodopa (Sinemet and others), chlorpromazine (Thorazine and others), cimetidine (Tagamet and others), citalopram (Celexa), clozapine (Clozaril and others), digoxin (Lanoxin and others), diphenhydramine (Benadryl and others), divalproex sodium (Depakote), doxepin (Sinequan and others), fluoxetine (Prozac and others), gabapentin (Neurontin), haloperidol (Haldol and others), indomethacin (Indocin and others), lamotrigine (Lamictal), lorazepam (Ativan and others), methylphenidate (Ritalin and others), olanzapine (Zyprexa), oxazepam (Serax and others), paroxetine (Paxil), phenytoin (Dilantin and others), primidone (Mysoline), propranolol (Inderal and others), quetiapine (Seroquel), risperidone (Risperdal), sertraline (Zoloft), tacrine (Cognex), topiramate (Topamax), valproic acid (Depakene and others), venlafaxine (Effexor), ziprasidone (Geodon).

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