Recognizing and Managing Antipsychotic Drug Treatment Side Effects in the Elderly

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Although atypical antipsychotics differ from conventional antipsychotics in their decreased ability to cause reversible drug-induced movement disorders/motor side effects such as dystonia, drug-induced parkinsonism, and akathisia and potentially persistent drug-induced movement disorders/motor side effects such as tardive dyskinesia, no antipsychotic agent completely eradicates this risk. Antipsychotic agents are frequently used in facilities for the elderly and in general hospitals to treat older patients with behavioral problems. Drug-induced movement disorders are more common and more persistent in elderly patients than in younger patients, and this problem is exacerbated by the fact that antipsychotic medications are often misused by practitioners lacking adequate psychopharmacologic training. Movement disorders can be detrimental to an elderly patient's quality of life and may transform what were otherwise routine activities into difficult tasks. Educational programs are needed to teach primary care physicians, specialists, and patients and their families how to identify and manage drug-induced movement disorders in order to achieve safer and more efficacious care for elderly patients. *(Prim Care Companion J Clin Psychiatry 2004;6[suppl 2]:14–19)*

Antipsychotic agents have been widely used since the 1950s, when they revolutionized the care of patients with severe psychiatric disorders. More than 20 of these agents have been introduced in the United States since that decade. With a generally good benefit-to-risk ratio, antipsychotic drugs have substantially improved functioning and quality of life for a number of patients with psychotic disorders. Antipsychotics that were in use through the 1980s are generally referred to as conventional antipsychotics, and newer agents developed in the 1990s are referred to as atypical antipsychotics. Atypical antipsychotics differ from conventional antipsychotics in their decreased tendency to cause reversible drug-induced movement disorders/motor side effects such as dystonia, drug-induced parkinsonism, and akathisia and potentially persistent drug-induced movement disorders/motor side effects such as tardive dyskinesia, while simultaneously reducing psychotic symptoms. Although all atypical antipsychotics have antipsychotic action with fewer motor side effects than conventional antipsychotics, no antipsychotic agent completely removes a patient's risk of developing a movement disorder or less harmful adverse events. Elderly patients are especially vulnerable to side effects of any medication, and antipsychotic agents are no exception.

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This article was derived from the planning roundtable "Using Atypical Antipsychotics in Primary Care," which was held June 2–4, 2002, in Washington, D.C., and supported by an unrestricted educational grant from Janssen Pharmaceutica, L.P.

Original funding for this work was provided by National Institute on Aging grant AG13785 (Dr. Saltz).

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ANTIPSYCHOTIC USE IN THE ELDERLY

Antipsychotic agents are frequently used in facilities for the elderly and in general hospitals to treat older patients with behavioral problems, which are not uncommon. In nursing home facilities, behavioral disturbances are seen in as many as 40% to 95% of residents—40% to 80% with dementia, 5% to 25% with depression, and 2% to 5% with schizophrenia.[1–3] However, although approximately 50% to 75% of all nursing home residents take antipsychotic medications,[4] only a relatively small proportion of residents actually see a mental health professional. In a study of the availability of mental health services in nursing homes, data indicated that 65% of nearly 2000 nursing home residents were found to have some type of mental disorder[3]; yet, the 1-month rate of contact with mental health professionals for this group was only 4.5%.[5] Additionally, only 2% with a diagnosis of dementia and 17% of residents diagnosed with chronic schizophrenia had seen a mental health specialist.[5]

Unfortunately, antipsychotic medications can be misused by practitioners who lack psychopharmacologic training.[6] Mental illnesses are frequently misdiagnosed, unrecognized, or undertreated in the elderly, partly because delirium and dementia may masquerade as depression or anxiety to the inexperienced observer. Additionally, compared with younger patients, elderly patients who receive antipsychotics are at an increased risk for developing reversible drug-induced movement disorders/motor side effects such as dystonia, drug-induced parkinsonism, and akathisia as well as potentially persistent drug-induced movement disorders/motor side effects such as tardive dyskinesia.

In an attempt to reverse the over-utilization and under-supervision of antipsychotic medications, Congress implemented federal regulations on October 1, 1990, for use in Medicare- and Medicaid-certified nursing homes in the United States. These regulations marked the first time in American history that a prescription drug had to be legally justified by indications recorded in a patient's medical chart. A study[7] that was conducted a year later found that if these regulations had been in effect from 1976 to 1985, 50% of antipsychotic drug use in almost 9,000 nursing homes would have been out of compliance with the federal regulations. Congress hoped that these regulations might influence medical practitioners to expand their knowledge of psychopharmacology.

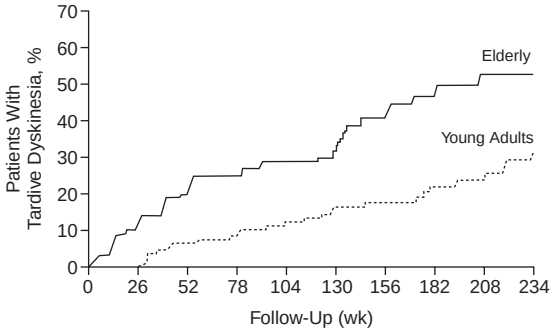
Although federal regulations have undoubtedly instigated some improvements in the prescribing patterns of many primary care physicians, these regulations have not addressed all of the challenges associated with antipsychotic use. Many primary care physicians have not had training in the use of antipsychotic agents. In recent years, many elderly patients have been switched to managed-care programs that require patients to seek primary care providers for their medical and mental health care. Therefore, as more elderly patients choose managed-care coverage, more primary care physicians will be prescribing antipsychotic agents.

Educational programs designed for primary care physicians and specialists such as nurses, psychologists, and social workers, as well as patients and their families, are clearly needed to achieve safer and more efficacious care for elderly patients. Learning to identify, distinguish, and manage drug-induced movement disorders associated with conventional, and sometimes atypical, antipsychotic agents can aid primary care physicians and others in achieving that end.

DRUG-INDUCED MOVEMENT DISORDERS IN THE ELDERLY

Drug-induced movement disorders/motor side effects are more common and more persistent in elderly patients than in younger patients.[8] Reversible and persistent drug-induced movement disorders/motor side effects are 3 to 6 times more prevalent in institutionalized elderly patients who take conventional antipsychotic medication than in elderly patients who do not.[9] My colleagues and I have studied the prevalence of tardive dyskinesia in the elderly and have determined that this disorder is considerably more common in elderly than in younger patients receiving antipsychotic treatment.[8,10,11] As demonstrated in Figure 1, in younger patients, the incidence of tardive dyskinesia after 1 year of exposure to an antipsychotic drug is approximately 5%.[10,11] In striking contrast, the incidence of tardive dyskinesia development reported in older adults is almost 25%.[8] After 3 years of continual treatment, the incidence of tardive dyskinesia had increased to only15% for the younger patients, yet as many as 43% of the older patients had developed the condition.[8]

Figure 1. Tardive Dyskinesia in Elderly Versus Young Adults[a]



[a]Adapted with permission from Mental Health Advocates, Inc.[12]

Movement disorders are often detrimental to an elderly patient's quality of life and may transform into extraordinarily difficult tasks what were otherwise routine daily activities such as eating, walking, and sleeping. These movement disorders are frequently difficult to distinguish from a patient's other medical problems, as well as from one another. There are 4 major categories of movement disorders/motor side effects that are associated with antipsychotic treatment—drug-induced parkinsonism, akathisia, dystonia, and tardive dyskinesia. Because movement disorders can compromise an elderly patient's quality of life, physicians should view them as serious medical conditions that need to be addressed and should be able to recognize each type of disorder in order to provide appropriate effective treatment (Table 1).

Drug-Induced Parkinsonism

Drug-induced parkinsonism is a common side effect of conventional antipsychotic treatment. Approximately 40% of older patients treated with conventional antipsychotics develop drug-induced parkinsonism even at very low doses.[11] Additionally, when parkinsonism develops, it may continue unabated as long as the treatment is continued.

Table 1. Neuromotor Side Effects of Antipsychotic Medications[a]

Side Effect	Reversible?	Symptom	Treatment
Parkinsonism	Usually	Tremor, increased muscle tone, bradykinesia or akinesia, drooling, postural instability, loss of spontaneity, micrographia, seborrhea	Lower dose Change to low-potency or atypical agent Add anticholinergic agent
Akathisia	Usually	Restlessness	Lower dose Add benzodiazepine, β blocker, or α-adrenergic agent (eg, clonidine)
Dystonia	Often, if during acute treatment; less often if it develops later	Sustained muscle contractions	Add anticholinergic agent or antihistamine Lower dose Change to low-potency or atypical agent
Tardive dyskinesia	Sometimes	Hyperkinesia, involuntary body movements (usually choreiform)	Lower dose or discontinue agent Change to low-potency or atypical agent Raise dose to mask effects

[a]Reprinted with permission from Saltz et al.[13]

Drug-induced parkinsonism can cause discomfort and often contributes to falls in older adults. The added difficulty of movement may contribute to a patient's social isolation and may create an additional burden on caregivers. Atypical antipsychotic agents usually cause fewer parkinsonian symptoms than do conventional agents when given in doses at the lower end of their therapeutic range, and therefore may be a better choice than conventional antipsychotics in treating psychosis or agitation in patients with idiopathic Parkinson's disease.

Tremors are one of the cardinal features of drug-induced parkinsonism.[13] These symptoms can occur at rest or upon movement, often disappear with sleep, and frequently worsen with stress and anxiety. Parkinsonian tremor is sometimes difficult to distinguish from lithium-induced tremor or tremor associated with thyroid, liver, or cerebellar diseases. However, these other tremors usually oscillate at a slightly faster frequency, and cerebellar disease tremor is often a more coarse form of tremor.[14] A pill-rolling movement of the hand may be seen, and rigidity of major joints and muscles often occurs in drug-induced parkinsonism. Affected muscles may also be continuously firm and tense, even when the patient appears quiet and relaxed, and the patient may display increased resistance to passive movement throughout the range of the affected limb—a condition known as cogwheel rigidity. Other signs of rigidity include stiff gait, difficulty initiating movement, or turning. The patient may additionally display bradykinetic movement with a general loss of spontaneity. In severe cases, the patient may not shift body position or posture, and may speak slowly or softly, exhibiting little spontaneous communication. In extreme cases, the patient may be mute or inanimate for long periods of time. Other features of drug-induced parkinsonism include increased salivation, drooling, seborrhea, and postural instability.

Other conditions such as idiopathic Parkinson's disease or severe depression may be confused with drug-induced parkinsonism; therefore, physicians should always examine a patient for movement disorders before prescribing antipsychotic medications. Patients with idiopathic Parkinson's may benefit from antipsychotic medication, but a neurologist or psychiatrist should be consulted first. One difference between idiopathic and drug-induced parkinsonism is that drug-induced parkinsonism does not usually exhibit the on-off phenomenon commonly seen in idiopathic Parkinson's disease. The psychomotor retardation of depression may also be difficult to differentiate from the bradykinesia of parkinsonism. To rule out depression as a cause of the bradykinesia of parkinsonism, physicians should inquire about mood and other depressive symptoms such as a change in appetite, insomnia, loss of interest in activities, feelings of guilt or worthlessness, and suicidal ideation.

The best way a physician can determine drug-induced parkinsonism is to observe the patient. Watching a patient perform incidental activities such as entering the examination room, removing shoes and socks, and exiting the examination room may reveal clinically important findings that may not otherwise be apparent. However, some patients do not spontaneously demonstrate symptoms. A movement disorder in these patients will only become apparent when elicited by the physician. The physician can ask the patient to extend both arms outward (horizontal to the floor), or give the patient a task such as drawing a spiral or writing a complete sentence, name, or address. These tests will provide the physician an opportunity to observe tremor and slowness as well as micrographia, which may be another feature of parkinsonism. Cogwheel rigidity can be detected by moving each of the patient's limbs at the wrist, elbow, shoulder, ankle, knee, and hip while looking for a ratchet-like resistance, which would be indicative of this condition. Additionally, these patients may demonstrate a slow and inhibited arm-drop. Testing may require diverting the patient's attention to prevent the patient from deliberately helping or resisting the examiner. A physician can identify postural instability by testing for lateropulsion, retropulsion, and anteropulsion. The physician should ask the patient to stand with his or her eyes open and arms limp and then gently push the patient's shoulders from left to right and forward to back, to see if

the patient can maintain balance against the slight degree of force.

The first strategy in managing these side effects of antipsychotic drugs is to consider other treatments. Antipsychotics are sometimes prescribed unnecessarily (for their sedative properties, for example) when other medications could be used. After careful consideration, if antipsychotic treatment is determined to be the appropriate treatment, then the physician should consider lowering the dose. If decreasing dosage is not effective or not advisable due to the severity of the patient's psychotic symptoms, then switching to a low-potency antipsychotic or—if the patient is not already receiving one—an atypical antipsychotic might improve symptoms, since atypical antipsychotics are associated with fewer motor side effects. If necessary, the physician might consider adding an anticholinergic agent.[13] Benztropine is commonly prescribed for the purpose of treating drug-induced parkinsonism. However, anticholinergic agents should be used sparingly, and only for a short time, because they may cause increased heart rate, memory loss, blurred vision, urinary retention, and constipation in older patients.

Akathisia

Akathisia is a common, drug-induced type of motor restlessness that should always be considered when evaluating agitated or restless older adults receiving antipsychotic treatment. It is typically accompanied by a feeling of inner restlessness (sometimes described as anxiety), an urge to move, and an inability to sit still.[15] Patients may describe themselves as feeling as if they are "jumping out of their skin." Akathisia most often involves the lower extremities but can also involve the upper body. The most common expressions of akathisia are shifting of body weight from one foot to another while standing and repeated swinging or crossing and uncrossing of the legs. In severe cases, patients may move their feet and legs or pace constantly. The most severely impaired patients may not be able to describe the subjective features of akathisia. In these patients, pacing or another persistent movement may be the only manifestation.

Many doctors confuse akathisia with tremor or anxiety, and akathisia and psychomotor agitation are often difficult to distinguish since purposeless movements can occur in both. While complex behaviors are more characteristic of psychomotor agitation, pronounced rhythmic or regular movements are more characteristic of akathisia. Akathisia should be carefully distinguished from psychomotor agitation, because an increase in antipsychotic medication in an erroneous attempt to control agitation may increase akathisia symptoms. Conversely, if a patient is experiencing agitation rather than akathisia, then agitation may worsen with an antipsychotic dose reduction. The response to a change in medication dosage may be the only way to distinguish between akathisia and agitation in some patients.

Akathisia usually disappears when antipsychotic treatment is discontinued. Other medications should be considered if antipsychotics are not absolutely necessary. If antipsychotics are necessary, however, changing the antipsychotic agent or reducing the dose is the best long-term management strategy. Treatment with a benzodiazepine, low-dose propranolol,[16] or the alpha-adrenergic drug clonidine[17] may be effective in treating akathisia; however, these medications can have adverse effects, including confusion, gait instability, and (rarely) addiction. Initial treatment should be for 5 to 10 days and should be followed by a gradual reduction in dose; however, some patients may require continual treatment for the duration of antipsychotic treatment.

Dystonia

Characterized by sustained contraction of muscles, dystonia generally causes twisting postures that most commonly affect neck and arm muscles and may be visible only when the patient is moving. The extraocular and periorbital eye muscles may also be affected, precipitating a painful event known as oculogyric crisis. In such cases, the patient's eyes rotate upward or to the side and remain in that position for a potentially lengthy period of time ranging from seconds to minutes or, in extreme cases, even hours. The patient's eyes may appear to have rolled up into the head or the physician may see forced eye closure. When dystonia affects the trunk and lower extremities, an associated gait disturbance is often apparent. Dystonia can occur shortly after treatment begins or it may appear after prolonged treatment. Acute dystonic reactions are substantially more rare in the elderly than in younger adults and require immediate treatment.

Almost all dystonic reactions respond to anticholinergic treatments such as benztropine or diphenhydramine, although intramuscular administration of these agents may be required. Dystonia is usually reversible unless it develops in the late stages of treatment. Once an acute dystonic episode is under control, the antipsychotic medication should be switched or the dosage should be lowered.

Tardive Dyskinesia

Tardive dyskinesia is a drug-induced movement disorder that may persist even after discontinuing treatment. It tends to be more prevalent in older adults. In the previously cited prospective study[8] of tardive dyskinesia in patients treated with conventional antipsychotics the incidence of tardive dyskinesia development in older adults was about 3 to 5 times greater than what has been found for younger patients. However, most cases of tardive dyskinesia in the elderly tend to be mild in severity and are not usually profoundly disabling. In fact, affected individuals may not even be aware of the presence of the disorder. Elderly patients who have been treated with electroconvulsive therapy or who have a history of diabetes or

alcohol abuse are at an increased risk of developing tardive dyskinesia. However, currently no test can accurately predict which patients will develop a mild form of the disorder and which patients will develop a more severe form.

Patients with tardive dyskinesia have involuntary movements of the muscles of the face, mouth, and tongue that are referred to as orofacial dyskinesias and are characterized by repetitive oral, facial, and lingual movements resembling grimacing, chewing, lip smacking, tongue protrusion (fly-catching), writhing movements of the tongue, or lateral tongue movements in the floor of the mouth (bon-bon sign). These movements are present in almost every elderly patient with tardive dyskinesia, and approximately 40% of elderly patients with tardive dyskinesia have no other dyskinesias.[8] The fingers, arms, trunk, legs, and toes may also be affected. Choreiform movements are most frequently seen, but choreoathetoid, ballistic, myoclonic, dystonic, and ticlike movements also occur. In the upper extremities, finger movements are the most common, and in the lower extremities, common tardive dyskinesia movements involve the toes, ankles, or legs at the knees or hips. Abdomen and pelvic muscle involvement may produce pelvic rocking. Although tardive dyskinesia movements of the neck and trunk are rare, when they do occur, they can be very disabling. Other examples of movements include repetitive and patterned hand waving, toe wiggling, head bobbing, and body rocking. Rarely, in very severe cases, the whole body may be affected, including the muscles that control breathing and swallowing. Respiratory involvement produces sudden, forced, audible expiration and inspiration or grunting. In rare instances, tardive dyskinesia can interfere with a patient's mobility. Most abnormal involuntary movements can be consciously suppressed for brief periods, and they often disappear completely during sleep. Symptoms are often exacerbated with anxiety or activation techniques during examination. In some patients, embarrassment about displaying unusual movements may lead to social withdrawal and isolation.

Movements indicative of tardive dyskinesia may resemble those of other disorders such as Huntington's chorea, antiparkinsonian drug-induced dyskinesia, psychostimulant-induced dyskinesia, autism, mental retardation, Rett's syndrome, restless leg syndrome, and akathisia. However, in patients with tardive dyskinesia these movements are usually not accompanied by additional symptoms of another condition (e.g., dementia in Huntington's chorea). Additionally, approximately 5% of elderly patients have spontaneous orofacial dyskinesias that are not related to drug exposure.[18] Patients with neurologic disorders also frequently have orofacial movements,[19] and problems associated with teeth or dentures may also give the appearance of orofacial dyskinesia. Therefore, it is important for a physician to examine a patient for dyskinesias prior to prescribing antipsychotic drugs. Also, before beginning an examination, the physician should ensure that the patient's mouth is empty and check for dental problems.

A physician can evaluate a patient for tardive dyskinesia by performing a systematic examination. The physician should begin by asking the patient to relax and look straight ahead, and then observe facial grimacing, tics, eye movements (such as forced eye closure), and lip movements (pressing, pouting, puckering, smacking, chewing, or other jaw movements). The physician should additionally note tongue movements, which may be observed at rest. While the patient is relaxed, a physician should also attempt to identify the sudden, forced audible inspiration and expiration or grunting indicative of symptomatic respiratory movements. Patients may also experience nutrition problems related to dyskinesias, and a physician should take notice of a dramatic loss or gain in weight.

Tardive dyskinesia movements can often be revealed or amplified by an activation technique since many patients need to be distracted before the disorder will visually manifest. To distract the patient, a physician might consider observing the patient with his or her mouth open for 20 to 30 seconds and then ask the patient to hold up his or her hand while tapping each finger to the thumb in sequence. Another technique is to have the patient display rapid, alternating movements by repeatedly and quickly pronating and supinating the hands at the wrists—either simultaneously or one on top of the other. The physician can also ask the patient to open and close each hand while the mouth is open. This will enable the physician to observe any curling or writhing movements of the tongue.

To date, no uniformly effective treatment for tardive dyskinesia or chronic tardive-type dystonias exists. When treating tardive dyskinesia, physicians should try lowering the dose, switching, or discontinuing the antipsychotic. However, occasionally, in the most severe versions of choreiform dyskinesia and dystonia, if symptoms persist, a dose increase may actually cause suppression of these movements. Since no treatment has proved to be effective in tardive dyskinesia, a primary care physician should consider other drugs as a first step in managing this side effect of antipsychotic agents. If antipsychotic medications are necessary for treatment, then the physician should apply the lowest effective dose and consider using an atypical antipsychotic, since these agents are associated with fewer neuromotor side effects than conventional antipsychotics.

CONCLUSIONS

Emphasis should be placed on prevention as the first strategy in managing side effects of antipsychotic use in the elderly. In general, antipsychotics should be used in older patients only when a psychosis is present and should not be used for disorders such as insomnia, anxiety, or depression—particularly since there are effective alterna-

tive treatments for these disorders that are associated with fewer risks. Patients receiving continual antipsychotic treatment should be advised of the risks associated with antipsychotic agents and should be examined periodically to screen for early manifestations of symptomatic movements. Additionally, the lowest effective dose should be used, and the need for these medications should be reassessed by a physician frequently, at a minimum of every 4 to 6 months. Antipsychotics should be discontinued if no longer indicated (e.g., patients who develop psychotic symptoms as part of a delirium may only need antipsychotic treatment until the medical cause of the delirium resolves). In the past, brief interruptions (drug holidays) were sometimes used in patients who required maintenance antipsychotic therapy. However, drug holidays from antipsychotics are now thought to increase the risk of persistent tardive movements and are therefore not recommended.

It is essential that primary care physicians understand the qualitative differences between the 4 drug-induced movement disorders, particularly since tardive dyskinesia may be irreversible. Additionally, elderly patients with these conditions experience a high risk of falling, and they may have nutrition problems related to dyskinesias. It is therefore essential to educate not only primary care physicians about the risks associated with antipsychotic use but also nurses, psychologists, social workers, and caregivers since they are in frequent contact with patients and can bring problems to the attention of psychiatrists or primary care physicians when they occur.

Drug names: benztropine (Cogentin), clonidine (Iopidine, Clorpres, and others), diphenhydramine (Benadryl and others), olanzapine (Zyprexa), propranolol (Inderal, Innopran), risperidone (Risperdal).

Disclosure of off-label usage: The authors of this article have determined that, to the best of their knowledge, benztropine is not approved by the U.S. Food and Drug Administration for the treatment of acute dystonia; clonidine and propranolol are not approved for the treatment of akathisia; diphenhydramine is not approved for the treatment of drug-induced parkinsonism/acute dystonia; and olanzapine and risperidone are not approved for the treatment of delirium and agitation and psychosis (nonschizophrenic).

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