Side Effects of Antipsychotics in the Elderly

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Side effects of antipsychotic medications are particularly problematic in elderly patients, who experience many age-related changes that may exacerbate medication side effects. Side effects of particular concern in the elderly include anticholinergic reactions, parkinsonian events, tardive dyskinesia, orthostatic hypotension, cardiac conduction disturbances, reduced bone mineral density, sedation, and cognitive slowing. In addition, elderly patients with schizophrenia often have comorbid medical illnesses—such as cardiovascular disease and dementia of the Alzheimer's type—and are thus likely to be taking multiple medications. The effects of polypharmacy must be carefully considered. Patients, caregivers, and family often have different perspectives on side effects. This article addresses the side effects of the currently available antipsychotic medications in light of these concerns.

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The side effects of antipsychotic medications, which can cause difficulties in any patient population, are particularly troublesome in the elderly. Elderly schizophrenic patients frequently have comorbid medical illnesses and take multiple medications.

Use of conventional antipsychotics in elderly patients has often been limited by adverse effects, but the newer atypical antipsychotics hold promise for elderly patients, including those who are unable to tolerate conventional antipsychotics. In a series of open and controlled studies as well as case reports, risperidone and olanzapine have shown efficacy in the treatment of elderly patients with psychosis.

The elderly experience age-related changes that can exacerbate or mimic the side effects of antipsychotic medications; pharmacokinetic changes affect drug absorption rates and excretion. Side effects of particular concern in the elderly include anticholinergic reactions, parkinsonian events, tardive dyskinesia, orthostatic hypotension, cardiac conduction disturbances, reduced bone mineral density, sedation, and cognitive slowing.

Elderly patients with schizophrenia often have comorbid medical illnesses such as cardiovascular disease or dementia of the Alzheimer's type. Treatment of these illnesses makes it likely that the elderly schizophrenic patient will be taking multiple medications; hence, combined medication side effects and drug interactions must be carefully considered. Established treatments for one illness may worsen aspects of a comorbid disorder. For example, Parkinson's disease presents particular treatment problems in the elderly. Dopaminergic agents are usually indicated, but these agents frequently cause psychotic symptoms. Agents that block dopamine, on the other hand, worsen mobility and tremor.

There are other side effects of antipsychotic medication that are more common, though not necessarily serious, in the elderly population. Anticholinergic side effects—including dry mouth, constipation, blurred vision, urinary retention, and confusion (particularly with low-potency conventional antipsychotics and with clozapine and olanzapine)—compound health problems in the elderly. The use of antipsychotic medications can cause or exacerbate anticholinergic delirium. Pseudoparkinsonian side effects include tremulousness, akathisia, akinesia, and dystonia. Tardive dyskinesia is another common side effect in elderly psychotic patients.

Zayas and Grossberg[1] point out that the high-potency neuroleptics (such as haloperidol and fluphenazine) have a higher affinity for dopamine receptors and less affinity for the α_1-adrenergic and muscarinic receptors. Accordingly, high-potency antipsychotics tend to cause extrapyramidal symptoms (EPS) or parkinsonian symptoms, akathisia, acute dyskinesia, and acute dystonic reactions. The intermediate-potency neuroleptics (such as perphenazine, loxapine, and molindone) have a greater affinity for the histaminergic, α_1-adrenergic, and muscarinic receptors. The researchers seldom recommend the use of low-potency antipsychotics (chlorpromazine and thioridazine), which can cause both peripheral and central anticholinergic side effects, including confusion, and can increase the risk of falls in the elderly, secondary to sedation and orthostasis.

The pharmacokinetics of antipsychotic medications are affected by age-related changes in the elderly. In particu-

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lar, drug levels can be affected by changes in hepatic metabolism and renal excretion.[2] Delayed absorption and onset of action may arise from the use of antacids and compounds with vast absorbing surfaces like psyllium husk fiber. Age-related changes in body composition also affect the pharmacokinetics of antipsychotic medications in the elderly. These changes include decreased lean muscle mass and total body water with concomitant increase in total body fat. Decreases in liver mass, hepatic blood flow, serum albumin levels, and renal blood flow and function occur as well. The hepatic cytochrome, however, is not affected by increasing age.

Since the half-life of a drug is directly proportional to the volume of distribution divided by the clearance of that drug, age-related increases in total fat mean that the volume of distribution is increased and the half-life of lipophilic and protein-bound medications is prolonged. As a result of these changes and others—including lower levels on measures of renal function, hepatic blood flow, serum albumin, and lean muscle mass—elderly patients should be given lower doses of lipophilic drugs such as phenothiazines and benzodiazepines.

CONVENTIONAL NEUROLEPTICS

Conventional neuroleptics have long been the treatment of choice for patients with schizophrenia, schizoaffective disorder, or schizophreniform disorder. Atypical antipsychotics—recently introduced—form a new generation of medications that are more effective and have a much more benign side effect profile than the conventional antipsychotics. Although conventional neuroleptics are effective in treating psychotic disorders, elderly patients are particularly susceptible to the adverse effects of conventional neuroleptic medications. Lanctot et al.[3] conducted a meta-analysis of 16 controlled, double-blind studies that investigated the side effects of conventional neuroleptics in dementia. Side effects occurred in twice as many patients receiving an active drug (50%) as in patients receiving placebo (25%). In this study, at least 21% of patients had an important side effect such as EPS, sedation, or orthostatic hypotension. The researchers concluded that conventional neuroleptics have been associated with a range of potentially serious side effects and should be prescribed with caution in elderly patients.

Tardive Dyskinesia

Elderly patients are at great risk for tardive dyskinesia, a potentially irreversible side effect of conventional neuroleptics. Yassa et al.[4] assessed 251 elderly, neuroleptic-naive patients on their first admission to an inpatient psychiatric hospital. Of the 162 patients available for follow-up, 99 had been treated with neuroleptics, and 35 of them (35.4%) developed tardive dyskinesia. Ten (4.0%) of the original 251 patients showed spontaneous tardive dyskinesia before neuroleptic therapy had begun. Eleven (22.9%) of the 48 patients who were exposed to neuroleptic therapy for 1 to 12 months developed tardive dyskinesia, while 7 (50.0%) of the 14 patients taking antipsychotics for 13 to 24 months showed the condition. Four (33.3%) of the 12 patients who received neuroleptics for 25 to 36 months developed tardive dyskinesia, compared with 8 (57.1%) of the 14 patients who were treated for 37 to 48 months. Five (45.5%) of the 11 patients who received antipsychotics for 49 to 60 months showed tardive dyskinesia.

Saltz et al.[5] presented preliminary data from a prospective study of tardive dyskinesia in the elderly. The researchers followed 160 elderly patients, ranging in age from 57 to 99 years (mean age = 77 years), for at least 1 month after initiation of neuroleptic therapy. The incidence of neuroleptic-induced tardive dyskinesia after up to 43 weeks of exposure in these neuroleptic-naive patients was 31%. The researchers noted that although this rate was not high compared with other prevalence rates for tardive dyskinesia, tardive dyskinesia occurred surprisingly early in treatment.

In a follow-up study of 261 neuroleptic-naive patients more than 55 years old, the cumulative rate of tardive dyskinesia was 25% after 1 year, 34% after 2 years, and 53% after 3 years of neuroleptic therapy.[6] On the basis of this and previous studies,[7,8] the researchers concluded that the rate of tardive dyskinesia in patients over 50 years old was 3 to 5 times greater than the rate among younger age groups. In most of the older patients, tardive dyskinesia was persistent and attained at least moderate severity levels. Jeste et al.[6] also found that the occurrence of tardive dyskinesia in elderly patients was directly related to length of exposure to neuroleptic medication.

Preliminary data show a reduced risk for tardive dyskinesia with atypical antipsychotics compared with conventional neuroleptics. Jeste et al.[9] compared the 9-month cumulative incidence of tardive dyskinesia in older patients with schizophrenia (N = 122) treated with risperidone or haloperidol. The median daily dose of each medication was 1 mg, and patients were assessed at baseline, 1 month, 3 months, 6 months, and 9 months by using the Abnormal Involuntary Movement Scale and the modified Simpson-Angus Scale for extrapyramidal symptoms. Life table analysis revealed that tardive dyskinesia was significantly more likely to develop in haloperidol-treated patients than in those treated with risperidone.

Neuroleptic Malignant Syndrome

It is difficult to establish the prevalence of neuroleptic malignant syndrome in the elderly and to compare it with the prevalence in young adults; there are few data about the elderly in any prospective study. However, since elderly patients are more likely to have organic brain syndrome and electrolyte disturbances—both risk factors for neuroleptic malignant syndrome—it seems likely that the syndrome is more common in the elderly.

ATYPICAL ANTIPSYCHOTICS

Four atypical antipsychotics have been approved to date by the U.S. Food and Drug Administration (FDA). Clozapine, the first to be approved, is used almost exclusively in patients with treatment-refractory schizophrenia due to the potentially fatal side effect of agranulocytosis. The remaining 3—risperidone, olanzapine, and quetiapine—are distinguished from their conventional predecessors by a much-improved side effect profile. They are differentiated from the conventional antipsychotics by a lower level of EPS but are associated with sedation (clozapine and olanzapine), weight gain (clozapine, olanzapine, and quetiapine), and increased prolactin levels (risperidone).

Clozapine

The reported side effects of clozapine include sedation, hypersalivation, tachycardia, hypotension, hypertension, constipation, urinary incontinence, fever, and agranulocytosis.[10] Patients taking clozapine are required to have their cellular blood count monitored weekly for the first 6 months of therapy and every 2 weeks thereafter. Physicians must monitor total white blood count as well as neutrophil counts. Patients should have tried and failed at least 2 previous neuroleptics before taking clozapine. Elderly patients taking clozapine should be monitored for all possible side effects, not just the well-known blood dyscrasias. Other clinically significant side effects of clozapine in elderly schizophrenic patients include lethargy, sedation, postural hypotension, confusion, and anticholinergic effects. In a case series[11] reporting on 4 patients, all 4 experienced adverse events temporally related to the initiation of clozapine therapy and possibly connected to it. Falls and bradycardia occurred in 2 patients each, although no other reports of falls or bradycardia with clozapine are found in the literature.

Side effects are commonly a reason for clozapine discontinuation in elderly patients. Chengappa et al.[12] studied 12 older women (mean age = 59 years) receiving 25 to 300 mg/day of clozapine. Six women took doses that were titrated rapidly to the maximum dose, while the other 6 took doses that were titrated slowly to that dose. All 6 in the rapid-titration group dropped out of the study because of side effects, compared with 1 patient in the slow-titration group. These findings reinforce the warning that clozapine doses must be titrated very slowly in older patients because they are often more intolerant of antipsychotic side effects than other populations. Sajatovic et al.[13] studied clozapine in 329 treatment-refractory or treatment-intolerant patients (mean age = 63.4 ± 6.5 years) for 5 years. The mean ± SD dose was 310 ± 223 mg/day. Adverse effects included sedation (1.2%), cardiovascular side effects (5.6%), neutropenia (4.7%), and agranulocytosis (1.9%). Almost one quarter (23.4%) of the patients withdrew due to side effects.

Lacro et al.[14] found that elderly schizophrenic patients taking clozapine are at greater risk for developing agranulocytosis than are their younger counterparts. In addition, mandatory weekly blood monitoring for agranulocytosis is problematic in this population. Patients with decreased mobility may have difficulty being present for monitoring; other elderly patients may experience bruising. Lacro and colleagues recommended that clozapine be started in elderly patients at doses of 6.25 to 12.5 mg/day and be titrated upward in increments of 6.25 mg/day.

Risperidone

There are a number of controlled studies, case reports, chart reviews, and open-label studies reporting on side effects of risperidone in elderly patients (Table 1).

Two large double-blind, placebo-controlled studies have been reported recently. Katz et al.[15] found that risperidone significantly improved symptoms of psychosis and aggressive behavior in 625 patients with severe dementia who received placebo, or 0.5, 1.0, or 2.0 mg/day of risperidone for 12 weeks. The most common dose-related adverse events were EPS, somnolence, and mild peripheral edema, but the frequency of EPS in patients receiving 1 mg/day of risperidone was not significantly greater than in those receiving placebo. Similarly, in terms of severity of EPS, risperidone did not significantly differ from placebo and was better than haloperidol in a 13-week study in 344 patients with dementia.[16] The authors found low-dose risperidone (mean = 1 mg/day) to be well tolerated and associated with reductions in the severity and frequency of behavioral symptoms, particularly aggression.

Webster and Wijeratne[17] looked at 2 patients with schizoid personality disorder or dementia who received risperidone doses of 1.0 and 2.0 mg/day, respectively. Adverse events included EPS and neuroleptic malignant syndrome. Meco et al.[18] observed 6 patients with Parkinson's disease receiving 0.25 to 0.50 mg/day of risperidone. Adverse events included hypersalivation and hypotension.

Madhusoodanan et al.[19] reported on a case series of 11 geriatric patients treated with risperidone for schizophrenia, schizoaffective disorder, bipolar disorder, or senile dementia. All patients had previously been treated with conventional antipsychotics, and their response was assessed by clinical observation of their behavior. Eight patients responded to treatment, 1 did not respond, and 2 discontinued treatment due to hypotension or dizziness. Somnolence, abdominal cramps, and headache also occurred. Four patients had preexisting EPS and symptoms of tardive dyskinesia that decreased in response to risperidone treatment. In addition, 4 patients were able to discontinue antiparkinsonian medications, and 2 were able to discontinue antihypertensive medications. Side effects related to the blockade of dopamine, histamine, and serotonin were negligible.

Table 1. Risperidone Safety in Elderly Patients: Published Studies[a]

Study	Diagnosis	N	Dose, mg/d	Adverse Events
Controlled studies				
Katz et al[15]	Alzheimer's disease, vascular dementia, mixed dementia	625	0.5, 1.0, 2.0	EPS, somnolence, peripheral edema
De Deyn et al[16]	Dementia	344	0.5–4	None
Case reports				
Webster and Wijeratne[17]	Schizoid personality disorder, dementia	2	1.0, 2.0	EPS, neuroleptic malignant syndrome
Meco et al[18]	Parkinson's disease	6	0.25–0.50	Hypersalivation, hypotension
Madhusoodanan et al[19]	Schizophrenia, schizoaffective disorder, bipolar disorder, senile dementia	11	4.9; range, 1.0–6.0	Hypotension, somnolence, dizziness, abdominal cramps, headache
Jeanblanc and Davis[20]	Dementia	5	1.5–2.5	EPS
Gallucci and Beard[21]	Delusional parasitosis	1	6.0	None
Raheja et al[22]	Dementia, bipolar disorder	2	3.0	None
Chart reviews				
Marciniak and Guay[23]	Dementia, OBS, parkinsonian psychosis	18	2.8	Lethargy, decreased appetite, tremor, gait disturbances, hypotension, drooling, slurred speech, confusion, incontinence
Aronson et al[24]	Dementia, schizophrenia, MDD with psychotic features, delusional disorder	32	2.72	None
Zarate et al[25]	Dementia, major mood disorder, other	122	0.25–8.0	Hypotension, symptomatic orthostasis, cardiac arrest (with fatality), EPS, delirium
Open-label studies				
Prado et al[26]	Dementia	18	0.5–4.0	Orthostatic hypotension
Berman et al[28]	Schizophrenia	22	5.2	Agitation, insomnia, movement disorder, anxiety, somnolence, constipation, confusion, SIADH
Goldberg and Goldberg[29]	Dementia	64	0.50–1.0	Rash, agitation, urinary retention, sedation (1 mg/d dose)
Gierz et al[30]	Schizophrenia, organic delusional disorder, bipolar disorder	35	1.8–5.6	Agitation, dizziness, light-headedness, sedation, oversedation, EPS after benztropine withdrawal
Lavretsky and Sultzer[32]	Dementia with agitation	15	0.5–3.0	EPS, cognitive decline

[a]Abbreviations: EPS = extrapyramidal symptoms, MDD = major depressive disorder, OBS = organic brain syndrome, SIADH = syndrome of inappropriate secretion of antidiuretic hormone.

Jeanblanc and Davis[20] studied 5 elderly patients with exacerbation of agitation or violent behavior associated with dementia who were treated with risperidone for 10–31 days. Risperidone was started at 1.5 to 2.5 mg/day and titrated upward according to response. Two patients showed EPS, which resolved with 100 mg/day of amantadine.

Gallucci and Beard[21] reported on a patient with delusions of parasitosis. The patient, treated with 6.0 mg/day of risperidone, did not show any adverse events. Raheja et al.[22] observed 2 patients with dementia or bipolar disorder. Treatment with 3.0 mg/day of risperidone produced no adverse events.

A chart review conducted by Marciniak and Guay[23] reported on 18 patients with dementia, organic brain syndrome, or parkinsonian psychosis. These elderly patients were treated with 2.8 mg/day of risperidone. Adverse events included lethargy, decreased appetite, tremor, gait disturbances, hypotension, drooling, slurred speech, confusion, and incontinence.

Aronson et al.[24] conducted a chart review of 32 elderly patients with dementia, schizophrenia, major depressive disorder with psychotic features, or delusional disorder. Patients were treated with 2.72 mg/day of risperidone without experiencing adverse events.

Zarate et al.[25] studied risperidone for agitation or psychosis due to dementia (53%), major mood disorder (29%), or other disorders (18%) in 122 hospitalized psychogeriatric patients. Seventy-seven percent of the patients had a comorbid medical illness, with 76% receiving other psychotropic medications during risperidone therapy and 70% receiving concomitant cardiovascular agents. Patients received a mean dose of 1.6 ± 1.1 mg/day of risperidone. Seventy-eight percent of patients received 2.0 mg/day. Risperidone appeared to be effective in 85% of patients but was discontinued in 18% due to side effects (11%) or lack of efficacy (7%). Adverse effects were reported in 32% of patients and included hypotension (29%), symptomatic orthostasis (10%), EPS (11%), and delirium (1.6%). Benefits of treatment were associated with younger age and male gender but not risperidone dose. Adverse events were associated with cardiovascular disease and its treatment, coadministration of a serotonin reuptake inhibitor (SRI) or valproate, and relatively rapid dose increase. (Both SRIs and valproate can increase serum concentrations of neuroleptics.) The researchers concluded that risperidone appeared to be effective and could be safe for many elderly psychiatric patients with comorbid medical conditions provided that doses were low and increased slowly. They emphasized that caution be exer-

cised when cardiovascular disease or coadministration of other psychotropic agents is present.

Prado et al.[26] studied risperidone in an open-label trial of 18 elderly patients with dementia. At doses of 0.5 to 4.0 mg/day, orthostatic hypotension was observed. The incidence of side effects was lower with risperidone than haloperidol in a study[27] of 228 patients (mean age = 72.4 years) with behavioral symptoms. Patients received haloperidol (N = 82), risperidone (N = 105), or olanzapine (N = 20). EPS appeared in 8 patients taking haloperidol, 5 taking risperidone, and none taking olanzapine. Sedation appeared in 1 patient taking haloperidol, 5 taking olanzapine, and 1 taking risperidone. Dizziness occurred in 1 patient taking olanzapine and confusion occurred in 1 patient taking haloperidol. Agitation appeared in 3 patients taking olanzapine.

Berman et al.[28] conducted an open-label study of risperidone in 22 schizophrenic patients. Adverse events included agitation, insomnia, movement disorder, anxiety, somnolence, constipation, confusion, and syndrome of inappropriate secretion of antidiuretic hormone (SIADH).

An open-label study of risperidone in 64 patients with dementia was conducted by Goldberg and Goldberg.[29] Patients received 0.5 to 1.0 mg/day of risperidone. Adverse events included rash, agitation, urinary retention, and (at the highest dose) sedation.

Gierz et al.[30] studied 35 patients with schizophrenia, organic delusional disorder, or bipolar disorder treated with 1.8 to 5.6 mg/day of risperidone. Side effects included agitation, dizziness, light-headedness, sedation, and (after benztropine was withdrawn) EPS.

Madhusoodanan et al.[31] conducted an open-label, 12-week trial of risperidone in 103 patients with psychosis. The mean dose was 2.4 ± 1.3 mg/day. Some patients took lorazepam (N = 42) or antiparkinsonian agents concomitantly. Eleven patients withdrew from the trial because of adverse events, the most commonly reported of which were dizziness (N = 23), insomnia (N = 17), agitation (N = 15), somnolence (N = 15), constipation (N = 11), and EPS (N = 10). Less than 10% of this sample developed EPS. These results emphasize that adverse events can be minimized with lower doses of risperidone.

Lavretsky and Sultzer[32] studied 15 patients with dementia and agitated behavior in a 9-week structured trial of risperidone. The optimal dose of risperidone was 0.5 mg/day. Eight patients developed EPS at some point during the trial, and 3 patients showed a decline in cognitive skills. The researchers concluded that risperidone is effective for agitation in elderly patients with dementia but noted that adverse effects can occur even at low doses.

High doses and rapid titration can lead to risperidone discontinuation. Davidson et al.[33] studied 180 elderly patients with a diagnosis of schizophrenia, schizophreniform disorder, or delusional disorder. The mean dose of risperidone at endpoint was 3.7 mg/day. Eighty-five patients dropped out of the study, 20 due to adverse events. The high dropout rate can be attributed to higher doses and rapid dose titration. Patients' mean scores on the Extrapyramidal Symptom Rating Scale (ESRS) at endpoint decreased by 0.7 on the questionnaire, 1.5 on the parkinsonism questionnaire, 0.1 on the dystonia questionnaire, and 0.4 on the dyskinetic movements questionnaire. Changes in ESRS scores at endpoint were –2.0 on the parkinsonism, dystonia, and dyskinetic movements questionnaire. Changes in patients' scores on the Clinical Global Impressions severity of illness scale were –0.2 on the CGI-severity of dyskinesia scale and –0.5 on the CGI-severity of parkinsonism scale. There were no cases of tardive dyskinesia. Many of these patients had been taking conventional neuroleptics before the study; 84 were also taking antiparkinsonian agents before the study. Only 46 patients required antiparkinsonian agents during the risperidone trial, however.

De Deyn et al.[34] studied 1008 elderly patients with dementia combined from 3 multicenter, controlled trials of risperidone, haloperidol, and placebo. EPS occurred in 8.8% of placebo-treated patients, 14.4% of risperidone-treated patients, and 24.3% of haloperidol-treated patients.

There tended to be little difference among treatment groups in rates of adverse events, which developed in 76.7% of placebo-treated patients, 81.6% of risperidone-treated patients, and 80.9% of haloperidol patients. Patients assigned to risperidone therapy were divided into 3 groups receiving < 0.75 mg/day, 0.75 to 1.5 mg/day, or 1.5 mg/day. Rates of adverse events tended to increase with the highest doses of risperidone.

Tardive dyskinesia. The risk of tardive dyskinesia is much lower in patients taking atypical antipsychotics than in patients taking conventional antipsychotics. Jeste et al.[35] studied tardive dyskinesia in 128 elderly patients with a mean age of 67 years. Patients taking risperidone (N = 64) were matched to patients taking haloperidol (N = 64). The median dose of risperidone was 0.8 mg/day; the mean dose of haloperidol was 1.0 mg/day. Patients taking haloperidol were 3.4 times more likely to develop tardive dyskinesia than those taking risperidone. Tardive dyskinesia that developed in patients taking risperidone appeared within the first 3 months of treatment.

Brecher et al.[36] conducted an open trial of tardive dyskinesia frequency and severity in 330 patients taking a mean modal dose of 0.96 mg/day of risperidone. The mean exposure to risperidone was 230 ± 130 days. The ESRS was administered every 3 months, and tardive dyskinesia appeared in 2.4% of patients. Dyskinetic movements declined by 5.2 and hyperkinesia by 1.9 at 12 months as measured by mean ESRS scores. Mean scores on the buccolinguomasticatory scale decreased by 3.6, and scores on the choreoathetoic limb movement scale decreased by 0.6, each after 12 months.

Olanzapine

Like clozapine, olanzapine appears to cause few, if any, EPS. Olanzapine produces high rates of sedation, however, that can lead to falls in the elderly. Street et al.[37] conducted a fixed-dose study comparing 5, 10, and 15 mg/day of olanzapine with placebo in nursing home patients with dementia of the Alzheimer's type. EPS were measured using the Simpson-Angus Neurologic Rating Scale, the Abnormal Involuntary Movement Scale, and the Barnes Rating Scale for Drug-Induced Akathisia. The rates for drug-induced EPS were equivalent to placebo or lower, even in patients taking the higher doses of olanzapine. Other adverse events occurred at a higher rate in patients taking olanzapine than in those taking placebo. For example, somnolence was reported in only 3 (6.4%) of 47 patients taking a placebo. This adverse effect was reported in 14 (25.0%) of 56 patients taking 5 mg/day of olanzapine, 13 (26.0%) of 50 patients taking 10 mg/day of olanzapine, and 19 (35.8%) of 53 patients taking 15 mg/day of olanzapine. In patients taking olanzapine, abnormal gait occurred in 11 (19.6%) of 56 patients taking 5 mg/day, 7 (14.0%) of 50 patients taking 10 mg/day, and 9 (17.0%) of 53 patients taking 15 mg/day, compared with 1 (2.1%) of 47 patients taking a placebo. Drowsiness and an abnormal gait increase the risk of accidental injuries such as falls and fractures. Twenty (37.7%) of 53 patients taking 15 mg/day of olanzapine reported accidental injuries, compared with 13 (27.7%) of 47 patients taking a placebo. Anticholinergic side effects—including constipation, fecal impaction, intestinal obstruction, dry mouth, urinary retention, and amblyopia—are of particular concern in patients with Alzheimer's type dementia. In the Street et al. study,[37] none of the groups of patients taking olanzapine differed from the placebo group in reported anticholinergic side effects. Most of the participants completed the study. Of those who dropped out, 4.3% of those receiving placebo, 10.7% receiving 5 mg, 8.0% receiving 10 mg, and 17.0% receiving 15 mg olanzapine did so due to adverse events.

Low rates of side effects were reported in a study comparing olanzapine with placebo in 238 elderly patients with Alzheimer's type dementia with psychosis (Eli Lilly and Company, data on file). However, the mean dose of 2.7 mg/day (range 1–8 mg/day) was extremely low and equal to placebo in efficacy. Agitation, somnolence, and confusion were the most common side effects in this study.

Another study[38] compared olanzapine with haloperidol in 59 patients at least 65 years old with schizophrenia or schizoaffective disorder. There were no differences in efficacy or dropout rates for side effects between patients taking olanzapine (5–20 mg/day) and those taking haloperidol (5–20 mg/day). Incidence of back pain, tremor, akathisia, and rhinitis was greater in patients taking haloperidol than in patients taking olanzapine.

Quetiapine

Quetiapine is the most recent atypical antipsychotic to be approved by the FDA, and there are few studies of this drug published to date. In an open-label study[39] of quetiapine in 151 elderly patients with idiopathic or organic psychosis, the mean dose of quetiapine in patients with idiopathic psychosis was 75 mg/day and the mean dose in patients with organic psychosis was 100 mg/day. Adverse events included somnolence (32%), dizziness (14%), and postural hypotension (13%). Overall, EPS improved during the course of the trial, with approximately 11% of patients receiving concomitant anticholinergic medications.

CONCLUSION

Elderly schizophrenic patients are especially prone to the side effects of antipsychotic medications. Age-related changes may be confused with side effects by caregivers, and pharmacokinetic changes affect the manner in which medications are metabolized. Elderly patients often have comorbid illnesses, and side effects of combined medications must be carefully considered. Patients' perspectives on side effects may be quite different from those of caregivers. For all of these reasons, careful attention to side effects is crucial when treating the elderly psychotic patient.

Drug names: amantadine (Symmetrel), benztropine (Cogentin and others), bromocriptine (Parlodel), chlorpromazine (Thorazine and others), clozapine (Clozaril and others), fluphenazine (Prolixin and others), haloperidol (Haldol and others), lorazepam (Ativan and others), loxapine (Loxitane), molindone (Moban), olanzapine (Zyprexa), perphenazine (Trilafon), quetiapine (Seroquel), risperidone (Risperdal), thioridazine (Mellaril and others).

Disclosure of off-label usage: The author of this article has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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