

# Treatment of Psychosis Among Older Adults in Residential Care Facilities: A Review of Clinical Cases Using Quetiapine

Franco Sicuro, MD



The psychiatric needs of older adults in residential care settings are significant. While increasing attention has been given to the mental health needs of elderly nursing home residents, other facilities, including assisted living facilities, board and care homes, and adult foster care programs, present unique treatment challenges for caregivers and physicians. The prevalence of psychiatric illness ranges from 65-90%, with dementia complicated by depression, psychosis, and behavioral disturbances, the most common disorder.<sup>1</sup> It is important to note that elderly patients with chronic mental illnesses including schizophrenia, bipolar disorder, major depression, panic disorder, posttraumatic stress disorder, and mental retardation also reside in nursing homes.<sup>2</sup> While assisted living facilities and other community residences have a lower prevalence of older adults with dementia, elderly patients who have chronic mental illnesses are often placed in these settings.<sup>3</sup>

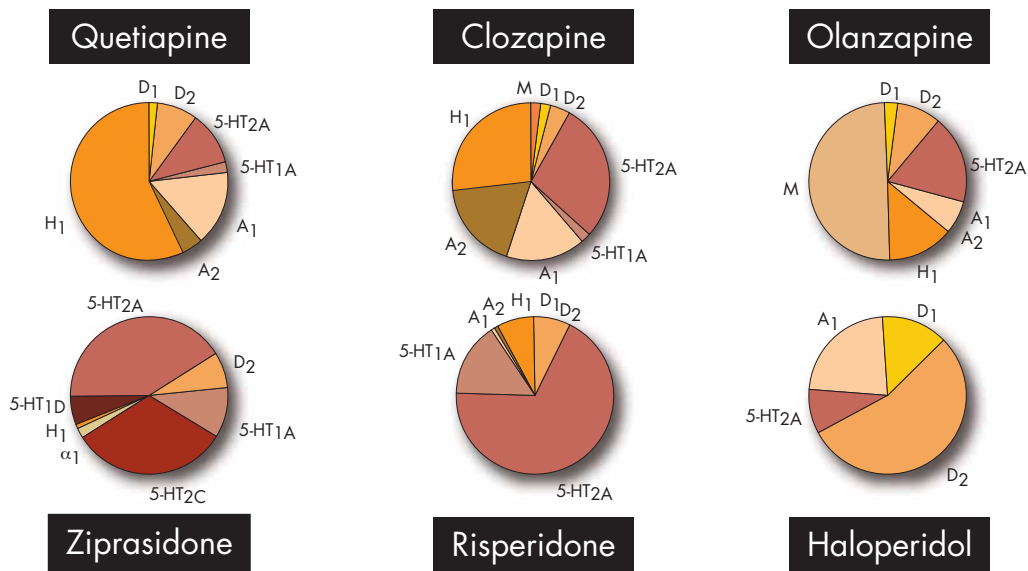
When dementia and other psychiatric disorders are accompanied by psychotic features, including delusions and hallucinations, the patient is more likely to have impaired functional status, display behavioral problems, and require a greater amount of care.<sup>4,5</sup> Treatment strategies for psychotic symptoms in the older adult must focus on medications that are efficacious and well-tolerated by this fragile population. The best outcome of medication treatment is the allevia-

Annals of  
Long-Term Care  
Clinical Care and Aging  
A Clinical Journal of the American Geriatrics Society

Clinical Geriatrics  
A CLINICAL JOURNAL OF THE AMERICAN GERIATRICS SOCIETY

Supplement to *Annals of Long-Term Care* and *Clinical Geriatrics*

A Freedom Magazines Publication



**Figure 1.** Antipsychotic receptor-binding profiles. Source: Goldstein JM. Atypical antipsychotic drugs: Beyond acute psychosis, new directions. *Expert Opinion on Emerging Drugs* 1999;4(1):127-151.

tion of psychotic symptoms, improvement in behavior and functioning, and an increase in socialization. Elderly patients have been difficult to treat with standard antipsychotic medications such as haloperidol and fluphenazine due to the sensitivity of older adults to the common side effects of these agents, including extrapyramidal symptoms (EPS) and tardive dyskinesia.<sup>1</sup> The ideal antipsychotic agent that a clinician looks for in treating psychosis in an older adult includes:

- Low potential for extrapyramidal symptoms
- Minimal cardiovascular side effects
- High degree of efficacy in reducing hallucinations and delusions
- No worsening of cognition
- Very little sedation
- Neutral effects on appetite
- Minimal effects on glucose, lipids, and diabetes control
- No anticholinergic side effects
- Low potential for tardive dyskinesia

The atypical or second-generation antipsychotics

include risperidone, olanzapine, clozapine, ziprasidone, quetiapine and the recently released medication aripiprazole. As a class, they have demonstrated significant advantages in safety and tolerability over the more traditional agents such as haloperidol.<sup>6,7</sup> The efficacy of these agents is comparable in terms of reducing psychotic symptoms.<sup>7</sup> The more favorable side-effect profile, including a significantly lower incidence of EPS and tardive dyskinesia, has resulted in these second-generation agents becoming the treatment of choice for psychotic symptoms in the elderly.<sup>1</sup> All second-generation antipsychotic agents share a common pharmacologic feature of relatively low dopamine D<sub>2</sub> receptor antagonism with a significant degree of serotonergic 5-HT<sub>2</sub> receptor antagonism (Figure 1).<sup>6</sup>

This review of clinical cases illustrates the use of quetiapine to treat the psychosis and behavioral problems that are common among patients living in residential care facilities.<sup>3,5</sup> Our experience comes from psychiatric consultations at several St. Louis area nursing homes and residential care facilities, and from a 20-bed geropsychiatric unit.

## CASE #1

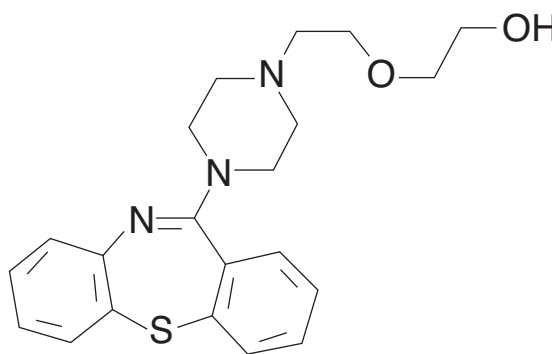
Ms. NV is a 69-year-old female with a history of bipolar illness, who suffered an exacerbation of her manic symptoms that included irritability, hypersexuality with masturbation in public, and resistance to redirection. Her sleep decreased and her appetite increased. The patient was also experiencing auditory hallucinations of persecutory type. Upon admission to our geropsychiatric unit, she was taking alprazolam 0.5 mg at bedtime, olanzapine 15 mg twice a day, fluvoxamine 50 mg at bedtime, and sertraline 100 mg at bedtime. During the first week in the hospital, she received several doses of temazepam as required for insomnia. Her concurrent medical conditions, including chronic obstructive pulmonary disease, non-insulin-dependent diabetes mellitus, and congestive heart failure, were clinically stable and did not require any medication adjustment.

Quetiapine was rapidly titrated in 1 week to 100 mg twice a day and 400 mg at bedtime without any side effects. By the second week, alprazolam, fluvoxamine, and olanzapine were discontinued, and quetiapine was increased to 100 mg twice a day and 450 mg at bedtime. Upon discharge to the nursing home, the patient had remarkably improved with no symptoms of hallucinations, insomnia, or hypersexuality.

In this case, the patient was suffering from an exacerbation of manic-depressive illness that was not controlled by high doses of olanzapine. The adjunct of quetiapine was successful in reducing the manic symptoms, and more interestingly, allowed the discontinuation of three psychotropic medications, alprazolam, fluvoxamine, and olanzapine. While there are no published controlled trials of quetiapine in the treatment of mania, case reports have described its successful use in the treatment of manic symptoms and hypersexuality.<sup>8,9</sup>

Quetiapine is an atypical antipsychotic agent in the

dibenzothiazepine chemical class (Figure 2). Quetiapine is a potent serotonin 5-HT<sub>2</sub> receptor antagonist with mild antagonism at dopamine D<sub>2</sub> receptors. It appears to bind to the D<sub>2</sub> receptor in a weak and reversible manner, which allows for antipsychotic effects with minimal EPS.<sup>10,11</sup> Quetiapine is also an antagonist at histamine H<sub>1</sub> and adrenergic alpha<sub>1</sub> and alpha<sub>2</sub> receptors. As a result, its most common side effects include sedation and orthostatic hypotension.<sup>12</sup>



**Figure 2.** Chemical profile of quetiapine.

While it is well studied in the younger schizophrenic population, published results of controlled clinical trials in the elderly have been limited. Tariot et al<sup>13</sup> studied 184 elderly patients with psychosis in an outpatient setting and found significant clinical benefits, safety, and tolerability with quetiapine treatment over a 52-week period. Schneider et al<sup>14</sup> demonstrated the efficacy of quetiapine in improving hostility in a subset of 78 of these patients who suffered from Alzheimer's disease with psychosis.

## CASE #2

Ms. J is an 87-year-old patient with history of bipolar disorder and vascular dementia in the mild-to-moderate range who is currently living in a nursing home. She has been admitted several times to our acute inpatient geropsychiatric unit for exacerbation of symptoms including agitation, grandiose ideation, and mixed affective symptoms of elation

and depression. This patient would cry for hours, and then sing and talk about her past dancing career or make sexually explicit comments. Evenings and nights would worsen the symptoms to the point of requiring as-needed tranquilization with either benzodiazepines or intramuscular antipsychotic agents.

Ms. J was given several medications, including olanzapine up to 20 mg, mood stabilizers such as valproic acid and carbamazepine, and many different antidepressants including serotonin reuptake inhibitors. We reviewed her recent hospitalization history and found that quetiapine was first used over 1 year ago at higher doses of 400-600 mg a day in combination with valproic acid and mirtazapine with improvement in mood and behavior. The patient was then discharged and the antipsychotic medication was slowly tapered in accordance with the Omnibus Budget Reconciliation Act of 1987 (OBRA '87) nursing home psychotropic prescribing regulations, while her symptoms were monitored.

Unfortunately, Ms. J did not remain stable on less than 200 mg of quetiapine, and she was rehospitalized with an acute exacerbation of symptoms. She improved when the dose of quetiapine was increased. She again suffered a relapse when olanzapine 10 mg once daily was used in place of quetiapine. As the patient had a prior history of improvement on quetiapine, the drug was resumed and increased rapidly over a 10-day period due to severe manic and psychotic symptoms. At discharge, the patient had very few crying spells and no sexual overtones. Currently, Ms. J is being treated with quetiapine 200 mg four times a day with a stable mood, and is able to socialize appropriately. She sleeps well, requires no additional medication, and has a good appetite. No side effects of sedation, hypotension, or EPS have developed.

The case of Ms. J illustrates that older adults with chronic mental illness may require higher doses of quetiapine even in the presence of comorbid dementia.<sup>12</sup> Despite the patient's age, she was able to safely tolerate high doses of quetiapine. In addition, the issue of interpretation of the federal OBRA '87 nursing home regulations regarding the use of antipsychotic agents may have been too stringent in the case of Ms. J. The physician must attempt dose reduction of antipsychotic agents unless clinical contraindications would place the patient at risk of relapse or harm. In this case, Ms. J has a history of severe and recurrent psychosis with multiple hospitalizations when her medication was changed. This history, if clearly documented, along with monitoring of current response, side effects, and need for ongoing treatment, would justify the need to continue the patient's medication regime.<sup>15</sup>

One study by Tariot et al<sup>16</sup> involved 284 nursing home patients who suffered from dementia with psychosis. Subjects were randomized in this flexible dose trial to receive quetiapine, haloperidol, or placebo. Findings suggest a better functional status on quetiapine compared to placebo and haloperidol, a statistically significant decrease in the incidence of EPS with quetiapine versus haloperidol, and fewer patient falls or fractures with quetiapine. Treatment-induced somnolence was statistically more significant with quetiapine.<sup>14,16</sup>

Mintzer et al<sup>17</sup> performed an open-label trial of quetiapine versus risperidone with 92 elderly outpatients who suffered from psychotic disorders or dementia with psychosis. The 16-week study was flexibly dosed, and both agents produced a reduction in the severity of psychotic symptoms. The quetiapine-treated group (mean dose = 237 mg per day) displayed a significantly lower incidence of EPS, rigidity, and akathisia than the group treated with risperidone (mean dose = 3.3 mg per day).

### CASE #3

Mr. H is an 85-year-old black male with a history of mixed dementia due to Alzheimer's disease and vascular features with agitation and psychosis. He was admitted to our geropsychiatric unit due to severe agitation and combativeness at the nursing home. While in the nursing home, the patient was briefly treated with risperidone 1 mg twice a day, which resulted in severe akathisia and cogwheel rigidity. His medical conditions included a history of bladder carcinoma in remission, gastroesophageal reflux disease, and alcoholism. The patient also had an acute urinary tract infection that was treated with levofloxacin.

Risperidone was immediately decreased to 0.5 mg twice a day and benztropine 0.5 mg was added to relieve EPS. Risperidone was then discontinued due to lack of efficacy, and olanzapine 7.5 mg at bedtime was given. The patient continued to display severe paranoia and behavioral disturbances. He barricaded himself in his room, continuously paced, broke the showerhead to "defend" himself, exposed himself in public, and was very difficult to redirect. A decision was made to discontinue olanzapine and start quetiapine 50 mg twice a day and 100 mg at bedtime. In 1 week, quetiapine was increased to 100 mg in the morning, 150 mg in the evening, and 200 mg at bedtime. The periods of agitation became sporadic, but he still required episodic doses of lorazepam for agitation and temazepam for insomnia. By the third week, Mr. H's quetiapine dose was increased to 200 mg three times a day, and he received trazodone 150 mg at night to help him sleep. The patient was still active and continued rearranging tables in the dining room, but he was easy to redirect, cooperative with care, and showed no aggressive behavior. He did not display any signs of EPS, no sedation, and was ambulating without difficulty.

*We felt that the patient had benefited remarkably from quetiapine, and we discharged him to his family, who had decided to bring him back with them on a trip to his hometown.*

Mr. H developed EPS within 24 hours from the start of risperidone treatment, and appeared to be extremely sensitive to the extrapyramidal side effects of antipsychotic agents. He was able to successfully tolerate relatively high doses of quetiapine, with no signs of EPS. Mintzer et al<sup>17</sup> have demonstrated a reduced incidence of extrapyramidal symptoms in elderly outpatients treated with quetiapine compared with those given risperidone. In addition, case reports have illustrated an improvement in tardive dyskinesia when quetiapine was used for the treatment of psychotic symptoms.<sup>18,19</sup> It is important to remember that no atypical antipsychotic agent eliminates the risk of tardive dyskinesia, particularly among elderly patients who are more sensitive to all types of EPS. The 1-year prevalence of tardive dyskinesia in elderly patients treated with the atypical agents risperidone or olanzapine ranges from 0.5-2.5% compared with 25% for haloperidol-treated patients.<sup>20</sup> At least one case report has described the emergence of tardive dyskinesia in a quetiapine-treated patient who had no prior antipsychotic exposure.<sup>21</sup> As the next case illustrates, however, quetiapine may be a safe and effective therapeutic agent for patients who are actively psychotic and also display significant dyskinesia.

### CASE #4

*Mr. J has a history of chronic paranoid schizophrenia and has spent most of his adult life in mental institutions. He currently resides in a nursing home after having been discharged from a state mental facility. Mr. J suffered an exacerbation of his acute paranoid symptoms and was hospitalized. He was very slender and frequently paced about the unit or remained isolated in his bed in constant motion with facial*

*grimacing, truncal spasms, and leg jerking. Severe tardive dyskinesia and tardive akathisia were noted on clinical examination. Mr. J was verbally aggressive, mostly toward staff members, and at times physically abusive during activities of daily living. He was a threat to the nursing home community because of paranoid behavior, poor compliance with treatment, and aggressive episodes. His appetite and sleep were maintained. Mr. J was initially treated with a medication regimen of risperidone up to 3 mg a day and vitamin E 800 IU twice a day for tardive dyskinesia, which resulted in some improvement in his paranoid symptoms and aggressive behavior. He continued to display paranoid ideation, and his symptoms of tardive dyskinesia were prominent. Risperidone was discontinued and quetiapine was quite rapidly titrated up to 200 mg four times a day in 2 weeks. Mr. J tolerated the medication very well without signs of sedation or hypotension. Upon discharge, he was able to sit more comfortably in the common area of the unit, although he still maintained very little social interaction. A significant improvement in his tardive dyskinesia and akathisia symptoms was noted. The truncal spasms were minimal, his facial grimacing was less intense, and his leg jerking was both less frequent and less intense. Mr. J was no longer striking out at staff.*

This patient is the product of chronic institutionalization and many years of treatment with traditional neuroleptics. As a result, he developed severe tardive dyskinesia with components of both dystonia and akathisia. Quetiapine has been associated with improvement in tardive dyskinesia in patients with schizophrenia.<sup>18,19</sup> Further studies are warranted to further evaluate the ability of quetiapine to improve dyskinesia in patients with psychosis.

## CASE #5

*Ms. D is a 72-year-old female with a history of Alzheimer's disease who presented to the hospital with anxiety and severe coughing. Her upper respiratory symptoms had been evaluated fully during approximately 20 visits to the emergency room during the past month, and were found to be psychosomatic in nature. Her caretaker was requesting nursing home placement as part of the discharge plan. Previous treatment with benzodiazepines had not provided any relief. The patient was admitted to the geropsychiatric unit in an agitated state with anxiety, somatic delusions, and compulsive coughing. An attempt was made to treat the patient with paroxetine up to 20 mg, and with donepezil. The patient became more confused and delusional. She became very agitated and displayed significant sleep disturbance, despite treatment with hypnotic medications. Paroxetine and donepezil were discontinued due to concerns of drug-induced delirium. Quetiapine 50 mg three times a day was started, after a trial dose of 50 mg was well tolerated by the patient. Ms. D was safely discharged to her husband at home. A follow-up visit 3 weeks later showed a much calmer patient who was sleeping well, coughing episodically but no longer somatically preoccupied, with little anxiety. She was tolerating the quetiapine well, with no signs of sedation or EPS.*

This case illustrates how the behavioral symptoms of dementia are often complicated by psychosis, depression, mood instability, and functional decline.<sup>4</sup> Treatment with multiple psychotropic medications often leads to worsening confusion due to the inherent problems of polypharmacy and the potential for drug–drug interactions. In this case, monotherapy

with quetiapine led to a reduction in paranoia, improved behavior, and an increase in functional status. In addition, this clinically significant improvement led to discharge home with her husband, which prevented her from requiring care in a more restrictive setting.

Quetiapine is metabolized extensively by the liver, primarily by the cytochrome P-450 enzyme CYP3A4. Drugs that are strong inhibitors or inducers of CYP3A4 may require a dose adjustment in quetiapine if these agents are utilized concurrently (Table I). Strong inducers of CYP3A4 such as carbamazepine may require an increase in quetiapine dose. Inhibitors of CYP3A4 including ketoconazole and fluvoxamine require caution, as the half-life of quetiapine may be doubled when administered with these drugs. The mean half-life of quetiapine is 7 hours in young adults, and may double in those over age 65.<sup>12</sup> Due to the significant hepatic metabolism of quetiapine, careful dose adjustments must be considered for patients with liver disease.<sup>6,11</sup>

**TABLE I** Potential Drug-Drug Interactions With Quetiapine

CYTOCHROME 3A4 INDUCERS	CYTOCHROME 3A4 INHIBITORS
May need dose increase of quetiapine	May need dose reduction of quetiapine
Barbiturates	Ketoconazole
Carbamazepine	Itraconazole
Phenytoin	Clarithromycin
Rifabutin	Erythromycin
Rifampin	Fluvoxamine
	Nefazodone
	Ritonavir
	Protease inhibitors
	Thioridazine
	St. John's wort
	Grapefruit juice

## CASE #6

*Sister L is an 87-year-old Catholic nun with a history of hypertension and vascular dementia who resides in a nursing home. She was referred for psychiatric consultation due to intense aggression and paranoia, which represented a marked change in her prior behavior and personality. The patient was loud, threatened residents and staff, and spoke in profanities. Sister L was treated with risperidone 0.75 mg per day and sertraline 25 mg once daily with minimal improvement. The risperidone was increased to 1.5 mg per day, and several different antidepressants were added to her regime with no response. Quetiapine at 25 mg twice a day and 50 mg at night was started. The risperidone and antidepressants were tapered and discontinued. Sister L's aggressive behavior slowly improved. For more than 18 months, the patient was stable on 150 mg per day of quetiapine. Episodically her paranoia has increased, and the quetiapine dose was temporarily raised to 100 mg three times per day. Her dementia has progressed, but Sister L has tolerated quetiapine well, with no signs of EPS, sedation, or falls.*

This patient, with vascular dementia complicated by marked psychotic symptoms and behavioral disturbances, responded well to monotherapy with quetiapine. This patient was able to tolerate 100 mg per day of the drug as a starting dose, but this is higher than typically recommended in a geriatric patient. A starting dose of 25 mg twice a day with increases of 25-50 mg every other day is commonly utilized. Cutler et al<sup>22</sup> has recommended an even more aggressive strategy when switching from other antipsychotics to quetiapine, utilizing starting doses of 50 mg per day of quetiapine and rapidly escalating over a 5-day period to doses up to 400 mg if needed. Monitoring for sedation, orthostatic hypotension, and falls is important, as these are the most common side effects in

an elderly population. Dose-related sedation is a common side effect, and often resolves by lowering the dose or improves over time in some patients.<sup>22,23</sup>

When using any antipsychotic agent for off-label or non-Food and Drug Administration (FDA)-approved indications, it is very important to clearly identify the target symptoms for treatment, rather than focus on the diagnosis.<sup>1</sup> This is particularly relevant in the nursing home setting, where the use of antipsychotic agents is heavily regulated and requires the identification of clear indications, contraindications, and monitoring of side effects of the medication. Patients with dementia are often extremely sensitive to the side effects of antipsychotic agents, even at very low doses. The need for an effective agent with minimal sedation, low risk of EPS, and a favorable cardiovascular profile is vital.

### CASE #7

*Ms. D is an 86-year-old woman with a history of Alzheimer's disease, coronary artery disease, and anemia, who was treated for depression with mirtazapine. This patient developed agitation and paranoid delusions about the theft of her money. She became combative when paranoid and was started on quetiapine 25 mg at bedtime with very little improvement. Quetiapine 50 mg at bedtime failed to provide any improvement in her symptoms. Ms. D was awake all night, accusing people of stealing from her. She would wander, pace, and appeared very restless. Her primary care doctor suspected that the restlessness was akathisia induced by quetiapine, and it was discontinued. Unfortunately, the patient's symptoms did not improve. We decided to restart quetiapine and increased the dose over a 2-week period to 125 mg per day. This produced a significant reduction in paranoia and agitation, although the patient is still having difficulty sleeping. A gradual increase in the bedtime dose of quetiapine is planned.*

This case illustrates that very low doses of atypical antipsychotics may not be effective for acute symptoms even in frail elderly patients. While the adage, "start low, go slow" is important to remember, gradual dose titration is safe and effective when properly monitored.<sup>17,22</sup> Mintzer et al<sup>17</sup> used doses above 200 mg per day in this study of elderly outpatients with psychosis. As the dose was individually titrated by the physician based on the patient's response, it shows that quetiapine may be safely increased as needed to achieve resolution of symptoms. In this case, the patient's wandering and pacing was in response to her paranoia, and not a sign of EPS. However, the physician is always correct in carefully evaluating the patient for any signs of emerging side effects during therapy with antipsychotic medications.

The low incidence of extrapyramidal side effects related to quetiapine has led researchers to study the interaction of the drug with the postsynaptic dopamine D<sub>2</sub> receptor.<sup>10</sup> Kapur et al<sup>24</sup> found that quetiapine has very limited occupancy of these receptors at therapeutic doses. Using positron emission tomography (PET) scan studies, quetiapine was found to occupy D<sub>2</sub> receptors in the range of 0-24% 12 hours after the last dose, and 58-64% within 3 hours after a single dose. This is in sharp contrast to typical agents such as haloperidol that appear to occupy D<sub>2</sub> receptors more than 80%, resulting in EPS and elevated prolactin levels.<sup>25</sup>

### CASE #8

*Mr. P is an 80-year-old widowed male with a 20-year history of Parkinson's disease. He has been treated with carbidopa/levodopa 25/100 mg four times per day. He moved in with his daughter following the death of his wife, but developed progressive dementia with periods of anger and hostility. He started getting up at night, calling out, and screaming. Mr. P believed that there was a party going on in the house, and reported people talking. He was treated with clozapine 25 mg at night*

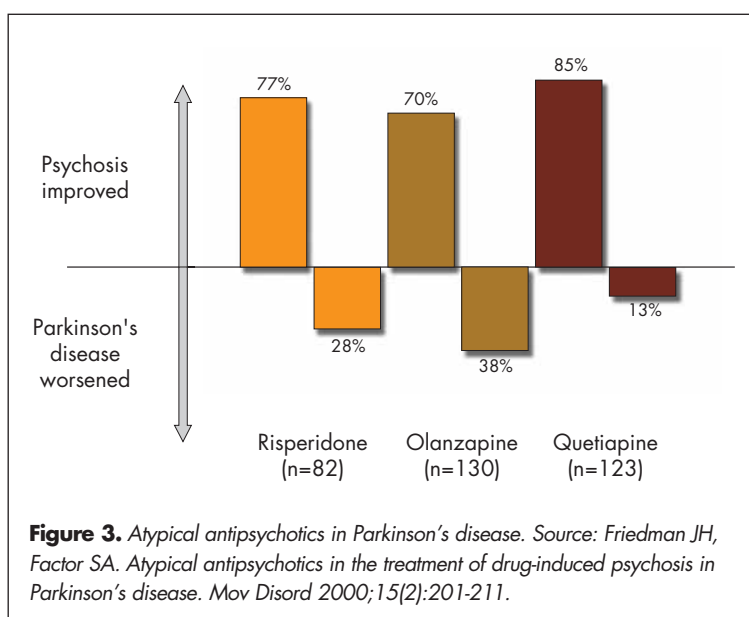
with improvement, but started refusing to have his blood drawn weekly. His neurologist switched the medication to olanzapine 5 mg at bedtime, but Mr. P became more rigid and was no longer able to toilet himself. His daughter reluctantly placed him in a nursing home. Mr. P was found to be very regressed and withdrawn following nursing home admission, and olanzapine was discontinued. He received physical therapy and became ambulatory with a walker. He began complaining of hearing people talking and laughing about him, and was very distressed by these hallucinations, often yelling "Shut Up!" and "Stop!" throughout the night. Mr. P was started on quetiapine 25 mg at bedtime with some improvement in his hallucinations and sleep pattern. The dose was increased to 50 mg after 2 weeks. His hallucinations resolved and he slept well at night. His motor function remained stable. Mr. P was eventually transferred to an assisted-living facility located next door to the nursing home, where he has his own apartment with support services.

Patients with Parkinson's disease who are treated with levodopa and other agents, such as dopamine agonists, frequently develop psychotic symptoms, particularly hallucinations. The treatment of psychosis in Parkinson's disease is complicated by the potential for all antipsychotic agents to worsen motor functioning. Fernandez and colleagues<sup>26,27</sup> studied a group of 87 patients with Parkinson's disease using quetiapine in doses of 50-75 mg per day. They described significant improvement in 70 of the 87 patients. Sedation and motor deterioration were limiting factors.<sup>26</sup> In addition, 10 out of 11 patients who suffered from Lewy body dementia displayed improvement with low-dose quetiapine treatment.<sup>27</sup> Reddy et al<sup>28</sup> found improvement in psychotic symptoms among 80% of patients with Parkinson's disease who were treated with a mean dose of 54 mg per day of quetiapine. Half

of this sample of 43 patients suffered from dementia, and these subjects were more likely to develop motor deterioration over the 10-month study period. Juncos et al<sup>29</sup> conducted a single-center, open-label trial of quetiapine in 40 patients with psychosis associated with Parkinson's disease who did not respond well to prior treatment with clozapine, olanzapine, or risperidone. The majority of patients displayed improvement in psychotic symptoms and behavioral disturbance, with no worsening of motor symptoms when monitored using the Unified Parkinson's Disease Rating Scale (UPDRS).<sup>29</sup> Friedman and Factor<sup>30</sup> studied 69 patients with Parkinson's disease who developed psychosis following initiation of dopaminergic therapy (Figure 3). Quetiapine treatment is often beneficial in patients with Parkinson's disease, but motor worsening may still occur. Clozapine may be a good choice for the psychosis that accompanies the treatment of Parkinson's disease, but many patients are not able to tolerate this agent.<sup>30</sup> (See Table II.)

## DISCUSSION

The atypical antipsychotic quetiapine appears to be well tolerated in geriatric patients, and may offer advantages in the treatment of the complex psychiatric problems that occur among residents of nursing homes and other care



**TABLE II** Summary of Quetiapine Studies of Elderly Patients with Psychosis

AUTHORS	DATE	NO. OF PATIENTS	DIAGNOSIS	MEAN AGE	PATIENT TYPE	MEDIAN DOSAGE	EFFICACY	TOLERABILITY	LENGTH
Tariot et al	2002	284	Alzheimer's disease	84	Nursing home	Up to 200 mg	Yes	Yes	10 wks
Tariot et al	2000	184	Alzheimer's disease; schizophrenia	76	Outpatient	137 mg	Yes	Yes	1 year
Schneider et al	1999	78	Alzheimer's disease	78	Outpatient	100 mg	Yes	Yes	1 year
Juncos et al	1999	40	Parkinson's disease	73	Outpatient	75 mg	Yes	Yes	1 year
Friedman et al	1999	69	Parkinson's disease	78	Outpatient	49 mg	Yes	Yes	4 wks
Juncos et al	2000	29	Parkinson's disease	73	Outpatient	62 mg	Yes	Yes	24 wks

facilities. As these case reports illustrate, quetiapine may be used safely for the treatment of the psychotic features that accompany Alzheimer's disease, vascular dementia, and Parkinson's disease, as well as the chronic psychiatric disorders that persist into late life, including bipolar mania and schizophrenia. In our practice of residential care psychiatry, we have found quetiapine to be particularly helpful in patients who display a combination of psychotic features and significant behavioral disturbances, including impulsivity and aggression.

Dose titration in the inpatient setting may be performed rapidly, but individual responses vary widely, as this series of cases illustrates. While some patients improved on as little as 50 mg per day of quetiapine, those who suffered from chronic psychiatric disorders or significant physical aggression required doses as high as 800 mg per day. This is the maximum recommended dose for quetiapine in any age group. In frail elderly patients we recommend a much more cautious titration in 25-mg increments and a maximum dose of 200 mg of quetiapine per day. If higher doses are required in patients with dementia, documentation regarding the diagnosis, indications, clinical rationale, and monitoring of side effects must be clear in order to comply with feder-

al OBRA '87 guidelines for nursing home residents.<sup>15</sup> The most common side effect is dose-related sedation, which often resolves within 72 hours. Dose increases may be made as often as every 2-3 days if clinically needed. If careful monitoring of sedation, hypotension, and falls is provided, elderly patients may respond well to higher doses of quetiapine when needed for treatment of refractory psychosis and severe behavioral disturbances.<sup>31</sup>

We found that patients who have neurodegenerative illness may benefit from quetiapine as the first-line drug, possibly due to the very low incidence of EPS associated with this agent. Some of these patients include those with Huntington's chorea,<sup>32</sup> Parkinson's disease, and dementias of the mixed type including Alzheimer's, alcohol-related, vascular, and diffuse Lewy body diseases. The safety and tolerability of the agent in the elderly population have led clinicians to use the drug for other conditions. Quetiapine has been used successfully to treat elderly patients suffering from posttraumatic stress disorder.<sup>33</sup> It also appears that some patients who suffer from significant EPS, akathisia, and tardive dyskinesia from other agents may show improvement with quetiapine.<sup>18-20</sup>

No specific laboratory monitoring is required during treatment with quetiapine. The metabolic abnormalities of

elevated glucose and triglycerides that have been reported with other agents appear less problematic with quetiapine.<sup>34</sup> However, individual patients may require additional monitoring due to comorbid medical conditions. While electrocardiogram changes, including QT and QTc prolongation, have been an issue with other atypical antipsychotic agents, no significant abnormalities have been reported with quetiapine.<sup>35</sup>

## CONCLUSION

No medication has been approved by the FDA for the treatment of psychosis and behavioral disturbances that accompany dementias, such as Alzheimer's disease or vascular dementia. The dementia resulting from neurodegenerative diseases, chronic alcoholism, and head trauma is also frequently accompanied by psychosis, which often requires pharmacologic intervention. As these case reports illustrate, the older adult with a psychiatric disorder is frequently cared for in a nursing home or other residential care setting. The need for an effective and well-tolerated agent to treat distressing psychotic symptoms is significant. Quetiapine, due to its efficacy, safety, and tolerability, with a wide range of dosing options to meet the needs of a variety of clinical scenarios, may be a beneficial treatment option for elderly patients.

## References

- Salzman C. Treatment of the agitation of late-life psychosis and Alzheimer's disease. *Eur Psychiatry* 2001;16(Suppl 1):25S-28S.
- Sherrell K, Anderson R, Buckwalter K. Invisible residents: the chronically mentally ill elderly in nursing homes. *Arch Psychiatr Nurs* 1998;12(3):131-139.
- Lyketsos CG, Steinberg M, Tszchanz JT, et al. Mental and behavioral disturbances in dementia: Findings from the Cache County Study on Memory and Aging. *Am J Psychiatry* 2000;157(5):708-714.
- Devanand DP. The interrelations between psychosis, behavioral disturbance, and depression in Alzheimer disease. *Alzheimer Dis Assoc Disord* 1999;13(Suppl 2):S3-S8.
- Devanand DP, Jacobs DM, Tang MX, et al. The course of psychopathological features in mild to moderate Alzheimer's disease. *Arch Gen Psychiatry* 1997;54(3):257-263.
- Goldstein JM. Atypical antipsychotic drugs: Beyond acute psychosis, new directions. *Expert Opin on Emerging Drugs* 1999;4(1):127-151.
- Tandon R. Safety and tolerability: How do newer generation "atypical" antipsychotics compare? *Psychiatr Q* 2002;73(4):297-311.
- MacKnight C, Rojas-Fernandez C. Quetiapine for sexually inappropriate behavior in dementia. *J Am Geriatr Soc* 2000;48(6):707.
- Vieta E, Parramon G, Padrell E, et al. Quetiapine in the treatment of rapid cycling bipolar disorder. *Bipolar Disord* 2002;4(5):335-340.
- Kapur S, Seeman P. Does fast dissociation from the dopamine d2 receptor explain the action of atypical antipsychotics? A new hypothesis. *Am J Psychiatry* 2001;158(3):360-369.
- Kapur S, Muller-Spahn F. Review of quetiapine and its clinical applications in schizophrenia. *Expert Opin Pharmacother* 2000;4(1):783-801.
- McManus DQ, Arvanitis LA, Kowalczyk BB. Quetiapine, a novel antipsychotic: experience in elderly patients with psychotic disorders. Seroquel Trial 48 Study Group. *J Clin Psychiatry* 1999;60(5):292-298.
- Tariot PN, Salzman C, Yeung PP, Pultz J, Rak IW. Long-term use of quetiapine in elderly patients with psychotic disorders. *Clin Ther* 2000;22(9):1068-1084.
- Schneider L, Yeung P, Sweitzer D, et al. Quetiapine may reduce hostility in patients with psychoses related to Alzheimer's disease. Poster presentation to the American Psychiatric Association; May 16-20, 1999; Washington, DC.
- Stoudemire A, Smith DA. OBRA regulations and the use of psychotropic drugs in long-term care facilities: Impact and implications for geropsychiatric care. *Gen Hosp Psychiatry* 1996;18(2):77-94.
- Tariot P, Schneider L, Katz I, et al. Quetiapine in nursing home residents with Alzheimer's dementia [abstract]. Presented at the Annual Meeting of the American Association for Geriatric Psychiatry; February 24-27, 2002; Orlando, FL.
- Mintzer J, Yeung P, Mullen J, Sweitzer D. Extrapyramidal symptoms in elderly outpatients treated with either quetiapine or risperidone [poster]. Presented at: 13th Annual Meeting of the American Association for Geriatric Psychiatry; March 12-15, 2000; Miami, FL.
- Vesley C, Fufferle B, Brucke T. Remission of severe tardive dyskinesia in a schizophrenic patient treated with the atypical substance quetiapine. *Int Clin Psychopharmacol* 2000;15(1):57-60.
- Farah A. Reduction of tardive dyskinesia with quetiapine. *Schizophr Res* 2001;47(3):309-310.
- Jeste DV. Tardive dyskinesia in older patients. *J Clin Psychiatry* 2000;61(Suppl 4):27-32.
- Ghaemi SN, Ko JY. Quetiapine related tardive dyskinesia. *Am J Psychiatry* 2001;158(10):1737.
- Cutler AJ, Goldstein JM, Tumas JA. Dosing and switching strategies for quetiapine fumarate. *Clin Ther* 2002;24(2):209-222.
- Scharre DW, Chang SI. Cognitive and behavioral effects of quetiapine in Alzheimer's disease patients. *Alzheimer Dis Assoc Disord* 2002;16(2):128-130.
- Kapur S, Barsoum SC, Seeman P. Dopamine D(2) receptor blockade by haloperidol: (3)H-raclopride reveals much higher occupancy than EEDQ. *Neuropsychopharmacology* 2000;23(5):595-598.
- Kapur S, Zipursky R, Jones C, et al. A positron emission tomography study of quetiapine in schizophrenia: A preliminary finding of an antipsychotic effect with only transiently high dopamine D2 receptor occupancy. *Arch Gen Psychiatry* 2000;57(6):553-559.
- Fernandez HH, Friedman JH, Jacques C, Rosenfeld M. Quetiapine for the treatment of drug-induced psychosis in Parkinson's disease. *Mov Disord* 1999;14(3):484-487.
- Fernandez HH, Trieschmann ME, Burke MA, Friedman JH. Quetiapine for psychosis in Parkinson's disease versus dementia with Lewy bodies. *J Clin Psychiatry* 2002;63(6):513-515.
- Reddy S, Factor SA, Malho ES, Feustel PJ. The effect of quetiapine on psychosis and motor function in parkinsonian patients with and without dementia. *Mov Disord* 2002;17(4):676-681.
- Juncos JL, Ewalt ML, Jewart RD, et al. Long-term quetiapine treatment for psychosis in patients with Parkinson's disease who fail treatment with other atypical antipsychotics. Presented at: American Psychological Association; May 13-18, 2000; Chicago, IL.
- Friedman JH, Factor SA. Atypical antipsychotics in the treatment of drug-induced psychosis in Parkinson's disease. *Mov Disord* 2000;15(2):201-211.
- Siuro F. Use of higher dose quetiapine in elderly inpatients: A chart review study [poster]. Presented at: American Association for Geriatric Psychiatry; March 1-4 2003; Honolulu, HI.
- Bonelli RM, Niedervieser G. Quetiapine in Huntington's disease: A first case report. *J Neural* 2002;249(8):1114-1115.
- Sattar SP, Ucci B, Grant K, et al. Quetiapine therapy for posttraumatic stress disorder. *Ann Pharmacother* 2002;36(12):1875-1878.
- Wirshing DA, Boyd JA, Meng LR, et al. The effects of novel antipsychotics on glucose and lipid levels. *J Clin Psychiatry* 2002;63(10):856-865.
- Mullen J, Jibson MD, Sweitzer D. A comparison of the relative safety, efficacy, and tolerability of quetiapine in outpatients with schizophrenia and other psychotic disorders. The Quetiapine Experience with Safety and Tolerability (QUEST) Study. *Clin Ther* 2001;159(2):255-262.

This special report was produced by  
MultiMedia HealthCare/Freedom, LLC, under an  
unrestricted educational grant from AstraZeneca.  
The views expressed in this publication are not necessarily  
those of AstraZeneca or the publishers.  
This publication may not be reproduced in whole or in part  
without the express written permission of  
MultiMedia HealthCare/Freedom, LLC.

Copyright © 2003 MultiMedia HealthCare/Freedom, LLC.  
All rights reserved. Office Center at Princeton Meadows, Building 400,  
Plainsboro, NJ 08536. Telephone: (609) 275-3800.

*Printed in USA.*

SR-02302