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Treatment of schizophrenia and delusional disorder in the elderly

Abstract With increasing longevity, greater numbers of patients with schizophrenia and delusional disorder will be surviving into advanced age. Antipsychotics form the core of the treatment for both of these psychotic disorders. Treatment of elderly patients with antipsychotics is, however, complicated by a much higher risk of adverse effects such as tardive dyskinesia. More is known about treating patients with schizophrenia than those with delusional disorder. The introduction of newer atypical antipsychotics may herald a new era in the pharmacotherapy of elderly psychotic patients. Nonetheless, judicious dosing is essential in the geriatric population. We discuss the benefits and limitations of the main forms of treatment.

Key words Geriatrics · Psychosis · Delusions · Antipsychotics · Dyskinesia

Introduction

The proportion of persons greater than 65 years of age is expected to greatly increase in both Europe and North America during the next 20 years. Overall, increases in the numbers of elderly people are expected to be coupled with correspondingly larger proportions of elderly patients with psychotic disorders. Clinicians need to be prepared to treat a growing number of psychotic patients who will be living into advanced age. Treatment of psychotic disorders in the elderly frequently involves differences in treatment response and sensitivity to side effects from those seen in younger adult patients [1]. Subtle changes in clinical presentation may also exist.

In contrast to the large amount of published literature on schizophrenia and delusional disorder in young adults, there is a relatively paucity of studies focusing on these psychoses in older age. Treatment of elderly patients with these disorders has generally involved extrapolating from studies of younger patients, extracting results from studies which included some elderly patients in the overall cohort, and gleaning information from small, uncontrolled studies of older subjects.

We discuss the assessment and treatment of schizophrenia and delusional disorder in the elderly. We first briefly consider the clinical picture and differential diagnosis of these disorders in the geriatric population, and then review their treatments. Schizophrenia is several times more common than delusional disorder. Nevertheless, we discuss published reports on delusional disorder at some length because the literature on this condition is very limited and rarely reviewed.

Clinical symptoms

Schizophrenia: early vs late onset

The issue of schizophrenia onset after 45 years of age has been controversial especially in the United States. In Europe this issue has been extensively investigated by Kay and Roth [2–4]. Patients with later onset of schizophrenia or schizophrenia-like symptoms have been diagnosed as having late-onset schizophrenia, paraphrenia, late paraphrenia, paranoid states, delusional disorder, psychosis not otherwise specified, etc. Unfortunately, there is still some confusion over these terms. In contrast to Kraepelin, Bleuler always believed that schizophrenia could manifest after 45 years of age [5]. The DSM-III restricted the diagnosis of schizophrenia to patients whose symptoms manifested before the age of 45 [6]. The DSM-III-R [7] eliminated the age restriction and added the term late-onset schizophrenia (LOS) for patients with onset of symptoms after age of 45 years [7]. The DSM-IV [8] does not include an age-of-onset criterion and has discontinued the specification of LOS, although the terms EOS (early-onset schizophrenia) and LOS are still useful for clinical and research purposes. Maurer and Häfner [9] have discussed

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in detail various methodological aspects in the assessment of age of onset in schizophrenia.

Most patients with schizophrenia have onset of symptoms in their adolescence or early adult years. Approximately 15% of all the patients with schizophrenia may, however, have onset of symptoms after the age of 45 years [10]. Clinically, LOS is similar to EOS in several respects. Positive symptoms, such as bizarre delusions and auditory hallucinations, are prevalent in both groups. Family history, prevalence of white matter hyperintensities on magnetic resonance imaging (MRI), and medication response appear to be similar between those with early vs late onset. The pattern of cognitive impairment is also comparable, although the degree of impairment is somewhat less severe in patients with LOS [1]. There are also several notable differences between EOS and LOS [1]. Late-onset schizophrenia is more common in women than in men. It is associated with fewer negative symptoms such as social withdrawal or emotional blunting. We have found larger thalamic volume on MRI in LOS compared with EOS patients [11]. Finally, effective doses of antipsychotic drugs for LOS tend to be as low as one third of those required for patients of similar age with EOS.

Although many patients with schizophrenia are surviving into old age, little is known about the long-term course of the illness. Follow-up research in the elderly is complicated by the social illusiveness of this population as well as the high prevalence of medical comorbidity. At least a quarter of patients with schizophrenia may experience significant symptom diminution and psychosocial remission in old age [12]. Schizophrenia is a chronic illness, however, and a majority of the patients continue to be disabled.

Delusional disorder

By DSM-IV definition [8], the diagnosis of delusional disorder applies to patients who present with nonbizarre delusions and do not have prominent hallucinations. Subgroups of this disorder, categorized according to the predominant delusional theme, are erotomanic, grandiose, jealous, persecutory, and somatic. In the general population of patients with delusional disorder, the persecutory subtype is the most common one. It has been estimated that the lifetime risk of developing delusional disorder is 0.05–0.1% [8]. Delusional disorder generally has its onset in middle or late life but can have onset in early adulthood.

Some patients may engage in disputes with the family members or other figures who are objects of their paranoid delusions and accusations, and these actions can create situations requiring emergency psychiatric intervention. Delusions usually cannot be altered by reasoning with the patient, and such attempts may produce agitation and rage. At these times, or when the delusion causes significant distress (to the patients or caregivers) or potentially dangerous behavior, psychotropic drug treatment is warranted.

The etiology, treatment, and prognosis of delusional disorder have been relatively poorly characterized. This is at least partly due to inconsistent nomenclature and diagnostic criteria. The term "delusional disorder" was preceded by "paranoia" and "paranoid disorder" in the DSM-III. "Paranoia" in the DSM-III was "paranoid disorder" of greater than 3 months' duration. The delusional content per DSM-III only included persecution or jealousy; the current delusional subtypes (erotomatic, grandiose, etc.) were added in the DSM-III-R.

Several risk factors for the development of delusional disorder have been investigated. Two studies have reported that patients with paranoid or delusional disorder [13] have an increased prevalence of schizophrenia in their families [14]. Some studies have implicated immigration and low socioeconomic status as playing a role [15], and persons with premorbid avoidant, paranoid, or schizoid personalities are reported to be at a heightened risk [6]. Flint et al. [16] examined CT scans of patients diagnosed with delusional disorder and paraphrenia [13]. The patients with delusional disorder had significantly more cerebral infarctions than those with paraphrenia. Other reports of late paraphrenia occurring in organic brain disease patients have also been reported [17].

In one study, Rockwell et al. characterized patients with late-onset psychosis with vs without somatic delusions (LOP+ and LOP–, respectively) [18]. Of the ten LOP+ patients, eight had delusional disorder and two had LOS [6]. Six of the LOP+ patients were immigrants to the United States or were first-generation U.S. born, and five had sensory components to their somatic complaints. The LOP+ group was compared with the nine patients without somatic delusions (LOP–; four with delusional disorder, four with schizophrenia, and one with psychosis NOS) and ten normal comparison subjects. Although the three groups had similar education levels, the LOP+ patients had lower mean full scale IQ scores than did the normal subjects and LOP– patients. The LOP– group had more negative symptoms than the LOP+ group. No specific structural lesions were seen on MRI in any of the patients.

A clinical and neuropsychological comparison of delusional disorder and patients with schizophrenia has recently been published by Evans et al. [19]. The authors compared 14 middle-aged and elderly patients (mean age 70 years) with delusional disorder with 50 patients with schizophrenia (mean age 64 years) who all had onset of illness after age 40 years [7]. Overall, the patients with delusional disorder had higher levels of psychopathology but had fewer psychiatric hospitalizations than the patients with schizophrenia. The delusional disorder group received a nonsignificantly lower daily neuroleptic dose than the schizophrenia group. On neuropsychological comparison, no significant differences were found between the two groups, although the delusional disorder group tended to have less severe impairment.

Differential diagnosis

Elderly patients who present with recent onset of psychosis should be examined for possible primary causes.

Several medical disorders, drug side effects, and other psychiatric conditions can have clinical presentations that are similar to schizophrenia and delusional disorder. These possible causes should be investigated in the differential diagnosis of schizophrenia and delusional disorder. In organic mental disorders, paranoid symptoms accompany cognitive dysfunction and a history of progressive intellectual decline may be present.

The potential of a mood disorder should also be considered in the differential diagnosis of schizophrenia and delusional disorder. Depressive symptoms frequently occur before the development of delusions. Paranoid ideas may also be present with either bipolar or unipolar mood disorders when the patient is experiencing emotional highs and lows.

Drug therapy

Gerontokinetics and gerontodynamics

Elderly patients typically require much lower doses of antipsychotic medications than young adults. Part of this difference in dosage requirement is likely to be secondary to gerontokinetics, or the pharmacokinetics due to age-related changes in physiology. The aging process is associated with decreases in total body water, decreases in muscle mass, and increases in adipose tissue. Elderly patients have lower plasma protein levels, and this may result in higher levels of unbound drug (drug which is able to exert its pharmacological action) [20]. Renal function declines with increasing age, and most psychotropic medications with their active metabolites are excreted slower than they are in younger patients.

Pharmacodynamics refers to the drug's effect on the body. It is likely that age-associated changes in pharmacodynamics contribute to lower dose requirements in the patients. Since pharmacodynamic studies involving the CNS are difficult, however, the relative effect of gerontodynamic changes on psychopharmacotherapeutics remains uncertain. Dopamine and acetylcholine receptors, among others, are known to decrease with age.

Typical antipsychotics

Typical antipsychotic medications may be grouped into the three potency categories: high potency (haloperidol, thiothixene, and fluphenazine), intermediate potency (acetophenazine, loxapine, molindone), and low potency (chlorpromazine, thioridazine). When given in therapeutic doses, all the typical antipsychotics are therapeutically equivalent in treating schizophrenia. It is plausible that these medications are also therapeutically equivalent in treating delusional disorder, however, there are inadequate comparative data to make a definitive conclusion.

The use of potency-related drug classes is, however, useful in characterizing side effect profiles that are important to the elderly patients. Even at relatively low doses, the sedative, anticholinergic, and adrenergic-blocking activity of low-potency antipsychotics may result in falls and confusion in elderly patients. In contrast, high-potency neuroleptics are associated with greater risks of extrapyramidal symptoms (EPS).

Typical antipsychotics in schizophrenia

The efficacy of typical antipsychotics in elderly patients with schizophrenia has been documented in several controlled trials. Honigfeld et al. conducted one of the early studies of middle-aged and elderly patients with schizophrenia [21]. In a 24-week double-blind study, these investigators compared the treatment of 308 men with schizophrenia (aged 54–74 years) and found that acetophenazine and trifluoperazine were both more effective than placebo in treating psychosis, conceptual disorganization, personal neatness, and social competence. In another investigation, haloperidol and thioridazine were compared in a 12-week double-blind study involving 50 patients who were 63 years or older [22]. Both medications were found to be equally effective in reducing anxiety, excitement, hostility, and other target symptoms. Other smaller or uncontrolled studies evaluating the efficacy of typical antipsychotics in treating elderly patients with schizophrenia have been conducted [3, 23–25]. A detailed review of these and other treatment studies for elderly patients with schizophrenia has been published by Jeste et al. [26].

Typical antipsychotics in delusional disorder

As compared with schizophrenia, there are very few published studies which exclusively evaluate the treatment of delusional disorder. One problem has been the inconsistent nomenclature and diagnostic criteria. Another difficulty with delusional disorder research is obtaining informed consent from patients who do not believe they have a psychiatric disorder. Several studies are limited by small samples sizes. Occasionally, information on the patients with schizophrenia is combined with that on other diagnostic groups [15]. Since patients with schizophrenia frequently do not comply with antipsychotic medication, treatment outcome studies are extremely difficult in these patients [27].

Of the typical antipsychotic agents, pimozide has perhaps received the greatest attention in delusional disorder studies, and some of these publications have exclusively involved elderly patients. McCoy et al. published a report of two older patients with delusional disorder [28]. The first patient was a 61-year-old woman with a 30-year history of persecutory delusions regarding her husband. After 2 days of receiving pimozide 1 mg/day, her husband noted that she was less hostile. At discharge, the patient's dose was 3 mg/day and there was no evidence of delusions. The second patient was a 67-year-old woman with delusional disorder, paranoid type. At admission, she received thiothixene 2 mg twice daily for a week and was then

switched to pimozide 4 mg/day. She was later discharged with the same dose and without evidence of delusions.

There was one published case report of treating litigious delusional disorder [7] with pimozide [29]. On admission, the patient was started on pimozide 2 mg/day, and the dose was increased to 6 mg/day. Side effects of psychomotor slowness, rigidity, and sialorrhea resulted in a dose reduction to 2 mg at bedtime, and the patient continued on this dose "without significant side effects". Following discharge, the patient underwent psychotherapy and continued taking pimozide. After 27 months, his litigious efforts had greatly diminished and the patient considered his previous delusional beliefs as no longer being important.

The problem of medication compliance associated with treating outpatients with late paraphrenia led Raskind et al. to study the use of fluphenazine ethanante, a depot preparation, in this population [30]. Thirteen patients diagnosed with late paraphrenia (mean age 71 years) were first treated with oral haloperidol, 2 mg three times a day. A second group of 13 late paraphrenia patients (mean age 72 years) was administered 5 mg of intramuscular fluphenazine ethanante every 2 weeks. At the end of the 6-week study, 3 of the haloperidol patients were described as markedly improved, one was minimally improved, 8 were unchanged, and one was worse. In contrast, the subjects who received the intramuscular fluphenazine experienced much greater improvement, with 4 subjects experiencing marked improvement and 7 having moderate improvement after 6 weeks of treatment; the other 2 subjects were unchanged. It is not clear how oral medication compliance was assessed in this study, but poor compliance likely influenced the outcome in the haloperidol group. The intramuscular fluphenazine was well tolerated in this elderly group (mean age 72 years); no EPS or cardiovascular effects were observed. Thus, in this study intramuscular antipsychotics produced superior results compared with oral agents in treating delusional disorder.

Chiu conducted a retrospective survey of 349 psychogeriatric inpatients and outpatients and reported that 7.2% had a diagnosis of delusional disorder [7, 31]. The author focused on 5 patients with jealous delusions; 3 of these patients (ages 73, 77, and 81 years) had delusional disorder. One patient treated with pimozide experienced improvement of the delusions in a few months, and the other patient remained unchanged. The third delusional patient was treated with thioridazine and improved after a few months. Unfortunately, specific treatment information such as dose, side effects, and trial duration were not provided for these patients.

Atypical antipsychotics

Atypical antipsychotics are generally defined as those blocking both dopamine and serotonin receptors. The side effect profile of each atypical antipsychotic varies, but the risk of EPS appears to be much lower in this newer class of antipsychotics as a whole. Examples of atypical antipsychotics are clozapine, risperidone, olanzapine, sertindole, quetiapine, and ziprasidone. Since these medications (except for clozapine) have been available for only a short period of time compared with the typical agents, there are relatively few studies of atypical antipsychotics conducted in elderly schizophrenia subjects. We are not aware of any treatment studies or case reports involving elderly patients with delusional disorder treated with atypical antipsychotics. We found only one report of two middle-aged patients with delusional disorder who were treated with clozapine and risperidone [32].

Clozapine

Clozapine was the first atypical antipsychotic agent approved in the U.S. Studies involving elderly psychotic patients have usually reported that very low initial doses (6.25–25 mg/day) and slow titration periods are required. Effective maintenance doses have usually ranged from 25 to 300 mg/day [33–36]. Even at these low doses, however, clozapine is poorly tolerated by many elderly patients. Excessive sedation, anticholinergic toxicity, and postural hypotension are side effects of clozapine that are especially problematic in the elderly. The necessity for weekly blood draws also makes clozapine treatment difficult in the aged. The use of clozapine in geriatric patients should usually be restricted to those who are resistant or intolerant of other treatments.

Risperidone

Risperidone is generally better tolerated than clozapine by elderly patients, provided it is used in low dosages. Effective doses in elderly patients usually range from 0.25 to 4 mg/day. When dosed judiciously, serious side effects of risperidone are usually not a problem. The more common side effects which may occur with risperidone use in the elderly are somnolence, hypotension, and (with higher doses) EPS [37–39]. There has been some interest in possible cognitive benefits of risperidone in elderly patients [40, 41].

Selected studies of clozapine and risperidone involving older psychotic patients with psychosis are reviewed in Table 1. Since these studies often included study cohorts with mixed diagnoses, we have included studies with at least some patients with schizophrenia.

Olanzapine

Olanzapine was recently approved for use in the U.S. Currently, there are no published studies on the dosing or side effect profile of olanzapine in the elderly patients with schizophrenia or delusional disorder. Although olanzapine blocks muscarinic receptors, the particular types of muscarinic receptors that are blocked are somewhat different from those blocked by clozapine.

Table 1 Selected studies of clozapine and risperidone involving older patients with psychosis. *TD* tardine dyskinesia; *EPS* extrapyramidal symptoms

Reference	Study design	Diagnosis	Mean age (range) years	Mean daily dose (range) mg/day	Results
Clozapine					
[36]	Case series	(Diagnostic criteria not specified) Chronic paranoid schizophrenia with dementia (n = 1) Chronic Undifferentiated schizophrenia with dementia (n = 1) Alzheimer's-type dementia and Parkinson's disease (n = 1) Recent-onset psychosis (n = 1)	74 (68–83)	26.6 (12.5–43.8)	Two patients had relief of psychotic symptoms. All 4 patients experienced side effects including falls, bradycardia, and delirium
[42]	Retrospective	(DSM-III-R) Depression with psychosis (n = 4) Chronic undifferentiated schizophrenia (n = 3) Parkinsonian dementia with levodopa-induced hallucinations (n = 1)	72 (68–80)	135 (12.5–400)	Six patients showed at least moderate improvement. All patients with parkinsonism or TD experienced diminishing of those symptoms. Two patients had marked orthostasis.
[34]	Retrospective	(DSM-III-R) Chronic paranoid schizophrenia (n = 7) Schizoaffective disorder (n = 3) Chronic undifferentiated schizophrenia (n = 1) Bipolar affective disorder (n = 1)	69 (61–82)	150 (25–300)	Psychotic symptoms improved moderately in 5 patients and markedly in 2. Seven patients experienced postural hypotension. One developed agranulocytosis but had successful clozapine rechallenge
[35]	Retrospective	(Diagnostic criteria not specified) Chronic schizophrenia (n = 13) "Acute psychosis" (n = 4) Dementia with psychosis (n = 2) Acute unspecified psychosis (n = 4) Chronic bipolar affective disorder (n = 1) Korsakoff's syndrome with psychosis (n = 1)	72 (65–84)	210 (75–350)	All patients experienced marked behavior improvements and minor decreases in psychopathology following clozapine; however, 10 patients discontinued due to adverse effects. Sedation/lethargy reported by 12 patients. Four developed serious respiratory complications (pneumonia, respiratory arrest), and 3 developed leukopenia
Risperidone					
[37]	Prospective forced dose titration	(Diagnostic criteria not specified) Schizophrenia (n = 12) Alzheimer's dementia (n = 8) Other (n = 2)	70 (66–81)	6	Psychopathology decreased and global cognition improved after risperidone was initiated. Nine patients required dose reduction due to side effects (hypotension, EPS, akathisia, and others)
[43]	Case series	(Diagnostic criteria not specified) Schizophrenia (n = 6) Schizoaffective disorder (n = 3) Bipolar affective disorder (n = 2) Senile dementia (n = 2)	69 (61–79)	4.9 (1.5–6)	Eight patients responded favorably to risperidone. EPS and TD were reduced in 4 patients. Two discontinued risperidone due to hypotension, but the drug was well tolerated by the other patients
[40]	Prospective forced dose titration	(DSM-III-R) Chronic schizophrenia (n = 10)	71 (66–81)	6	Nine patients experienced lessening of psychopathology. Mean scores on several cognitive measures also improved following risperidone. One patient required a dosage reduction to 4 mg/day due to drooling. Risperidone was well tolerated by the other patients
[38]	Prospective forced dose titration	(DSM-III-R) Schizophrenia (n = 15)	54 (45–64)	6	Nine patients reached the target dose of 6 mg/day. Of 11 patients who completed most of the study, 7 had improved psychopathology over their previous typical neuroleptic. Lethargy, sedation, and dizziness resulted in 4 patients discontinuing risperidone. Three patients required a dose reduction to 4 mg/day due to similar side effects

Table 1 (continued)

Reference	Study design	Diagnosis	Mean age (range) years	Mean daily dose (range) mg/day	Results
[38]	Retrospective	(DSM-III-R) Chronic undifferentiated Schizophrenia ($n = 6$) Organic delusional disorder ($n = 2$) Chronic late-onset schizophrenia ($n = 1$) Bipolar affective disorder ($n = 1$)	67 (47–79)	3.9 (0.5–8)	Seven patients markedly improved and 2 moderately improved. One patient required a dose decrease due to daytime sedation. One patient worsened. No major side effects were observed in the other 8 patients
[44]	Retrospective	(DSM-IV) Schizophrenia ($n = 18$) Other psychotic disorders ($n = 4$) Schizoaffective disorder ($n = 2$) Bipolar affective disorder ($n = 2$)	70 (65–85)	3.8 (1–8)	Twenty patients had marked or moderate improvement with risperidone. Two showed no improvement and two were lost to follow-up. Risperidone was discontinued due to elevated liver enzymes in 1 patient and diaphoresis, hypotension, and tachycardia in another
[39]	Retrospective	(DSM-III-R) Schizophrenia ($n = 4$) Delusional disorder ($n = 3$) Other ($n = 7$)	71 (54–100)	1.7 (0.25–6)	Twelve patients markedly or moderately improved. Two patients worsened. No major side effects were observed in the other 12 patients

Side effects of antipsychotics

Sedation

Sedation is one of the most common side effects of antipsychotics experienced by elderly patients. Low-potency agents with strong sedative activity may be helpful for patients with insomnia or daytime agitation. Acute treatment with highly sedating antipsychotics may also be helpful in situations where rapid tranquilization is desired (e.g., acute agitation) [45]. Impaired mental functioning and disorientation may occur in the morning and afternoon following a nighttime dose. The sedative side effects of an antipsychotic usually diminish after 1–3 weeks of treatment, although this period may be longer in the elderly.

Hypotension

Drug-induced hypotension is common in the elderly and places the patient at risk for a fall or a even stroke. Most low-potency and atypical antipsychotics have significant α_1-adrenergic blocking activity. Young adult patients may not experience an orthostatic episode. Elderly patients, however, are at a much higher risk for orthostasis due to age-related losses in postural reflexes and reduced CNS vasoregulartory ability. Risks for orthostatic hypotensive episode are greatest early in antipsychotic treatment especially after a dose increase.

The risk of an orthostatic episode (and possibly a fall or stroke) can be decreased by patient education; when antipsychotics with high α_1-adrenergic activity are prescribed to an elderly patient, the patient and caregivers should be instructed that the patient should rise slowly from seated or supine position. The is no specific drug treatment for antipsychotic-induced hypotension. Ephedrine or amphetamine may precipitate or aggravate psychotic symptoms, and epinephrine may further lower blood pressure from its β-adrenergic blocking activity. General treatment measures include reducing the dose, changing antipsychotics, and maintaining fluid/electrolyte balance.

Anticholinergic side effects

Since cholinergic function decreases with age, the use of medications with strong anticholinergic activity can result in serious peripheral and central side effects [46]. Peripheral anticholinergic manifestations include dry mouth, constipation, urinary retention, and worsening of glaucoma. Dry mouth may be a particularly undesirable side effect, especially for patients with dentures. Central anticholinergic manifestations include confusion, disorientation, irritability, and impaired recent memory [47–49]. In more severe cases of anticholinergic toxicity, the patient may experience agitation, assaultiveness, and visual hallucinations. Anticholinergic medications, such as diphenhydramine and benztropine, which are commonly used to

treat EPS induced by high-potency neuroleptics, are also likely to cause similar toxic symptoms at higher doses.

Clozapine and low-potency typical agents all have substantial antimuscarinic properties which may be problematic in elderly patients. Olanzapine avidly blocks muscarinic receptors; however, it appears to block somewhat different muscarinic receptors than does clozapine. Risperidone, sertindole, and ziprasidone have very little antimuscarinic activity, and quetiapine has virtually no antimuscarinic activity [50].

Anticholinergic symptoms from antipsychotics are best treated by reducing the dose of the offending agent or changing to a higher potency antipsychotic. Cholinergic medications have their own side effects (e.g., depression), making them impractical in most of such cases.

Cardiovascular

Antipsychotics with strong anticholinergic activity may also affect the sinoatrial node and result in tachycardia. Elderly patients receiving these agents may have heart rates of 90 or more beats per minute. Treatment with thioridazine may cause nonspecific T-wave abnormalities on electrocardiogram. Pimozide and sertindole may cause prolongation of QT interval, although the clinical significance of this is uncertain. Pimozide has also been reported to cause flattening, notching, and inversion of T-waves and an appearance of U-waves.

Extrapyramidal symptoms

Extrapyramidal symptoms (EPS) include akathisia, drug-induced parkinsonism, and dystonic reactions. The risk of each of these EPS varies with each agent and with dose. Extrapyramidal symptoms can be painful or at least inconvenient and may result in medication non-compliance. Some aspects of EPS prevalence are different in the elderly as compared with younger adults.

Dystonic reactions

Dystonic reactions involve acute muscle spasms and usually occur within 72 h after initiation of an antipsychotic. Acute treatment of dystonic reactions involves use of diphenhydramine or benztropine. These reactions are fortunately rare in the elderly.

Akathisia

The clinical presentation of akathisia is similar in elderly and young patients, although akathisia tends to be more common in the elderly. Akathisia can be very distressing. Treatment consists of decreasing the antipsychotic dose. Benzodiazepines, β-blockers, and anticholinergic medications have been used in its treatment, but the results are inconsistent.

Drug-Induced Parkinsonism

Drug-induced parkinsonism (DIP) is characterized by bradykinesia, rigidity, and tremor, and phenomenologically it is often indistinguishable from idiopathic Parkinson's disease [51]. It is important to avoid DIP in elderly patients since gait impairment results in a higher risk of falls [52]. Treatment of DIP may involve lowering the antipsychotic dose or switching to a lower potency or an atypical antipsychotic. Adding medications such as amantadine, levodopa, ritanserin, and anticholinergic drugs has been partially successful, but these agents have their own side effects.

Tardive Dyskinesia

Tardive dyskinesia (TD) is probably the best known long-term side effect of antipsychotic drugs. Essential features of TD are involuntary movements of tongue, face, jaw, and sometimes the extremities and trunk. The clinician should be aware of the differential diagnosis of TD which includes poorly fitting dentures, and tongue movements secondary to dry mouth from medications.

Advanced age and greater cumulative amount of typical neuroleptics are the predominant risk factors for development of TD [53]. We recently reported on a prospective 3-year longitudinal study of 266 middle-aged and elderly patients (mean age 66 years) [54]. The subjects received an average daily dose of 150 mg chlorpromazine equivalents of typical neuroleptics. The cumulative annual incidence of TD in this group was 26%, a rate that was 5–6 times higher than that reported in younger adults. Significant risk factors for developing TD were longer antipsychotic treatment duration, greater cumulative antipsychotic amounts (especially for the high-potency drugs), history of alcohol abuse or dependence, and subtle movement disorder at baseline.

The presence of dentures may increase the severity of orofacial TD. African–Americans also appear to be at a higher risk for developing TD than do Caucasians. It appears that Asians probably have a similar or slightly lower risk for developing TD than do Caucasians [55]. Other suggested TD risk factors include use of depot antipsychotic and history of drug interruptions.

Severe TD is not rare in older patients. Caligiuri et al. [56] followed 378 middle-aged and elderly patients who were recently started receiving antipsychotics. After 36 months of follow-up, the cumulative incidence of severe TD was 23%. Risk factors for the development of severe TD were found to be greater cumulative amount of antipsychotic dose prescribed and greater severity of worsening negative symptoms.

There is no consistently effective treatment of TD. The antipsychotic dose should be evaluated to assure that it is

the lowest necessary dose. β-blockers and benzodiazepines may occasionally be helpful in reducing the severity of the dyskinetic movements. Several studies have examined the role of antioxidants in reducing the severity of TD, and a review of these studies has been published by Lohr and Browning [57]. The efficacy of vitamin E in treating TD is currently being tested in a multicenter cooperative study sponsored by the U.S. Department of Veterans Affairs.

Adjuvant medications

Benzodiazepines

In patients with schizophrenia, benzodiazepines can be used to treat episodes of acute agitation. Patients with schizophrenia may benefit from both acute and short-term treatment with benzodiazepines [58]. Since patients with delusional disorder are frequently unwilling to accept antipsychotic agents, they may be more receptive to receiving benzodiazepines; these agents do not diminish the delusion but may ease the sharpness of the delusion. Unfortunately, most of the available literature on adjunctive benzodiazepines in psychosis involves younger adults.

The effects of benzodiazepines last longer in the elderly than they do in younger adults. Long-acting benzodiazepines, such as diazepam and flurazepam, are best avoided in the elderly, since their sedative activity may result in daytime sedation and an elevated risk of falls [46]. Relatively short-acting benzodiazpines (e.g., oxazepam) are less likely to result in prolonged sedation.

Other adjunctive medications

Some studies have examined the adjunctive use of lithium in treating schizophrenia. Some studies involving lithium with antipsychotics in young adult patients have reported modest improvements in areas such as anxiety and depression [59, 60]. One consideration before combining lithium with antipsychotics in an elderly patient is a reported higher risk of neurotoxicity when these medications are combined in the aged [61]. Carbamazepine and valproate may offer some benefit when either is conjunctively used with an antipsychotic [62–64]. We are not aware of any studies involving adjunctive use of these medications in elderly patients with delusional disorder or schizophrenia.

Medication compliance

Poor compliance with antipsychotic medications is a common reason for hospitalization of patients with schizophrenia and continuation of the delusions in those with delusional disorder. Continual surveillance of medication compliance and education are warranted for both groups. Medication compliance can be assessed with several methods including clinical outcome and pill counts. The Rating of Medication Influences (ROMI) is a scale to assess compliance in patients with schizophrenia [65]. To our knowledge, there have been no published reports of its use in elderly patients. In general, the area of medication compliance in the psychotic elderly is largely uncharacterized [66].

Depot neuroleptics may be an improved method of antipsychotic dosing for the patient with questionable compliance. But safety studies with depot preparations in the elderly are lacking. A particular disadvantage of parenteral depot antipsychotics, such as haloperidol decanoate and fluphenazine ethanante, is the high risk of EPS.

Electroconvulsive therapy

Electroconvulsive therapy (ECT) is a controversial treatment in the U.S., especially for nonaffective disorder patients. Remington and Jeffries reported the results in three patients with erotomanic delusions [7] who had responded to ECT after failed antipsychotic treatment [67]. Only one of these patients, however, was elderly. The use of ECT to treat delusional disorder is not generally recommended and is conceivably difficult given the problems of obtaining informed consent.

Psychosocial management

Pharmacological and somatic treatments do not cure schizophrenia or delusional disorder. Psychosocial treatment (supportive therapy, social assistance, etc.) are vital in the management of the patient. In addition, close family members and friends of the patient may also benefit from a better understanding of the nature of the disease and its treatment.

Conclusions

Elderly patients require lower doses of antipsychotics and are at a much higher risk for medication side effects than are younger adults. Typical neuroleptics are effective in treating positive symptoms but also have a high risk of causing TD. Atypical antipsychotics may minimize the risk of EPS. Delusion disorder in the elderly remains poorly characterized and relatively little is known about its treatment. Psychosocial aspects of management are critical in the overall treatment of elderly patients with schizophrenia or delusional disorder.

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Note added in proof An open-label study of olanzapine (mean dose 7 mg/day) in 15 elderly Parkinson's disease patients with psychotic symptoms was recently published [68]. While most patients had an improvement in psychotic symptoms, one patient discontinued the drugs due to drowsiness. At present no other atypical antipsychotics have been approved by the U.S. Food and Drug Administration for use in the United States. Several drugs are, however, expected to receive approval in the near future. Such agents include sertindole, quetiapine, and ziprasidone. The number of published studies on the use of these drugs in elderly patients is very limited. In a double-blind placebo-controlled dose-escalation study of sertindole, 16 elderly dementia patients were titrated to 16 mg/day dose over 12 weeks [69]. The main side effects reported were somnolence, dizziness, and arthralgia, although no clinical evidence of cardiotoxicity was seen. Finally, in an open-label multicenter trial, elderly patients with schizophrenia and other psychotic disorders were generally found to tolerate quetiapine well [70]. The most frequently reported side effects were somnolence, dizziness, and postural hypotension.

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