REVIEW

Antipsychotic prescribing in older people

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Abstract

Antipsychotic medications have made a significant contribution to the care of the mentally ill people over the past 50 years, with good evidence that both typical and atypical agents are effective in the treatment of schizophrenia and related conditions. In addition they are widely used to good effect in other disorders including psychotic depression, dementia and delirium. Both typical and atypical agents may cause severe side-effects and, in the elderly in particular, there is an increased propensity for drug interactions. If used with care, antipsychotics are usually well tolerated, especially the atypical drugs.

Although antipsychotics are effective at reducing psychotic symptoms their limitations should be recognised. They do not ‘cure’ the underlying illness, and the management of psychotic and behavioural symptoms must take into consideration treatment of physical illness as well as psychosocial interventions. In addition, the antipsychotic effect may take one to two weeks to be evident so doses should not be increased too rapidly. Often small doses are effective in the elderly if they are given sufficient time to work.

As our understanding of the mechanisms of psychosis improves it is hoped that new drugs will be developed with novel mechanisms of action with improved efficacy and reduced side-effects. There are several drugs in development, some sharing similarities to currently available agents whilst others have novel mechanisms of actions involving glutamate and nicotinic receptors. Pharmacogenetics is also likely to be increasingly important over the next few years. As the genetic basis of many psychiatric disorders becomes more clearly established it is likely that drugs specifically designed for particular sub-groups of receptors will be developed.

Finally, although the pharmacological treatment of psychotic disorders in younger people has been given considerable attention, there is a paucity of good quality research on antipsychotic drug use in older people. There is a need to redress this balance to ensure that the prescribing of antipsychotics in older people is evidence based.

Keywords: antipsychotics, psychiatry, older people

Introduction

It is now 50 years since chlorpromazine, the first modern synthetic antipsychotic was launched. Since this time, further antipsychotics have been developed with improved efficacy, side-effect profiles, tolerability and safety. The 29 preparations now licensed for use in the UK are used in the treatment of both psychomotor excitement and psychosis, whether secondary to dementia, delirium, schizophrenia, depression or mania. The newer generation of drugs (‘atypicals’) are up to 30 times more expensive than their older counterparts [1] and this has led to an intense debate about their cost-effectiveness. Although prescribing guidelines on the use of antipsychotics in schizophrenia from the National Institute of Clinical Excellence are welcome, extrapolation of their recommendations to the use of antipsychotics in older people will need to be made with caution. In addition, other published guidelines for the treatment of schizophrenia and psychosis do not provide specific information about older people [2–5]. This population has an increased risk of developing side-effects and drug
interactions yet there is relatively little primary research into the use of these drugs in older people. The National Service Framework for Older People contains a Medicines Code with a short section on antipsychotic medication [6], and also highlights the abuse of these drugs in older people. This paper seeks to highlight some of the key issues related to prescribing antipsychotics and provides an evidence-based rationale for the treatment of common psychiatric conditions in older people.

**Terminology and classification**

A number of terms including ‘neuroleptic’ (the ability to produce a state of ‘neurolepsis’, or calm indifference, without loss of consciousness), ‘major tranquiliser’ (because of their use in major psychoses) and ‘antischizophrenic’ have historically been proposed to describe this group of drugs. However, the term ‘antipsychotic’ is currently the preferred term. A number of classification systems exist for these drugs based on their chemical structure (Table 1), neuropharmacology and clinical action. The most commonly used system divides antipsychotics into ‘typical’ and ‘atypical’ agents. The atypicals are broadly defined as being less likely to produce extrapyramidal side-effects (EPSEs), tardive dyskinesia or to raise prolactin levels.

**Mechanism of action**

There are three principal dopamine-containing tracts in the brain: the mesolimbic tract (ventral segmental area to amygdala, pyriform cortex, lateral septal nuclei, nucleus accumbens, frontal cortex and septohippocampal regions), the nigrostriatal tract ( substantia nigra to caudate nucleus and putamen), and the tuberoinfundibular tract (arcuate nucleus of the hypothalamus to the median eminence). Antagonism of dopamine activity in these sites is associated with antipsychotic effects, EPSEs and endocrine effects respectively.

All antipsychotics have clinically relevant affinities for the D2 receptor, with most showing a mixture of D1 and D2 antagonism, in conjunction with varying degrees of non-dopaminergic receptor involvement (e.g. muscarinic, adrenergic, serotoninergic and histaminic). In addition, the atypicals show antagonism at D3 and D4 receptors (Table 2). Although the precise functional significance of these multiple receptors remains to be clarified, this high D3 and D4 selectivity may account for the low EPSE rates observed with atypical antipsychotics [7]. Phenothiazines (e.g. chlorpromazine) are predominantly D1 and D2 antagonists whereas the butyrophenones (e.g. haloperidol) and diphenylbutylpiperidines (e.g. pimozide) are mainly antagonists at D2. The former have, in addition, a higher affinity for adrenergic, muscarinic and histaminic blockade compared with the relatively more receptor specific butyrophenones, giving rise to their distinctive side-effect profiles as below.

**Side-effects of antipsychotics**

Older people tend to experience side-effects more frequently and with greater severity compared with younger people and receptor binding characteristics of antipsychotics largely determine the side-effects experienced by patients (Table 3). Typical drugs such as haloperidol have high affinities for D2 receptors and thus are particularly

**Table 1. Classification of antipsychotics**

<table>
<thead>
<tr>
<th>Chemical structure</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenothiazine</td>
<td>Chlorpromazine*</td>
</tr>
<tr>
<td>Piperidine</td>
<td>Thoridazine*</td>
</tr>
<tr>
<td>Piperazine</td>
<td>Trifluoperazine*</td>
</tr>
<tr>
<td>Butyrophone</td>
<td>Haloperidol*</td>
</tr>
<tr>
<td>Diphenylbutylpiperidine</td>
<td>Pimozide*</td>
</tr>
<tr>
<td>Thiothixene</td>
<td>Flupenthixol*</td>
</tr>
<tr>
<td>Substituted benzamide</td>
<td>Sulpiride*</td>
</tr>
<tr>
<td>Dibenzoazepine</td>
<td>Clozapine*</td>
</tr>
<tr>
<td>Thienobenzodiazepine</td>
<td>Olanzapine*</td>
</tr>
<tr>
<td>Dibenzoazapine</td>
<td>Quetiapine*</td>
</tr>
<tr>
<td>Benzisoxazole</td>
<td>Risperidone*</td>
</tr>
<tr>
<td>Dibenzothiepine</td>
<td>Zotepine*</td>
</tr>
</tbody>
</table>

*Typical antipsychotic

*Atypical antipsychotic

**Table 2. Relative receptor binding affinities of antipsychotics**

<table>
<thead>
<tr>
<th>Example</th>
<th>D&lt;sub&gt;1&lt;/sub&gt;</th>
<th>D&lt;sub&gt;2&lt;/sub&gt;</th>
<th>D&lt;sub&gt;3&lt;/sub&gt;</th>
<th>D&lt;sub&gt;4&lt;/sub&gt;</th>
<th>M&lt;sub&gt;1&lt;/sub&gt;</th>
<th>α&lt;sub&gt;1&lt;/sub&gt;</th>
<th>5HT&lt;sub&gt;2&lt;/sub&gt;</th>
<th>H&lt;sub&gt;1&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amisulpride</td>
<td>–</td>
<td>+ + + +</td>
<td>+ +</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Clozapine</td>
<td>+ +</td>
<td>+ + + +</td>
<td>+ +</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>+ +</td>
<td>+ +</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>– + + + +</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+ + + +</td>
<td>+ +</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>+ + + +</td>
<td>+ +</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Risperidone</td>
<td>– + + + +</td>
<td>+ +</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Zotepine</td>
<td>+ + + +</td>
<td>+ +</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+ + + +</td>
<td>+ + + +</td>
<td>+ + + +</td>
</tr>
</tbody>
</table>

+ + + + = Very high affinity; + + + = High affinity; + = Weak affinity; – = Absent affinity (D = Dopaminergic; M = Muscarinic; α = Adrenergic; 5HT = Serotoninergic; H = Histaminic) (Adapted from [8, 9]).
associated with a high prevalence of extrapyramidal side
effects. These symptoms are more likely to occur in older
people and in patients with dementia and up to 21% of
patients with dementia experience extrapyramidal side-
effects when treated with typical antipsychotics [10]. Of
particular concern in older people is the potential to
develop tardive dyskinesia. The prevalence in older
people is 3–5 times higher than in younger age groups [11].
In addition, typical antipsychotics have a number of
other side-effects including sedation and anticholinergic
side-effects, especially with chlorpromazine, causing
acute confusional states and memory impairment.
Recently, concerns have been raised about QT interval
abnormalities with ventricular tachycardia and sudden
death in patients of all ages receiving doses of thioridazine
within BNF limits [12]. As a consequence, restrictions on
its use have been made, limiting it to specialist-only
prescribing for a limited range of clinical indications
including schizophrenia [13]. For similar reasons,
droperidol has been withdrawn.

In comparison, atypical antipsychotics are associated
with significantly fewer serious side-effects [14–16].
Risperidone has minimal sedation and negligible
anticholinergic effects. The most frequently reported
side-effects include insomnia and postural hypotension,
the latter is especially common in those with pre-existing
cardiovascular conditions [17]. Olanzapine has a low
propensity to cause EPSEs [18, 19] but sedation is seen
in approximately 11% [17]. Olanzapine is also associated
with significant weight gain and concerns have been
expressed about an increased risk of diabetes with olan-
zapine [20–22], but further prospective studies need to be
undertaken to clarify this. Side-effects of quetiapine
include somnolence, dizziness and hypotension and an
increased risk of QT interval prolongation [18, 23], and
amisulpride causes insomnia, agitation, dry mouth and
weight gain, but few cardiovascular effects [24]. Clozapine
causes significant anticholinergic side-effects [11] as well
as orthostasis, hypersalivation and a high risk of neutro-
penia [18]; the incidence of agranulocytosis in older people
is approximately 0.4% [18]–5 times higher than in the
younger population [25].

**Drug interactions**

Drug interactions are more significant in older people in
part because of co-morbid physical illness. Drugs with
anticholinergic side-effects (e.g. typical antipsychotics)
reduce gastric emptying and slow absorption. Metabolism
can also be influenced by the induction (anticonvulsants)
or inhibition (antipsychotics) of hepatic enzymes.
Table 4 highlights some of the clinically important drug
interactions.

**Table 3. Side-effects of antipsychotics**

<table>
<thead>
<tr>
<th>Receptor type</th>
<th>Clinical examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopaminergic (especially D2)</td>
<td>Extrapyramidal side-effects (EPSE) (i.e. parkinsonism, acute dystonia, akathisia, tardive dyskinesia), galactorrhoea, gynecomastia, pigmentation, tremulousness</td>
</tr>
<tr>
<td>Muscarinic (anticholinergic)</td>
<td>Dry mouth, reduced sweating, blurred vision, raised intraocular pressure, urinary retention, constipation, impotence, tachycardia, confusion, memory impairment, delirium, cardiotoxicity</td>
</tr>
<tr>
<td>Adrenergic (α)</td>
<td>Orthostatic hypotension, tachycardia, arrhythmia, insomnia, tremor</td>
</tr>
<tr>
<td>Serotoninergic</td>
<td>Weight gain</td>
</tr>
<tr>
<td>Histaminergic</td>
<td>Sedation, hypotension, weight gain</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Photosensitivity and pigmentation (especially phenothiazines), neutropenia (especially clozapine), reduced seizure threshold (mainly typical drugs)</td>
</tr>
</tbody>
</table>

**Table 4. Principal drug interactions with antipsychotics**

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Drug interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine</td>
<td>Carbamazepine increases olanzapine clearance; activated charcoal decreases olanzapine bioavailability; ciprofloxacin increases olanzapine plasma levels; seizures reported when combined with clomipramine</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Carbamazepine reduces quetiapine plasma levels; increased plasma level of olanzapine with erythromycin, ketoconazole, and decreased levels with phenytoin and rifampicin. Quetiapine also increases lithium plasma levels and there is an increased risk of QT interval prolongation when combined with terfenadine</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Severe EPSEs have been reported when combined with donepezil or phenytoin</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Enhanced hypotension with diltiazem and enalapril; increased risk of leucopenia/neutropenia with a range of antibiotics including clindamycin, lincomycin, sulphonamides, trimethoprim, isoniazid, rifampicin and metronidazole; significant sedation with lorazepam; increased risk of agranulocytosis with chloramphenicol, penicillamine, sulphonamides, phenylbutazone, co-trimoxazole and pyrazolone analogues; increased plasma levels with erythromycin, fluroxetine, fluvoxamine, paroxetine, sertraline and decreased levels with phenytoin, rifampicin and valproate</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Enhanced hypotensive effect with ACE inhibitors; decreased absorption with activated charcoal; increased risk of ventricular arrhythmias with amiodarone; decreased plasma level with antaeds; increased plasma level with propranolol; chlorpromazine increases the plasma levels of valproate and phenytoin</td>
</tr>
</tbody>
</table>
Clinical indications

Patients with psychotic symptoms are frequently distressed and frightened and this often results in disturbed behaviour such as aggression and wandering. Managing patients with psychotic symptoms in acute medical settings can be difficult and antipsychotics have a useful role to play. Smaller dosages appear to be used in clinical practice but research in this area is very limited.

Physical illness

The choice of antipsychotic will depend in part on the patient’s physical health. Patients with conditions such as glaucoma and prostatism should not be prescribed drugs with significant anticholinergic side-effects (e.g. chlorpromazine), as these can exacerbate these conditions. Patients with Parkinson’s disease are particularly sensitive to the side-effects of typical antipsychotics, particularly those causing extrapyramidal side-effects such as haloperidol. About 20–30% of patients with Parkinson’s disease develop psychotic symptoms [26], making this an important clinical area. A number of atypical antipsychotics have been found to be helpful and well tolerated in treating psychotic symptoms in Parkinson’s disease, including quetiapine [27, 28] and olanzapine [29]. In addition, a review by Schweitzer [30] has recommended low dose risperidone for the treatment of psychotic symptoms in patients with Parkinson’s disease. More research is needed in this area.

Dementia

The prevalence of dementia increases from approximately 0.7% of those aged 60–64, doubling every 5 years to nearly 40% in those aged 90–95 years [31]. The symptoms and signs consist both of features attributable directly to defects in cognitive function and also to non-cognitive features including disturbed behaviours (e.g. aggression, wandering, eating disorders) and psychiatric symptoms (e.g. hallucinations and delusions). Psychotic symptoms cause considerable distress for patients and carers and they frequently lead to residential placement. These symptoms occur in up to 90% of patients with dementia at some time in their illness [32] and antipsychotics can be helpful in reducing symptoms [33].

There are different approaches to behavioural disturbance involving psychological and environmental interventions. When these are ineffective, psychotropics are commonly prescribed, with over 40% of patients with dementia in residential placements receiving antipsychotics [34, 35]. Typical antipsychotics show only modest response rates, with no consistent evidence that one agent is more effective than another [36]. In addition, their use is limited by their side-effects and particularly their propensity to cause delirium (e.g. chlorpromazine). However, a recent Cochrane review of haloperidol has shown that it is effective in the management of behavioural symptoms in dementia [37] but in comparison, risperidone has a better risk/benefit profile in this patient group [38].

In a 12-week, multicentre, double-blind, randomised, placebo-controlled trial of placebo versus risperidone in 625 severely demented patients with behavioural disturbance, all of whom were in a hospital or nursing home, significantly greater reductions in symptoms in patients taking risperidone were found compared with placebo [32]. Similar results have been found in other studies, with particular benefit in the management of aggression in patients with dementia [39]. In this context, Katz et al. [32] has recommended using 1 mg/day although other authors suggest using a smaller starting dose (0.25–0.5 mg/day) gradually increasing to a maximum of 2–3 mg/day depending on clinical response and tolerability [36].

Olanzapine (5 mg, 10 mg and 15 mg) and placebo were compared in 206 nursing home patients with severe Alzheimer’s dementia with behavioural disturbance and psychotic symptoms [40] over 6 weeks. The study found significant improvements with 5 mg and 10 mg/day compared with placebo but not with 15 mg/day. A further study comparing low dose risperidone, olanzapine and haloperidol in nursing home patients with psychiatric disorders, Frenchman [41] found that of the 123 patients with dementia, behavioural symptoms improved in 85% of patients treated with risperidone, in 44% of patients treated with olanzapine and in 43% of patients treated with haloperidol. Overall, risperidone was reported to be better tolerated with fewer side-effects [42]. In contrast, an open-label study involving nearly 1000 hospitalised patients with dementia with behavioural disturbance compared risperidone (n = 500), haloperidol (n = 289) and olanzapine (n = 209) reported significantly greater overall improvement in symptoms with olanzapine [43]. An intramuscular preparation of olanzapine is now available and this was evaluated in a double-blind randomised study involving 272 agitated patients with dementia. At 2 hours, olanzapine 2.5 mg and lorazepam 1 mg (intramuscular) were equally effective and both were superior to placebo. At 24 hours, only olanzapine remained superior to placebo [44].

The management of psychotic symptoms in patients with dementia with Lewy bodies can be difficult because of the increased risk of EPSEs. The atypicals are preferred but should be prescribed cautiously, usually starting with a low dose. In a recent double-blind, randomised, placebo controlled study involving 29 patients with dementia with Lewy bodies, olanzapine 5 mg and 10 mg significantly reduced psychotic symptoms without worsening the parkinsonism [45]. There is also limited evidence of benefit and safety with clozapine [46], risperidone [47], and quetiapine [48] but considerably more research is needed.

Delirium

Delirium is an organic psychiatric syndrome characterised by acute onset, fluctuating levels of consciousness
and global impairment of cognitive functioning. It is particularly common in the elderly [49] and especially in those with pre-existing cognitive impairment [50], and 14–56% of all elderly hospitalised patients have an episode of delirium at some point during their admission [49]. Common causes include infections (43%), prescribed medications (20–40%) as well as endocrine, fluid and electrolyte imbalances and constipation. Despite this, non-detection rates are high and range between 33–66% [50, 51]. However, detection and treatment are important because of the increased mortality [52], longer hospital stay and increased likelihood of subsequent residential care associated with delirium [50].

Standard approaches to treatment include specific interventions to address any underlying physical illness and management of associated symptoms such as agitation and hallucinations. Attention to environmental and psychological factors is also important [53]. If behavioural disturbance is prominent, antipsychotic medication may be indicated. Antipsychotics are highly effective, mainly due to their rapid onset of action, high therapeutic index and minimal effects on respiration. In addition, they do not lead to chemical dependency and it is unlikely that tolerance will develop.

Until recently, thioridazine was widely used but this is no longer recommended because of the increased risk of QT interval prolongation. Haloperidol has also been widely used and the benefits of this have been highlighted in a recent review [50]. In older people a small dose of oral haloperidol is frequently very effective (e.g. 0.5–2 mg) but intramuscular haloperidol may be needed if the patient is very disturbed. Small doses of lorazepam (1–2 mg) can also be useful if this is not clinically contraindicated and if antipsychotics cannot be given. There is very little good quality research on haloperidol in delirium but it remains the treatment of choice [54]. In a survey of 28 general hospitals in Japan haloperidol accounted for nearly 70% of antipsychotic prescriptions for delirium [55]. Sipahimalani and Masand [49] evaluated the efficacy of olanzapine versus haloperidol at conventional dosages in a non-randomised, uncontrolled case series of 11 patients with delirium of diverse aetiologies. Although both drugs had similar peak response times, olanzapine was better tolerated and this has been confirmed by a more recent series of case reports [56]. In a further study, Breitbart et al. [57] reported an open-label study of 79 hospitalised cancer patients with delirium treated with olanzapine. Seventy-six percent had a complete resolution of their delirium and the medication was well tolerated. In addition, there is also limited evidence of clinical benefit with risperidone (1.5–4 mg/day) [50] and quetiapine [58] but further work is needed to confirm this.

‘Early-onset’ schizophrenia

The life course of schizophrenia into later adulthood is not well studied, although it is generally recognised that, whereas psychotic symptoms tend to remit with time, the negative symptoms (e.g. social withdrawal and emotional apathy) increase in frequency and intensity with advancing age [18]. It is estimated that 0.1–1.0% of the over 65 population has schizophrenia [18], including up to 12% of all nursing home patients [59].

Older patients with long standing schizophrenia may have been taking high dose intramuscular antipsychotics (depots) for many years. If patients are experiencing side-effects, particularly EPSEs, or if there is limited clinical benefit, patients can be switched to atypical antipsychotic. In a recent study involving 51 older patients with schizophrenia, patients were successfully switched from typical antipsychotics to risperidone. The change was clinically effective, well tolerated and significantly less antiparkinsonian medication was needed [60]. However, because of the risk of relapse, this should usually be done in collaboration with psychiatric colleagues. In general, the depot can be stopped and the oral medication introduced when the next depot is due. The development of long acting atypical intramuscular preparations such as Risperdal consta will increase therapeutic options but safety and efficacy in older people needs to be clearly established.

Atypical antipsychotics have been shown to be as effective as typical agents in treating the psychotic symptoms of schizophrenia and more efficacious at reducing negative symptoms [18]. In addition, there is increasing evidence that their prescription may be cost-effective in the longer term [61].

Risperidone is an effective treatment for schizophrenia [62] but there have been no double-blind controlled studies of atypical antipsychotics in older people with schizophrenia. However, a number of open studies have demonstrated benefit with risperidone [63, 64] and particularly improved cognition [17, 18].

Olanzapine is also an effective treatment for schizophrenia [65]. There have only been a few reports of olanzapine use in older schizophrenics, most of which have involved small numbers [18]. However, the consensus of opinion is that olanzapine is both well tolerated and efficacious.

Clozapine is the only atypical antipsychotic with a clearly demonstrated superiority in treatment-resistant schizophrenia in younger patients [18] but there is very little information available in older patients. Of the studies involving older patients, there is evidence for both a significant behavioural improvement (especially in violence and aggression) reduced mortality from suicide, a modest reduction in psychotic symptoms and improved compliance [18]. However, these benefits must be balanced against the increased risk of agranulocytosis. Clozapine is restricted for the management of treatment-resistant schizophrenia or those unable to tolerate conventional antipsychotics. Its dispensing is controlled by the Clozaril Patient Monitoring Service (CPMS) which ensures regular monitoring of white cell count. As with most antipsychotics, the initial recommended dose in older people is less than for younger patients and should be gradually increased over several weeks [18].
Evidence for the use of other atypicals in older people is limited though they have been demonstrated to be effective in younger people e.g. quetiapine [23], amisulpride [24] and zotepine [66]. However, quetiapine has also been shown to be effective and well tolerated in older people with psychotic symptoms in schizophrenia, affective disorders and dementia [67].

Very-late-onset schizophrenia

Ten percent of all first admissions over 60 years of age to psychiatric hospitals are diagnosed with late onset paranoid disorders [68]. Patients are typically single, socially isolated women living alone, often with concomitant hearing impairment. Late-onset schizophrenia (illness onset after 40 years of age) and very-late-onset schizophrenia (illness onset after 60 years of age) [69] tends to follow a relatively benign course, with predominant positive symptoms and fewer negative symptoms, although relapse is frequent often as a consequence of medication non-compliance. Some paranoid presentations in later life may be prodromal for dementia.

There is a relative paucity of good quality psychopharmacology research in older patients with late onset schizophrenia. Case reports and open studies reveal conflicting conclusions with respect to treatment response [18]. No single antipsychotic has been shown to be proven more effective and in clinical practice choice of antipsychotic will be influenced in part by individual patient characteristics and side-effect profiles. However, in a recent review, typical antipsychotics were found to be as effective as atypicals [70] but compliance is much better with atypical antipsychotics [71].

Depression

The prevalence of depression in older people living in the community is 10–15% and this can rise significantly in residential and hospital settings [72]. Although mild and moderate forms respond well to the combination of antidepressants and psychological therapies, there is a relative lack of research into the effective management of severe depression with psychotic features in older people. Parker et al. [73] in a meta-analysis of 44 studies found that ECT was superior to drug therapy but combination therapy (an antipsychotic and an antidepressant) was more effective than either medication alone. More recently, a small 10-week, open-label study involving seven older patients with psychotic depression reported significant benefit with olanzapine 10–20 mg/day [74], and there have been a few case reports demonstrating similar benefit with risperidone [75]. There is clearly a need for further research in this area.

Bipolar affective disorder (BAD)

The prognosis of elderly patients with manic symptoms is generally worse compared with depressed patients. In particular, there is a higher prevalence of cognitive dysfunction, persistent symptoms and greater mortality [76]. However, there are few prospective studies focusing on older patients with mania and, as a result, most recommendations are extrapolations from data relating to younger patients with BAD or older patients with unipolar depression or dementia [77]. The initial treatment of an agitated, manic patient usually includes antipsychotics and benzodiazepines as adjunctive therapy. However, risperidone is reported to have a dramatic effect in elderly patients with mania, although other reports suggest it may induce mania in some patients [77]. Clozapine is safe and effective in the treatment of mania in the elderly but does not have demonstrated effectiveness in treating the depressed phase of bipolar patients [78]. There are no published studies of the use of olanzapine, amisulpride, quetiapine or zotepine in the elderly, although olanzapine has been approved for the treatment of mania in the US.

Anxiety disorders

Chlorpromazine and trifluoperazine have been widely used in the treatment of anxiety and related disorders, but the evidence to support this is very limited. Only one randomised controlled trial has been conducted into the use of the latter [79], concluding an improvement in anxiety symptoms compared with placebo but significant side-effects were reported. More recently the antidepressant venlafaxine (a serotonin and noradrenaline re-uptake inhibitor) has been licensed for anxiety disorders and consequently, the role of antipsychotics in the pharmacological treatment of anxiety is diminishing. However, in the acutely disturbed or highly agitated patients, antipsychotics do have a useful role [80] with haloperidol (0.5–10 mg) remaining the treatment of choice.

Key points

- Antipsychotics are effective for the treatment of psychosis and behavioural disturbance in a range of disorders including schizophrenia, depression, delirium, dementia and anxiety disorders.
- The starting dose should usually be small and gradually increased over several weeks as the antipsychotic effect can take one to two weeks.
- Side-effects, drug–drug interactions and tolerability are usually better with the atypical antipsychotics.
- Considerably more evidence-based research is needed on the use of antipsychotics in older people.

References


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Antipsychotic prescribing in older people


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