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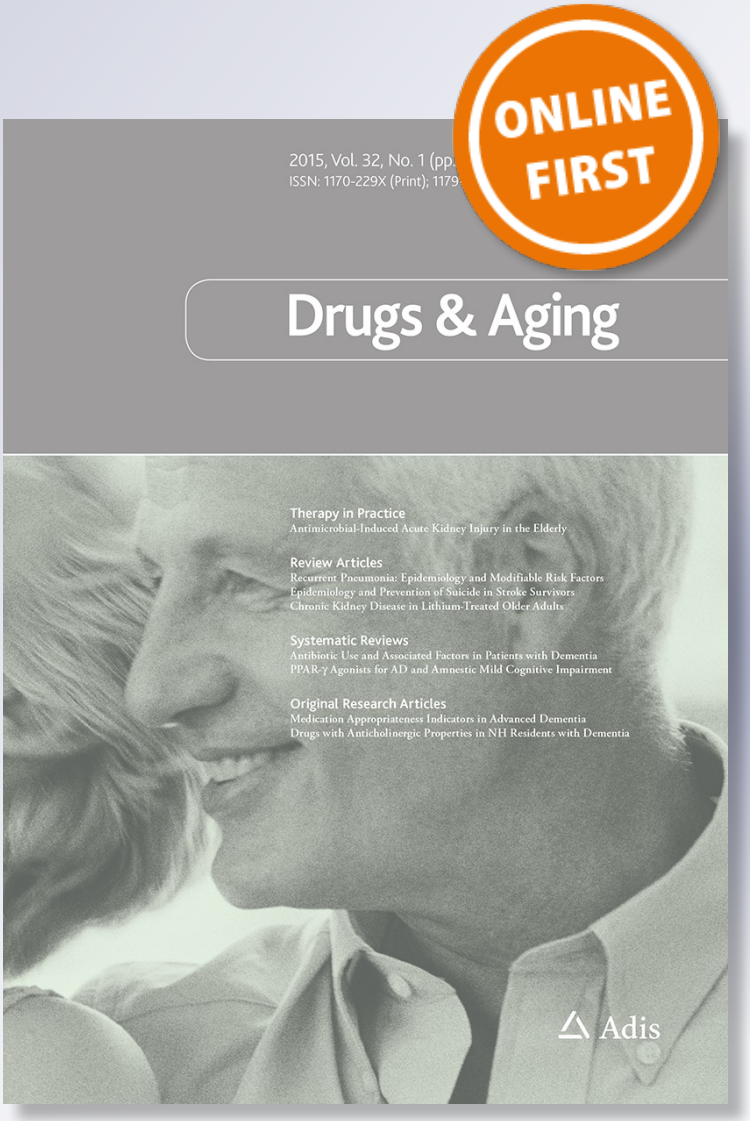

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REVIEW ARTICLE

Pharmacological Management of Behavioral and Psychiatric Symptoms in Older Adults with Intellectual Disability

Nicole Eady · Ken Courtenay · André Strydom

Abstract Given medical and social advances, the life expectancy of individuals with intellectual disability (ID) has increased dramatically, leading to a generation of older individuals with such disabilities. This review focuses on the pharmacological treatment of behavioral and psychiatric symptoms and disorders in older adults with ID. Older adults with ID often present with medical co-morbidities and mental health issues. Medication management of behavioral and psychiatric problems is complicated by a higher risk for adverse events, lack of decision-making capacity, and complex care networks. Some studies have shown that individuals with ID and co-morbid mental disorders are undertreated in comparison with those with similar disorders in the general population, resulting in poorer outcomes. However, older adults with ID are also at risk of polypharmacy, and older age is a risk factor for development of side effects. A general principle is that medication treatment for psychiatric disorders in older individuals with ID should be started at low dosages and increased cautiously while monitoring response and side effects. The use of psychotropic drugs for older individuals with ID and behavioral problems remains controversial, particularly in those with dementia.

Key Points

The growing population of older adults with ID has an increased risk for aging-related health issues such as dementia, on a background of lifelong disabilities and physical health and psychiatric co-morbidities.

Medication management of behavioral and psychiatric problems may be complicated by a higher risk for adverse events, lack of decision-making capacity, and complex care networks.

Medication management of specific conditions is, however, beneficial, but medication should generally be started at low doses, with careful titration against response, and regular monitoring for side effects.

1 Introduction

Intellectual disability (ID) is defined by the World Health Organization (WHO) as significant cognitive impairment associated with impairment of skills manifested during the developmental period. Cognitive impairment in people with ID is categorized as two standard deviations below the norm for intellectual quotient (IQ), with a level below 70 in the ID range. The development of social and adaptive skills is central in the definition of ID where the person requires support to maintain their level of functioning. Such deficits

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must have their origins in childhood, which contrasts with cognitive impairment acquired in adulthood. Classification systems categorize levels of IQ into mild, moderate, severe, and profound. In general, people with mild ID require less support in daily living skills than others but they are often more vulnerable to exploitation by others and engage in more high-risk lifestyle activities, for example, cigarette smoking. People with intellectual impairment account for 2.5–3 % of the general population based on statistical estimates in the population where ID is two standard deviations below the norm for IQ, but the global prevalence estimate of ID (i.e. intellectual and functional impairment) is 1.03 % [1].

ID is associated with greater degrees of health inequalities than seen in the general population, and people have more co-morbid conditions affecting all body systems, especially the nervous system [2]. The prevalence of epilepsy for example, is greater in people with ID than in the general population [3]. The prevalence of mental disorders and behavioral problems associated with related disorders such as autism is greater in people with ID [4]. Therefore, people with ID are, from childhood, more likely to require drug therapy to manage such long-term conditions and, as such, are exposed to the risks of using medication throughout their lives.

The life expectancy of people with ID has risen over the past 50 years [5], which could be due to advances in medical technology and improved social care benefitting people with moderate to severe ID. Changes in societal attitudes towards people with ID and awareness of health inequalities have also had beneficial effects. The life expectancy of people with Down syndrome (DS) has risen from 12 years in the 1940s to 60 years currently, largely because of cardiac surgery interventions [6]. In spite of this, people with ID continue to die younger than their peers in the general population, which is in part due to health and social factors that may be amenable to change [7]. Nevertheless, increasing numbers of older adults with ID may require considerable care inputs. The average annual cost of care for older individuals with ID in the UK is approaching £50,000 ($US71,952; €54,034 at 2013 rates for purchasing power parity), most of which is accounted for by personal care rather than healthcare costs, with mental health problems being an important predictor of costs) [8]. Appropriate treatment and management of behavioral and psychiatric symptoms may therefore help to reduce the burden on caregivers as well as the cost of care.

In this review, we focus on the behavioral and psychiatric symptoms associated with aging in ID and the implications for medication management of these conditions in this population.

2 Physical Health Issues

A review of medication management in the ID population would not be complete without acknowledging the complex health needs of this population, which affect the selection of treatments for behavioral and psychiatric symptoms, and their effectiveness and tolerability. People with ID are more vulnerable to developing acute and chronic health problems for a variety of reasons related to either dependency as a consequence of ID or to lifestyle factors (e.g. diet). An example of an acute health condition is the development of bronchopneumonia in a person with severe ID who has difficulties swallowing because of impaired reflexes. Older people with ID are more disposed to long-term conditions such as diabetes mellitus [9]. Their management often requires drug interventions in the long-term and thus exposure to the side effects of medication over a long period of time as they age.

People with ID often use combinations of medication that potentially interact with each other and have implications for other drugs added to current drug regimens. Clinicians need to be aware of the regimens already in use when prescribing new medication because of the pharmacokinetics of drugs that could affect the metabolism of other agents through enzyme induction or competitive binding to proteins, thus affecting serum levels of drugs. Equally, clinicians need to consider the impact of weight-inducing medication on the long-term health of the person and their subsequent quality of life.

People with ID experience the same range of physical and mental health difficulties as people in the general population, but their level of functioning and cognitive impairment may predispose them to developing health problems. The rates of cardiovascular diseases in older adults with ID are similar to those in the general population [9, 10], while neurological disorders, especially epilepsy, occur at higher rates in people with ID [3]. Overweight and obesity is also an increasing problem [9]. In a recent large-scale survey of older adults (age $\geq$55 years) with ID in Europe, rates of smoking and use of alcohol were lower than in the general population but were higher with older age. More than 60 % of older adults with ID had a sedentary lifestyle. Cataract, hearing disorder, diabetes, hypertension, osteoarthritis/arthrosis, and osteoporosis were positively associated with advancing age in those with ID, but rates of epilepsy declined with age [11]. The etiological factors for these health problems are multifactorial based on the etiology of the ID (e.g. neurological development) or on environmental and social factors such as poor housing or impoverished diet and sedentary lifestyle.

3 General Issues Regarding Medication Management in Individuals with Intellectual Disability (ID)

Prescription of medication for the treatment and management of behavioral and psychiatric symptoms in individuals with ID requires careful consideration. A full discussion of all the issues is beyond the scope of this review, and these have been reviewed elsewhere [12, 13]. The general principles of medication treatment of psychiatric disorders in individuals with ID include the following:

- Decision-making capacity should be assessed, and if the person does not have capacity to decide about their own treatment, appropriate legal and ethical frameworks should be followed to enable treatment depending on the jurisdiction.
- Safe management and dispensing of medication should be carefully considered, and the use of blister packs, dosette boxes, and medication alarm systems may be useful, as well as identifying a responsible person to assist with appropriate management of medication.
- Individuals with ID often have complex care networks, and it is important that all those involved be informed of any changes of treatment.
- Side effects and response to treatment should be monitored, using standardized instruments if possible, with due consideration to the communication needs of the individual. The carers of those with limited communication abilities should be provided with clear instructions on how to monitor for side effects.

4 Mental Health Disorders in Older Adults with ID

Mental health disorders have a greater prevalence among people with ID, with higher rates of psychosis, dementia, and mood disorders than the general population [4, 14, 15]. Drug management of such disorders in people with ID is important because of the benefits to the person in treating the disorders, but the choice and management of medication should be undertaken by a clinician knowledgeable in the mental healthcare of people with ID. However, there is very little evidence to guide prescribing of behavioral and psychiatric symptoms in this population because people with ID have been historically under-represented in randomized controlled medication trials [16]. We summarize generally accepted recommendations, and highlight specific findings if available.

4.1 Treatment of Mood Disorders in Older Adults with ID

Depression is common in adults with ID [4] and is more likely to follow a chronic course [17]. In older adults with ID, increased depressive symptoms were significantly and positively correlated with age, and were also associated with chronic diseases such as heart failure, stroke, chronic obstructive pulmonary disease, coronary artery disease, diabetes mellitus, and malignity in the previous 5 years [18]. In a large survey of depression in older adults with ID (aged $\geq$50 years) in the Netherlands, major depressive disorder was prevalent in 7.6 % (95 % confidence interval [CI] 5.2–11.0), anxiety disorders in 4.4 % (95 % CI 2.6–7.0), and both disorders in 0.7 % (95 % CI 0.2–1.6). There was no relationship with gender, age, or level of ID [19] https://www.nice.org.uk/guidance/cg90.

In Taiwan, patients with ID and bipolar affective disorder were younger than patients with bipolar affective disorder without ID, but had longer periods of hospitalization and were more likely to remain as in-patients, possibly due to receiving significantly lower dosages of medication such as antipsychotics, mood stabilizers, and lithium [20]. These findings are unlikely to be unique to Taiwan and suggest that mood disorders remain under-recognised and undertreated in individuals with ID, which affect longer-term outcomes. However, use of antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) has been increasing in the ID populations since the mid-1990s in the USA [21]. The increased use of SSRIs with fewer side effects was interpreted as evidence for improving skill in diagnosing and treating depressive disorders in this population.

We were not able to identify specific studies or guidelines for medication treatment of depression in older individuals with ID. In general, the treatment guidelines for depression in the general population are appropriate to use, including the UK's National Institute for Health and Care Excellence (NICE) guideline [22] and the American Psychiatric association's practice guideline [23].

4.2 Use of Antipsychotic Drugs in Older Adults with ID

A large survey of antipsychotic prescribing to 2,319 adults with ID (all ages) in the UK found that the most common indications were for psychotic illness (42 %) and anxiety (42 %), while behavioral problems such as aggression (38 %), threatening behavior (30 %), and self-harm (13 %) were also common indications [24]. Risperidone was the most prescribed antipsychotic, particularly for agitation and anxiety, at a median dose of 2 mg per day, followed by olanzapine, which was most often prescribed for psychotic symptoms. The second most common drug for psychosis was quetiapine. Use of older antipsychotics was common, particularly chlorpromazine, which was used for overt aggression, and haloperidol, used for agitation and anxiety. This survey was undertaken before the use of aripiprazole

became more common in the UK, and it is likely that this drug may increasingly be used for psychosis or behavioral disturbances associated with ID or autism following some evidence of efficacy [25, 26]. Guidelines have been produced for the use of newer antipsychotic drugs, as well as for clozapine [28], in individuals with ID [27], which included practical drug review checklists. These drugs need to be used cautiously in older adults with ID, particularly in those with co-morbidities:

- Dementia and cerebrovascular disease are relative contraindications for newer antipsychotics due to an increased risk for stroke.
- Olanzapine and quetiapine have potential antimuscarinic activity, which, in combination with other medications with antimuscarinic activity, may significantly impact on cognition in older individuals with ID, as well as cause problems with gastrointestinal motility, urinary retention, and narrow-angle glaucoma [27].
- Clozapine, quetiapine, olanzapine, and risperidone may cause hypotension, and clinicians should use these drugs cautiously in older adults with ID prescribed with antihypertensives.
- Metabolic syndrome is a well-known complication of newer antipsychotics (particularly olanzapine and clozapine), and risk factors such as obesity and diabetes are common in older adults with ID, particularly those with mild intellectual impairment. Concomitant use of medications known to elevate blood glucose or cause weight gain should be avoided as far as possible in older adults with ID. It is also recommended to document weight, body mass index (BMI), glucose levels, glycosylated hemoglobin levels, electrolytes, and liver function tests before starting these drugs [27], though this is often not done in practice [29]. The use of newer (atypical) antipsychotics was associated with higher diastolic blood pressure and elevated fasting glucose in adults prescribed antipsychotic drugs for more than 1 year [30].

4.3 Medication Management of Problem Behavior in Older Adults with ID

There is some evidence for the use of medication for problem behavior in adults with ID, particularly those with co-morbid autism [13]. The best evidence is for risperidone, with multiple trials showing its efficacy [26]. The management of problem behavior in people with ID can include the use of other medications to help manage behavior that could be attributed to mental disorder, for example, anxiety, mood disorder, or psychosis. The etiological cause of the problem behavior can be difficult to elucidate, and medication is often used to manage it without clear indications. For example, anti-psychotic drugs can be used for their sedative or anxiolytic properties rather than to treat psychotic signs. In doing this, the person may be exposed to the adverse effects of medication, particularly if used over a prolonged period of time, with the potential of interacting with other drugs, particularly in older individuals. Furthermore, a controlled discontinuation study of long-term antipsychotics for behavioral disturbance in individuals with ID (aged 15–66 years; $n = 98$), in which 43 achieved complete discontinuation, showed that a significant proportion of individuals benefited from reduction or withdrawal of the medication, with improvement in clinical symptoms [30]. Most guidelines concerning medication use for problem behavior therefore recommend careful titration against response, regular monitoring for side effects and the use of short treatment periods if possible [12]. In general, one medication should be used at a time, within a standard recommended dosage range, and the opportunities for monotherapy should be exhausted before a combination therapy is considered. Appropriate follow-up visits must be arranged, and the potential for dosage reduction or discontinuation of medication should be regularly considered during the course of treatment [16].

5 Dementia in Older Adults with ID

As the average life expectancy in the ID population increases, so does the number of individuals experiencing the complications of older age, such as dementia. Dementia is defined as a chronic, progressive mental disorder that adversely affects higher cortical functions, including memory, language, and orientation [31] and is associated with increasing morbidity and mortality and imposes significant costs [32]. It is therefore important that evidence-based treatments for dementia in ID are developed and evaluated.

Dementia in ID often has an atypical presentation. Changes in behavior or personality may precede the traditional cognitive symptoms, particularly in those with more severe ID and DS, and the onset of seizures is also common [8].

A number of anti-dementia medications, including acetylcholinesterase inhibitors (AIs) such as donepezil, rivastigmine, and galantamine, and the N-methyl-D-aspartate (NMDA) antagonist memantine, have been developed, and there is a strong evidence base to support their prescription in the non-ID population [33]. These medications are noted to have a beneficial effect on the behavioral and psychiatric symptoms of dementia in addition to maintaining cognitive functions in the short to medium term [34]. The prescription of anti-dementia medication is supported by national

and international guidance, including that in the UK [35], USA [36], and Europe [37].

AIs and NMDA antagonists are not believed to have disease-modifying properties and are therefore not used to prevent the long-term histopathological progression of disease. However, in the short to medium term, they have been shown to slow clinical deterioration.

5.1 Management of Dementia in Down Syndrome (DS)

DS is neuropathologically associated with the risk of developing an Alzheimer-like dementia [38]. Donepezil, from the anticholinesterase class of medications, is the most commonly prescribed anti-dementia medication in this population. A review of the literature found a few small controlled studies [39–41] that confirm that donepezil is well tolerated in the DS population. These studies have some methodological flaws, including the small sample size, choice of controls, and length of follow-up. Other than commenting on safety and the side effect profile, it is not possible to draw conclusions on the efficacy of donepezil on cognition or functioning, or the control of associated behavioral and psychiatric symptoms in the DS dementia population. Further evidence is required, including from non-randomized designs, as it may not be possible to complete further randomized control studies.

No studies on the efficacy of galantamine in the DS population have been published.

A recent small non-randomized observational study showed a significant difference in cognitive functioning ($p = 0.048$) and behavior ($p = 0.05$) between a non-treatment group with DS and those prescribed rivastigmine either as an oral or as a transdermal formulation [42]. The authors noted that transdermal rivastigmine had improved compliance and was well tolerated in the DS population. Another small placebo-controlled trial of rivastigmine in older adults with DS showed a reduction in the rate of deterioration on markers of cognition and behavior between the treatment and control groups after 24 weeks [43]. The differences between the control and treatment groups were not statistically significant. Both of the above studies have the limitations of being small and having short follow-up periods.

The current literature on memantine does not support its use in clinical practice in DS. A recent prospective double-blind, randomized control trial compared memantine with placebo in patients with DS [44]. All participants in the study were over 40 years of age, and one-third had a diagnosis of dementia. There was no statistical significance between the groups at 1 year in measures of functioning, behavior, or cognition. The authors concluded that memantine is not effective in the treatment of dementia in the DS population.

5.2 Management of Dementia in the Non-DS ID Population

Among people with ID, those with DS are most at risk of developing dementia. Dementia may also be more common in older adults with ID who do not have DS, with prevalence rates of up to 18 % in those aged 65 years and older [14]. Incidence rates peak at age 70–75 years [45].

However, among people with ID who do not have DS (non-DS ID), there is no published research on the pharmacological treatment of dementia despite a recent estimate of the incidence of dementia among them being up to four times higher than the general population [45]. Current clinical practice varies widely, with clinicians often referring to the evidence base for the DS population and the non-ID population. Clinicians, carers, and patients often lack awareness of the early signs of dementia, which can result in a delay in offering dementia-specific treatments [46].

5.3 Management of Behavioral and Psychiatric Symptoms Associated with Dementia in ID

Dementia in ID is frequently associated with co-morbidities, including psychiatric presentations (e.g. depression, and behavioral problems) [8]. Some of these psychiatric co-morbidities, including problem behavior, may be noted to improve with the prescription of dementia medication listed above. Antipsychotic drugs have been widely used to treat psychosis, aggression, and agitation in patients with Alzheimer's disease in the general population; however, a large randomized trial concluded that adverse effects offset advantages [47]. In some countries, such as the UK, recent guidelines consequently suggested that antipsychotics are overused in older adults with dementia in the general population and that the potential benefit of their use is likely to be outweighed by the adverse effects in many cases. Whilst not prohibiting the use of such drugs, a key recommendation was to avoid the prescription of newer antipsychotics in adults with dementia [48]. Pharmacological treatment of any co-morbidity would therefore need to be in accordance with guidance on managing co-morbidity in general guidance by the relevant national body, such as the American Psychiatric Association (USA) or the Royal College of Psychiatrists (UK).

Medical co-morbidities are a common cause of mortality in the older adult ID population and require prompt review in any person presenting with a change in behavior. The prescriber should also be aware of the associated risk of polypharmacy and drug interactions in this population. Although outside the scope of this review, changes in support plans and access to psychological interventions

both have an important role in the treatment of the behavioral and psychiatric symptoms of dementia [49].

Sleep difficulties are noted to increase in older age groups, especially in those with dementia [50]. Behavioral difficulties secondary to the day–night routine is common. Melatonin is noted to be effective in reducing sleep-onset latency in the ID population [51], although there are no published trials reviewing the safety or efficacy of melatonin prescription in the ID dementia population.

6 Polypharmacy and Prescribing Patterns

A large study of psychotropic prescribing patterns in the USA, which compared individuals with ID with a dual diagnosis of co-morbid psychiatric disorders against those with normal ability with psychiatric diagnoses, found that antidepressants and antipsychotics were prescribed at lower rates for those with ID, suggesting that psychiatric conditions in the ID population were often undertreated. However, polypharmacy rates were higher for adults with ID [52], and rates of prescribing of antipsychotics and antidepressants have been increasing over the past few decades [21].

Prescribing patterns are changing. Prescribers are moving away from medication management of behavioral issues, as found in a recent study of psychotropic drug prescribing in adults of all ages (mean age 49 years) with ID in New York State [21]. Although 58 % of these adults with ID were prescribed one or more psychotropic drug, in most cases the indication was a diagnosed co-morbid mental disorder and only 13 % were prescribed psychotropic drugs solely for control of behavioral problems [21]. Age had no effect on the likelihood of being prescribed antipsychotics.

One group from the Netherlands described the side effect profiles associated with longer-term (more than 1 year) antipsychotic use for behavioral problems in individuals with ID with a mean age of 49.8 years [30]. Extrapyramidal symptoms were present in 53 %, overweight and obesity in 46 %, and the metabolic syndrome in 11 %. Hyperprolactinemia was present in 17 %. Older age and more severe ID were associated with increased rates of side effects, particularly dyskinesia.

7 Conclusions and Further Research

Older adults with ID often present with medical co-morbidities and mental health issues. Many older individuals may have been prescribed long-term medication for psychiatric disorders such as autism, but they may be more sensitive to the development of side effects, particularly those of anti-psychotics. Some studies have shown that individuals with ID and co-morbid mental disorders are undertreated compared with individuals with similar disorders in the general population, resulting in poorer outcomes. However, older adults with ID are also at risk of polypharmacy, and older age may be a risk factor for development of some side effects. A general principle is that medication treatment for psychiatric disorders in older individuals with ID should be started at low dosages and be increased cautiously while monitoring response and side effects. The use of psychotropic drugs for those with ID and behavioral problems remain controversial, particularly in older adults with dementia, and current guidelines are to use alternative treatments such as behavioral interventions as first-line options. If psychotropic drugs are used, they should be carefully monitored and used for short periods. It remains to be seen whether the latest generation of antipsychotics such as aripiprazole are safer or better tolerated in older individuals with ID.

Dementia is a common problem in this population, and medication treatments for dementia in those with ID are broadly safe and well-tolerated. Sleep problems may respond to treatment with melatonin. However, there remains a lack of strong evidence to support the clinical effectiveness of most medication treatments in this population given the current lack of well-designed, adequately powered studies.

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