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REVIEW

Evaluation and treatment of older-age bipolar disorder: a narrative review

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Abstract

Objectives: This narrative review aims to synthesize information from the literature regarding older-age bipolar disorder (OABD) in order to provide up-to-date information on this important illness.

Methods: We searched Ovid (Medline, Embase and PsychInfo) on October 1, 2020, using the keywords "bipolar disorder", "older adults" and "elderly" to identify relevant articles on OABD. Additionally, the bibliography of identified articles was reviewed for pertinent studies.

Discussions: OABD is a term that is used to describe bipolar disorder (BD) occurring amongst individuals ≥50 years of age. Evidence indicates that OABD accounts for a quarter of all cases of BD. When compared to individuals with early-onset BD, individuals with OABD have a greater association with cerebrovascular disease and other neurological disorders, less family history of mood disorders, and utilize almost four times the total amount of mental health services. In addition, they are four times more likely to have psychiatric hospitalizations when compared to age-matched controls. Despite a dearth of controlled studies on the use of pharmacotherapy amongst individuals with OABD, available evidence from mixed-age studies indicates the efficacy of commonly used medications in individuals with early-onset BD. Additionally, psychosocial treatments have been found to be effective as adjunctive management strategies amongst individuals with OABD. Furthermore, electroconvulsive therapy may be effective in the treatment of refractory cases of OABD.

Conclusions: There is a great need for an improved understanding of the phenomenology and neurobiology of OABD. Additionally, research into effective treatments for this serious psychiatric disorder will mitigate the suffering of individuals with OABD.

Keywords: antipsychotics, bipolar disorder, early-onset bipolar disorder, electroconvulsive therapy, lithium, mood stabilizers, older-age bipolar disorder, psychosocial treatments.

Citation

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Introduction

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), describes bipolar disorder (BD) as an illness characterized by recurring episodes of mania or hypomania and depression.[1] The bipolar and related disorders chapter in the DSM-5 describes bipolar I disorder (BD-I) and bipolar II disorder (BD-II) as the two major subtypes of BD. BD-I is diagnosed when individuals who meet the criteria for a manic episode also report major depressive episodes sometime during the course of their life. BD-II is diagnosed when individuals report at least one episode of major depression and at least one hypomanic episode during their lifetime. Other diagnoses that are included in the bipolar and related disorders chapter are the cyclothymic disorder, substance or medication-induced bipolar and related disorder, bipolar and related disorder due to another medical condition, other specified bipolar and related disorder, and unspecified bipolar and related disorder. In this review, we focus only on BD-I and BD-II.

Although not as common as amongst younger adults, BD can occur amongst older adults.[2] Available evidence indicates that the number of individuals with older-age BD (OABD) is expected to increase significantly over the next few decades.[3] Available evidence indicates that the relative frequency of OABD had increased from 1% to 11% between 1980 and

1998.[4] In this review, we describe the various aspects of OABD, including the evidence-based treatment for this disorder.

Methods

The principal author (RRT) searched Ovid [Medline (1946-), Embase (1974-) and PsychInfo (1806-)] on October 1, 2020, using the keywords "bipolar disorder and older adults" AND "bipolar disorder and elderly" to identify relevant articles on OABD. The initial search for studies was not restricted by the language of publication of the study. However, in the final analysis, we only included studies involving human patients published in English language journals or with official English translations. In addition, the bibliography of identified articles was reviewed for pertinent studies. PRISMA guidelines were not followed as this article was intended as a narrative review and not a systematic review.[5] After a review of abstracts and the removal of all duplicates, a total of 310 articles were initially identified. The author selected a total of 63 articles that provided the core information regarding OABD for full-text review. An additional 25 articles were included to provide general information regarding BD and to also provide important information regarding topics like suicide and risk for death with antipsychotics. The core articles were selected irrespective of the type of study (randomized controlled trials (RCTs), meta-analysis, systematic reviews, scoping reviews, narrative reviews, etc.) if they provided relevant information regarding the epidemiology, neurobiology, assessment and treatment of individuals with OABD.

Review

Epidemiology

According to the International Society for Bipolar Disorders, Task Force OABD is defined as BD that occurs amongst individuals ≥50 years of age.[6] Available evidence indicates that approximately 25% of all cases of BD occur amongst individuals aged ≥60 years, with >10% occurring amongst individuals aged ≥70 years.[7]

The point prevalence of OABD is between 0.1% and 0.5%, with a lifetime prevalence of 0.5–1.0%.[8] Additionally, 10–25% of all older adults who are diagnosed with a mood disorder have BD.[9,10] It is estimated that approximately 10% of individuals with OABD develop their first-onset mania episode in association with a neurovascular disorder.[3] Approximately 6% of all geriatric psychiatry outpatient visits and 8–10% of all geriatric inpatient admissions involve individuals with OABD.[11] Individuals with OABD account for approximately 17% of all older individuals undergoing psychiatric evaluation in the emergency department. Additionally, the prevalence of BD amongst older adults living at residential care psychiatric facilities is approximately 17.4%. It is estimated that approximately 3% of older nursing home residents and 9.7% of chronically institutionalized older individuals have a diagnosis of BD. Evidence indicates that approximately 70% of all individuals with OABD are women.

Comparison between OABD and EOBD

Depressive episodes are the most common presenting symptom amongst individuals with OABD when compared to hypomania or manic episodes.[12–14] Additionally, individuals with OABD tend to present with depressive episodes that are more frequent and severe.[15] Furthermore, longer latency periods are noted between the first and subsequent mood episodes amongst individuals with OABD when compared to individuals with early-onset BD (EOBD).[13] They also have a lower family history of mood disorders when compared to individuals with EOBD.[12,16] It has been noted that individuals with OABD, when compared to age-matched controls, experience more stressful life events.[17]

A greater association with cerebrovascular disease and other neurological disorders is seen amongst individuals with OABD when compared to individuals with EOBD.[8] Manic episodes are often associated with vascular changes in the right cerebral hemisphere amongst these individuals, whereas vascular lesions in the left cerebral hemisphere are associated with depressive symptoms.[18,19]

It has been noted that individuals with OABD tend to have, on average, three to four medical comorbidities.[20–23,] Common comorbidities include metabolic syndrome, respiratory and cardiovascular diseases, and endocrine disorders. These comorbidities appear to worsen outcomes amongst individuals with OABD, including increasing the rates for suicide.[22,23] The rates of comorbidities appear to be similar amongst individuals with OABD and age-matched controls.[23]

Neuroimaging studies indicate that individuals with OABD have greater structural abnormalities in the brain when compared to individuals with EOBD.[19] These include a greater amount of white-matter hyperintensities especially in the frontal, parietal and putaminal areas of the brain.[24–26] Some studies indicate that there is greater cortical sulcal widening and lateral ventricle-brain ratio scores amongst individuals with OABD when compared to individuals with EOBD, although the majority of studies indicate no significant difference in grey matter, white matter and total brain volumes amongst these individuals.[27,28]

Psychiatric comorbidities have been found to be common amongst individuals with OABD when compared to age-matched controls, but these rates are lower than what is noted amongst individuals with EOBD.[29] Common comorbidities include alcohol use disorder (12-month and lifetime prevalence rates, 38.1% and 38.1%, respectively), dysthymia (12-month and lifetime prevalence rates, 7.1% and 15.5%, respectively), generalized anxiety disorder (12-month and lifetime prevalence rates, 9.5% and 20.5%, respectively) and panic disorder (12-month and lifetime prevalence rates, 11.9% and 19.0%, respectively).[29] A higher prevalence of alcohol use/alcohol use disorder is seen in men with OABD, whereas women have a

greater prevalence of panic disorder when compared to age-matched controls. Psychotic symptoms appear to occur at a similar rate amongst individuals with OABD when compared to individuals with EOBD.[11]

Available evidence indicates that older adults are at greater risk for suicide when compared to younger adults.[30] The rates of suicide are higher amongst older men when compared to older women. Known risk factors for suicide amongst older adults include the presence of a psychiatric disorder, having chronic illnesses and disabilities, bereavement and social isolation, and a history of non-fatal self-harm. It has also been noted that suicide attempts amongst older adults are often of greater determination and lethality. A population-based case-control study of individuals aged ≥66 years from Canada found that, amongst the psychiatric disorders that are associated with completed suicide, the odds ratio (OR) for suicide was highest for BP (OR, 9.20) followed by depression (OR, 6.44), psychotic disorders (OR, 5.09) and anxiety disorders (OR, 4.65).[22] In this study, death by firearms was the most frequent method for suicide amongst men and self-poisoning was the most frequent method amongst women. It was noted that the majority of individuals who committed suicide had been evaluated by a physician in the month prior to their death when compared to controls (75% *versus* 49%; $p<0.001$). Additionally, 75% of these individuals were registered for more than three visits with their physician. Furthermore, individuals who committed suicide visited a psychiatrist more often in the preceding week when compared to controls (6% *versus* 0.2%; $p<0.001$).

Available evidence indicates that individuals with OABD, when compared to age-matched controls, have been found to have lower scores on a variety of cognitive screening tools, including the Mini-Mental State Examination (MMSE) ($p=0.0007$) and the Mattis Dementia Rating Scale (DRS) ($p=0.0003$) after adjusting for age and education.[31] However, there was no correlation noted between the MMSE score (Pearson $r=0.07$) or total DRS score ($r=0.20$) and the Young Mania Rating Scale (YMRS) scores. When compared to individuals with EOBD, individuals with OABD have been found to be more impaired on word fluency, mental flexibility and psychomotor performance, but these impairments were not attributable to age, education or cerebrovascular risk factors.[32] When compared to age-matched and education-matched controls, approximately half of euthymic individuals with OABD had a score ≥1 standard deviation (SD) below the mean on the MMSE and the DRS and 1–2 SD below the mean on executive functioning.[33] Amongst individuals with OABD, a greater number of vascular risk factors and hospital admissions are related to worse outcomes of cognitive functioning.[34]

When compared to age-matched individuals with unipolar depression, individuals with OABD have an earlier age at onset of illness, greater overall symptom severity and have been found to be more impaired with reference to living skills in the community.[35] Additionally, they utilize approximately four times the total amount of mental health resources and are four times more likely to be hospitalized psychiatrically over the past 6 months when compared to age-matched individuals with unipolar depression.

A comparison between OABD and EOBD is provided in Table 1.

Diagnosis

A definitive diagnosis of OABD can be made via a thorough history.[8] The development of mood symptoms can also occur due to a comorbid medical illness, a neurological disorder and/or due to the effect of prescribed medications or illicit drugs. A focused physical examination will assist in identifying comorbid medical and/or neurological disorders that may cause instability of mood amongst older adults.[8] Common conditions that cause mood fluctuations include metabolic disorders such as diabetes and/or thyroid disorders. These disorders can be identified via laboratory tests. Common tests include a

Table 1. Differences between late-onset and early-onset bipolar disorder.[8,11–35]

Features	OABD	EOBD
Age of onset	≥50 years	≤50 years
Family history	Less likely	More likely
Presenting symptom	Depression	Mania or hypomania
Manic symptoms	Less likely	More likely
Latency between first and second episodes	Longer	Shorter
Cerebrovascular disease	More likely	Less likely
Medical comorbidities	More likely	Less likely
Psychiatric comorbidities	Less likely	More likely
Cognitive dysfunction	More likely	Less likely
Healthcare service utilization	Greater use	Lesser use

EOBD, early-onset bipolar disorder; OABD, older-age bipolar disorder.

complete blood count, a complete metabolic panel, including blood urea nitrogen and creatinine, thyroid function tests, vitamin B12 level, folic acid level, tests for syphilis including rapid plasma reagin or Venereal Disease Research Laboratory test, test for HIV, and the evaluation of urine, including analysis, culture and drug screen. Amongst individuals with OABD who present with evidence for cerebrovascular disease and/or cognitive dysfunction, neuroimaging studies, including a CT scan or an MRI scan will assist in identifying the aetiologies for the mood symptoms.[8]

There are no specific rating scales developed for use amongst individuals with OABD; however, some of the scales used for EOBD can also be used for OABD.[36] These scales can assist with the quantification and qualification of the symptoms of BD and help assess their progress. The Mood Disorder Questionnaire is a common screening tool used for the identification of BP amongst adults.[37] Although it has good sensitivity and specificity for the detection of a lifetime history of mania or hypomania, its routine use can result in the potential over-diagnosis of BD.[38] Available evidence indicates that, for the detection of manic symptoms amongst individuals with OABD, the YMRS is most commonly used.[36] For the detection of depressive symptoms, the Hamilton Depression Rating Scale (HDRS) and the Montgomery–Åsberg Depression Rating Scale (MADRS) are often used. The most commonly used clinical assessment tool amongst individuals with BD is the Structured Clinical Interview from the DSM-IV.[39] Finally, a diagnosis of BD can be confirmed using the criteria from the DSM-5.[1] A flow diagram for the assessment of bipolar disorder amongst older adults is provided in Figure 1.

Treatment

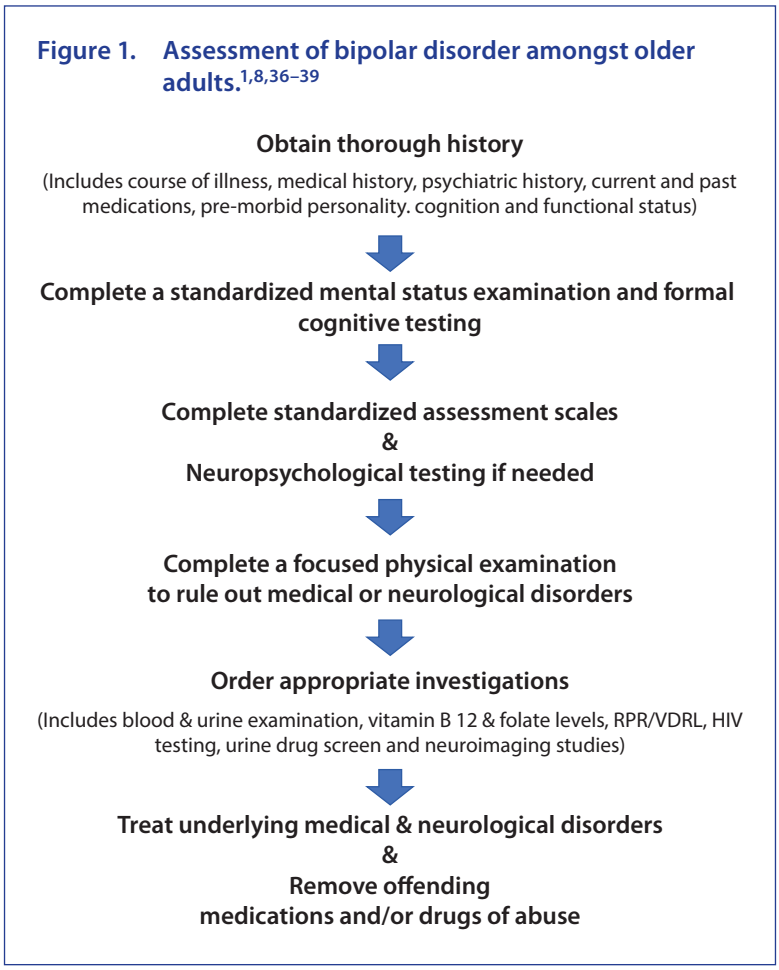
Psychosocial therapy

The available evidence for using specific psychotherapies for OABD is limited and often extrapolated from mixed-age studies or from anecdotal evidence.[3] Medication adherence skills training (the MAST-BD intervention) amongst individuals with OABD has been found to improve their ability to manage medications, compliance with medications, symptoms of depression and certain domains of health-related quality of life with medium effect sizes (Cohen's d, 0.30–0.57).[40] A manual-based medical care model was found to improve patient satisfaction rates, dropout rates and follow-up rates amongst individuals with OABD.[41]

Pharmacotherapy

Current evidence for pharmacotherapy for OABD is based on a limited number of clinical practice guidelines and RCTs.[42] Efficacy has been noted for lithium, anticonvulsant

Figure 1. Assessment of bipolar disorder amongst older adults.[1,8,36–39]



medications, antipsychotic medications, antidepressant medications and benzodiazepines as well as for electroconvulsive therapy (ECT).[42] Dols et al. evaluated data from 34 national and international guidelines and found that, in a majority of these guidelines, there was no specific section dedicated to the treatment of OABD.[43] The general principles of pharmacotherapy for OABD are similar to those of individuals with EOAB albeit with the need for closer monitoring for side effects, comorbid conditions and the coprescription of medications. However, the therapeutic serum levels of lithium amongst individuals with OABD are suggested to be lower than those in individuals with EOBD, although this recommendation is not based on extensive research evidence. Below, we discuss the common pharmacotherapeutic modalities used for the treatment of individuals with OABD.

Lithium

The prototypical drug for the treatment of OABD has been lithium.[42,44,45] Lithium appears best suited for individuals who have euphoric mania and for individuals who have minimal comorbid neurological disorders.[46] Evidence also indicates that lithium decreases suicide risk and the risk for cognitive decline.[47,48] Amongst individuals with OABD, lithium remains the drug of choice for maintenance treatment using monotherapy;[49] the daily dose of lithium should be 25–50% of the recommended daily adult dose.[50] Additionally, the lithium level target amongst individuals with OABD is between 0.4 and 0.7 mEq/L.[42] Prior to starting treatment with lithium, it is recommended that thyroid, cardiac and renal functions be evaluated.[51] Lithium appears to cause more adverse effects amongst individuals with OABD when compared to individuals with EOBD.[42,46] Common adverse events noted with lithium use include cognitive impairment, oedema, gait impairment, hypothyroidism, renal dysfunction, sedation and weight gain.[42,46,52] Lithium should be prescribed with caution amongst individuals who are also coprescribed a thiazide or loop diuretic, angiotensin-converting enzyme inhibitors, or NSAIDs.[42,50–52] Amongst individuals with OABD, the risk for developing lithium toxicity is higher amongst those individuals who have multiple medical comorbid conditions and are coprescribed multiple medications.[42,46,53]

Anticonvulsants

The evidence regarding the use of anticonvulsant mood stabilizers amongst individuals with OABD is limited.[42] It has been noted that, amongst individuals with OABD, the use of valproic acid (VPA) appears to be more prevalent despite a lack of evidence that it has greater efficacy or tolerability when compared to lithium.[42,46,54] The daily dose of VPA required to maintain levels that are therapeutic amongst individuals with OABD is lower than what would be expected for younger adults.[42,54] When prescribing VPA for OABD, care must be taken as it may interact with other drugs commonly prescribed to older adults, including acetylsalicylic acid, warfarin, phenytoin and phenobarbital, thereby causing serious adverse effects.[42] Combining VPA with lithium may be beneficial amongst individuals with OABD in whom the symptoms are partially responsive to lithium monotherapy or amongst those individuals who present with a rapid cycling type of illness.[55,56]

In the first and only RCT evaluating the efficacy and tolerability of medications for OABD, the researchers compared lithium carbonate to divalproex in individuals with BP-I.[57] They included 224 individuals aged ≥60 years who presented with a manic, hypomanic or mixed episode. The participants were randomly assigned under double-blind conditions to receive either lithium or divalproex. The targeted serum concentrations for lithium and VPA were 0.80–0.99 mEq/L and 80–99 µg/mL, respectively, for 9 weeks. Amongst those individuals who had an incomplete response to the drugs after 3 weeks, the use of open adjunctive risperidone was permitted. The investigators found that at 9 weeks, the response rates amongst the lithium and divalproex groups were not significantly different (79% and 73%, respectively). However, the response rates favoured lithium when compared to divalproex in the longitudinal mixed model. In both the lithium and divalproex groups, a similar proportion of individuals achieved the targeted concentrations of the respective drug (57% and 56%, respectively) and the need for adjunctive risperidone was low (17% and 14%, respectively). Furthermore, the rates of attrition were also similar (14% and 18% at week 3 and 51% and 44% at week 9, respectively). Additionally, there was no significant difference in the rates of sedation between the two groups. However, tremors were commonly noted in the lithium group when compared to the divalproex group.

A retrospective review that evaluated individuals aged ≥55 years with BP-I who were treated with lamotrigine, lithium or placebo, the investigators found that lamotrigine delayed the time to intervention for any mood episode and for a depressive episode when compared to placebo.[58] Additionally, when compared to placebo, lithium delayed the time to intervention for any manic/hypomanic/mixed episode. Back pain and headaches were the most common adverse effects in the lamotrigine group. However, no rashes were reported in this group. Dyspraxia, tremors, xerostomia, headaches, infection, amnesia, dizziness, diarrhoea, nausea and fatigue were the most common adverse effects in the lithium group. It has also been noted that the cognitive profile of lamotrigine is more favourable when compared to other anticonvulsant mood stabilizers.[42] This would be beneficial when used amongst individuals with OABD.

Current evidence does not include any RCT of carbamazepine amongst individuals with OABD.[8,9,59] Data from mixed-age population studies indicate that carbamazepine is not as effective as lithium or VPA in the management of acute mania episodes or for maintenance treatment.[60,61] Carbamazepine may be beneficial for individuals presenting with non-classical or atypical features of BD.[8] However, due to its significant drug–drug interactions, this drug may be less well tolerated by individuals with OABD.[42]

The routine use of gabapentin, oxcarbazepine, topiramate or zonisamide cannot be recommended amongst individuals with OABD as there are no controlled studies of these medications amongst this population.[42]

Antipsychotics

Atypical antipsychotic medications that are approved for the treatment of BD by the FDA in the United States include aripiprazole, asenapine, olanzapine, quetiapine, quetiapine extended release, risperidone and ziprasidone.[62] Additionally, olanzapine-fluoxetine combination, quetiapine and lurasidone are approved for the acute treatment of bipolar depression.[63] The olanzapine–fluoxetine combination and quetiapine are approved as monotherapies, and lurasidone is approved for both monotherapy and as an adjunct to either lithium or divalproex.

Amongst individuals with OABD, risperidone was found to be effective in a small case series.[64] An open trial found that clozapine showed efficacy in treating symptoms of mania and psychosis amongst three older institutionalized males with BD.[65] These individuals were either refractory to or were unable to tolerate monotherapy or combination treatments of lithium, VPA, benzodiazepines and other antipsychotics. Symptoms showed sustained improvements at an average of 11 months and no significant reductions in the granulocyte count were noted.

A post hoc analysis of pooled data from two quetiapine monotherapy trials indicated that a dose of quetiapine 400–800 mg daily when compared to placebo resulted in significant improvements in symptoms of mania from baseline to day 21 amongst individuals with BD who were aged ≥55 years.[66] Amongst these individuals, sustained improvements in mania scores were apparent by day 4 of treatment. The most common adverse effects that were noted in the quetiapine group were dry mouth, somnolence, postural hypotension, insomnia, weight gain and dizziness.

Two studies evaluated the use of asenapine amongst older adults with BD.[67,68] In the first study including 11 individuals with acute bipolar mania and a mean age of 67.7 years who were consecutively admitted to a psychogeriatric unit, the use of asenapine 10 mg orally twice daily as monotherapy for 4 weeks resulted in improvements in manic symptoms amongst all participants by the end of week 4.[67] The remission rate amongst this group was 64% (7/11 participants). The asenapine mean dose was 20 mg daily and the adverse effects noted were as follows: mild sedation (n=3), development of a rash (n=1) on day 6 of treatment and the development of peripheral oedema (n=1) on treatment day 14. The rash and peripheral oedema resolved within 3 days of discontinuation of asenapine. In the second study, which included 15 older adults (mean age, 68.6 years) without dementia with a suboptimal previous response to BD treatments, the use of adjunctive asenapine produced significant improvements in symptoms from baseline as noted on the Brief Psychiatric Rating Scale (BPRS; p<0.05), the Clinical Global Impression Scale – Bipolar version (CGI-BP; p<0.01), and the CGI-BP mania (p<0.05) and depression (p<0.01) subscales.[68] The mean dose of asenapine was 11.2 mg daily, and gastrointestinal discomfort (33%) followed by restlessness (13%), tremors (13%), cognitive difficulties (13%) and sluggishness (13%) were the most common adverse effects noted amongst individuals treated with asenapine.

A post hoc analysis evaluated the use of lurasidone when compared to placebo from two RCTs amongst individuals who were aged ≥55 years with a DSM-IV-TR diagnosis of BP-I depression.[69] The first study was a monotherapy study that compared fixed flexible-doses of lurasidone 20–60 mg daily or 80–120 mg daily with placebo.[70] The second study compared flexible doses of lurasidone 20–120 mg daily as adjuncts to either lithium or VPA when compared with placebo.[71] In both studies, 17.4% and 15.5% of the participants were aged ≥55 years. In the first study, the lurasidone group did much better on the mean change in the MADRS total score at week 6 when compared to the placebo group (p=0.003, effect size 0.83). In the second study, the mean change on the MADRS total score at week 6 did not show any superiority for the lurasidone group when compared to the placebo group (p=0.398, effect size 0.26). The discontinuation rates due to adverse events in the lurasidone group when compared to placebo were similar in both studies (6.8% *versus* 6.9%) and (3.8% *versus* 7.1%), respectively. Metabolic laboratory values were minimally affected by the use of lurasidone.

The FDA has a black box warning for increased mortality when antipsychotic medications are used amongst individuals with dementia.[72] It is prudent to exercise caution when prescribing antipsychotic medications to older adults especially those individuals with dementia, as evidence indicates that these drugs increase the risk for cerebrovascular adverse events and deaths amongst this vulnerable group of individuals.[72]

Antidepressants

The use of antidepressants amongst older (≥66 years) individuals with BD was found to decrease the risk of hospitalization for manic/mixed episodes (adjusted rate ratio, 0.5) but not for depressive episodes (adjusted rate ratio, 0.7) when compared to individuals in the control group, who did not receive an antidepressant during the same period in a population-based retrospective cohort study.[73]

Benzodiazepines

Evidence regarding the efficacy and safety of the use of benzodiazepines amongst individuals with OABD is limited.[42] Morishita and Aoki evaluated the use of clonazepam for 4 weeks amongst a mixed-age population of individuals with both unipolar depression (53.6±13.7 years) and bipolar depression (50.4±10.7 years).[74] The investigators found that, amongst the bipolar depression group, only 10.5% (2/19 participants) of the individuals fulfilled the response criteria (80% reduction) on

the HDRS when compared to 84.2% (16/19 participants, $p<0.05$) of the individuals in the unipolar depression group. Clonazepam was well tolerated as there were no side-effects noted amongst the study participants. In a retrospective chart review, Winkler et al. also included older individuals (56.3±16.5 years) with BD who were treated with clonazepam either as monotherapy or as adjunctive therapy to lithium for individuals who did not respond to lithium.[75] The investigators found that individuals with BD did not have any benefit from the use of clonazepam for either their manic or hypomanic episodes nor for their depressive episodes. However, the individuals with unipolar depression had less depressive episodes after treatment with clonazepam ($p=0.026$).[75]

Electroconvulsive therapy

Amongst individuals with BD, ECT remains the definitive treatment when there is a need for rapid and significant clinical improvements.[8] ECT is particularly effective amongst individuals with BD who present with imminent suicide risk, homicide risk, catatonic state, refractory psychotic state, agitated state or a medically unstable condition.[8,42] ECT has been noted to be effective in approximately 80% of the cases with BD.[42,76] Controlled studies of ECT amongst older individuals with BD are still lacking.[42,77] In clinical situations where symptoms are unresponsive to pharmacotherapy or where a quick and significant response to treatment is required, ECT remains the treatment modality of choice amongst individuals with OABD.[42,78] Amongst individuals with depression, available evidence indicates equal efficacy for both right unilateral and bilateral treatments.[42,79] However, bilateral treatments are associated with longer postictal recovery time and greater impairments in memory.

Treatment algorithm

Current evidence does not include any specialized algorithm for the treatment of individuals with OABD.[43] Evidence suggests that the initial trial of medication for individuals with OABD should be of at least 3–4 weeks duration.[42] A judicious combination of medications should be considered if monotherapy does not provide the desired results. For individuals with OABD who have responded adequately to a medication or a combination of medications, these agents should be continued for a period of approximately 6–12 months. For those individuals in whom the symptoms are in remission for a period of at least 12 months, a gradual reduction and discontinuation of adjunctive medications could be attempted.[78] Available evidence indicates that, amongst individuals with OABD, the use of combination medications is very common, with one study indicating that approximately 82% of these individuals have two or more psychotropic medications prescribed.[80] In this study, which included 1443 individuals aged ≥66 years who were discharged from a psychiatric hospital and information on psychotropic medications prescribed within 30 days of discharge was available, the most common medications were atypical antipsychotics (75.3%) followed by benzodiazepines/zopiclone (42.3%) and antidepressants (38.5%). VPA (35.4%) and lithium (23.4%) appeared to be used less commonly amongst these individuals. Surprisingly, only 1.4% of these individuals were treated using lithium monotherapy. Additionally, only 4.4% and 15.7% of individuals were prescribed antidepressant or atypical antipsychotic monotherapy, respectively. About 8.9% of individuals were prescribed two or more atypical antipsychotics. It has been noted that only about 1 in 10 individuals with OABD experience sustained clinical improvements with standard treatment strategies.[81] Poor adherence to pharmacotherapy, comorbid substance use disorders and co-occurring neurological illnesses have been found to reduce the responsiveness to treatment amongst people with OABD.[6] In addition, pre-existing levels of psychosocial functioning, residential status and occupational position affect the functional outcomes amongst these individuals.[5]

An algorithm for the treatment of bipolar disorder amongst older adults is provided in Table 2.

Conclusions

OABD is not an uncommon condition. Available evidence indicates that individuals with OABD have more comorbid

Table 2. Proposed algorithm for the treatment of older-age bipolar disorder.[3,8,9,40–79]

Type of mood episode	Medication/medication class	Additional information
Manic episodes	Lithium	Better for: 1. Manic episode 2. Depressive episode 3. Maintenance treatment Dose: 25–50% of adult dose Recommended level: 0.4–0.7 mEq/L Tolerability: less than amongst younger individuals

(Continued)

Table 2. (*Continued*)

Type of mood episode	Medication/medication class	Additional information
Manic episodes (*Cont*)	Anticonvulsant mood stabilizers	Better for: 1. Mixed episodes 2. Rapid cyclers 3. Individuals with medical and psychiatric comorbidities 4. Maintenance treatment Dose: 25–50% of adult dose Tolerability: less than amongst younger individuals
	Atypical antipsychotics	Better for: 1. Manic episode 2. Maintenance treatment Dose: 25–50% of adult dose Tolerability: 1. Less than amongst younger individuals 2. Metabolic syndrome with prolonged use 3. Higher risk of cerebrovascular events and death amongst individuals with dementia
Depressive episode	Lithium	As above
	Anticonvulsant mood stabilizers	Lamotrigine appears to be better for bipolar depression than mania
	Atypical antipsychotics	Quetiapine extended release and lurasidone are FDA approved for bipolar depression; olanzapine–fluoxetine combination is also FDA approved for bipolar depression
	Antidepressants	Adjunctive treatment with: 1. Lithium 2. Anticonvulsants 3. Antipsychotics Dose: usual adult dosing Tolerability: 1. As well as amongst younger individuals 2. Risk of manic/hypomanic switch less than previously thought
Partial response or refractory cases	Electroconvulsive therapy	Beneficial for individuals with refractory psychotic or catatonic symptoms Efficacy: bilateral = unilateral Tolerability: 1. Less than amongst younger individuals 2. Side-effect are bilateral > unilateral
Adjunctive treatments	Benzodiazepines	Adjunct treatment for manic or hypomanic episodes Dose: 25–50% of adult dose Tolerability: 1. Less than amongst younger individuals 2. High risk of cognitive and functional impairments
	Psychosocial therapies	Adjunctive treatment to medications Tolerability: as well as amongst younger individuals

medical conditions but a lower genetic predisposition when compared to individuals with EOBD. Individuals with OABD also have higher morbidity, higher rates of service utilization and overall poorer outcomes when compared to age-matched controls. When evaluating individuals with OABD, it is prudent to evaluate the effect of underlying medical/neurological disorders, prescribed medication or substances of abuse, as they may precipitate or perpetuate symptoms of OABD.

Although there is a scarcity of controlled pharmacotherapy trials for the treatment of individuals with OABD, available evidence from mixed age population studies indicates the efficacy for commonly used medication classes that are used in the treatment of individuals with EOBD. Individuals with OABD also find psychosocial treatments to be beneficial as adjunctive treatments. Evidence indicates that ECT is often an effective treatment for refractory cases. There is a significant need to

have a better understanding of the phenomenology and neurobiology of OABD. In addition, more research into effective treatments for this serious psychiatric disorder amongst older adults is needed. Effective treatments will mitigate the suffering of individuals with OABD and reduce the morbidity and mortality of this condition.

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