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SEPTEMBER NEWSLETTER

Choosing an Antidepressant Based on Comorbidities in Older Adults

The prevalence of depression is estimated to range from 5-10% in community-dwelling older adults age 65 or older,[1,2] and up to 14% lifetime prevalence as found in the 2018 NESARC-III national survey,[3] with 8-16% experiencing clinically significant depressive symptoms.[4] This is accompanied by impaired physical, mental, and social functioning that warrants antidepressant use and specialized attention and care.[4] Current pharmacological treatments of depression demonstrate efficacy in the older population; however, older adults are at higher risk of adverse events from the use of antidepressants, such as increased risk of falls, fractures, osteoporosis, sexual dysfunction, gastrointestinal bleeding with concurrent NSAID /anticoagulant/ antiplatelet use, hyponatremia, QTc prolongation, and serotonin syndrome with use of multiple serotonergic medications.[5] Despite the risks of antidepressants, their use may still be appropriate based on risk-benefit analysis and close monitoring. When selecting an antidepressant, we should consider specific side effects in the presence of co-existing medical conditions to maximize the management of depression simultaneously with other co-morbidities. This

assessment also reduces polypharmacy by treating multiple conditions with a single medication and by minimizing medication cascades. The following table presents comorbidities and their appropriate antidepressant treatment options. **Tricyclic antidepressants (TCAs) should be avoided in older adults, as they are highly anticholinergic and may cause mental status changes. Monoamine oxidase inhibitors (MAOIs) should also be avoided due to their many drug-drug interactions and dietary restrictions.**

Table 1. Potential Choice of Antidepressants Based on Comorbidities

Comorbidities	Preferred Agents	Agents to Avoid or Use with Caution	Comments
Anxiety	SSRIs: Citalopram, escitalopram, sertraline SNRIs: Venlafaxine, desvenlafaxine, duloxetine Alternatives: Mirtazapine, vortioxetine	TCAs, fluoxetine, bupropion	- Patients may require higher doses of SSRIs and SNRIs for the treatment of GAD - Activating agents, such as fluoxetine and bupropion, can initially worsen anxiety in the first few weeks of treatment - Mirtazapine, vilazodone, and vortioxetine have shown benefit in limited studies
Benign Prostatic Hyperplasia	Non-anticholinergic antidepressants	Anticholinergic antidepressants: TCAs, paroxetine	- TCAs and paroxetine may decrease urinary flow and cause urinary retention due to anticholinergic properties
Bleeding risk	Bupropion, mirtazapine	SSRIs, SNRIs	- SSRIs and SNRIs are associated with elevated risk for upper GI bleeding with concurrent use of NSAIDs, anticoagulants, and antiplatelet agents. However, the absolute risk remains low (0.5%, or 1 in 200[6]) - Platelets require uptake of serotonin for appropriate platelet aggregation. SSRIs and SNRIs also inhibit platelet's ability to reuptake serotonin and can reduce platelet aggregation.[7] - Patients with no signs or symptoms of bleeding can use SSRI/SNRIs. Patients with history of bleeding may use with caution, depending on risk/benefit profile. - Sertraline has the most antiplatelet effects among all SSRIs
Chronic neuropathic pain	SNRIs (particularly duloxetine)	N/A	- Duloxetine is indicated for fibromyalgia, chronic musculoskeletal pain, and neuropathic pain associated with diabetes - There is evidence that treating mood disorders is beneficial in pain reduction, and vice versa. Other antidepressants may be beneficial in this way, but do not have mechanisms specific to pain reduction

Cardiovascular risk	Sertraline	TCAs, MAOIs Arrhythmias: Citalopram, escitalopram Orthostasis: Trazodone, TCAs, MAOIs, SSRIs, SNRIs	- QTc prolongation: maximum recommended dose of citalopram and escitalopram are 20 mg daily and 10mg daily respectively in adults > 60 years old due to concerns of dose-dependent QTc prolongation - Orthostasis: Antidepressants should be initiated at low doses and titrated slowly to the lowest effective dose - SNRIs contribute to hypertension by increasing circulating norepinephrine
Hypertension	SSRIs	SNRIs, bupropion, TCAs, MAOIs	- If SNRI is indicated, duloxetine generally causes less BP increase than venlafaxine
Insomnia	Mirtazapine	Fluoxetine, bupropion, venlafaxine, sertraline	- Lower doses of mirtazapine produce more sedation compared to higher doses - Fluoxetine has the most activating effects among SSRIs and has a very long half-life, causing prolonged effects in older adults - Trazodone is not recommended for treatment of depression, as high doses (200mg-600mg daily) are required for therapeutic response. Patients experience excessive sedation and orthostasis at high doses. Trazodone is typically used to treat insomnia at lower doses (25-100mg nightly). - TCAs often used at low doses for insomnia. These doses are far lower than therapeutic doses for depression and would not be considered to be treating co-morbid conditions.
Obesity	Bupropion	Mirtazapine, paroxetine, TCAs, MAOIs	- SSRIs & SNRIs may lead to weight gain or weight loss. Paroxetine is highly associated with weight gain among SSRIs.
Osteoporosis/ Bone Fractures	Bupropion, mirtazapine	SSRIs, SNRIs, TCAs	- SSRIs are associated with reduced BMD; BMD testing should be considered during SSRI therapy, especially if patients have other risk factors for fracture - Fluoxetine is most known SSRI that accelerates bone loss
Sexual dysfunction	Bupropion, mirtazapine, vortioxetine, vilazodone	SSRIs, SNRIs, TCAs, MAOIs	- Most concerning SSRIs: citalopram, escitalopram, fluoxetine, paroxetine, sertraline - Most concerning SNRIs: venlafaxine, desvenlafaxine, duloxetine - Vortioxetine carries risk of accumulation due to long half-life (66 hours)
Seizure	SSRIs or SNRIs	Bupropion, amoxapine, clomipramine, maprotiline	- Bupropion lowers seizure threshold, and it should be used with caution in patients with eating disorder due to electrolyte imbalance and abrupt discontinuation of alcohol, benzodiazepines, and antiseizure agents.
Weight loss/Anorexia	Mirtazapine	Bupropion	- Studies suggests the incidence rate of weight gain in patients taking mirtazapine ranges from 8-77% - Bupropion may lead to weight loss (14-28%)

Abbreviations: SSRIs, selective serotonin reuptake inhibitors; SNRIs, serotonin norepinephrine reuptake inhibitors; TCAs, tricyclic antidepressants; MAOIs, monoamine oxidase inhibitors.

Patient Case: RD is a 79 YO F with newly diagnosed MDD, and a PMH significant for Type 2 diabetes (T2DM), neuropathy, hyperlipidemia (HLD), hypertension (HTN), obesity (BMI 31), and insomnia. Patient endorses insomnia due to neuropathic pain. She reported that she recently felt her daily activities lacked purpose which exacerbated her loss of self-motivation. She was referred by her PCP to a psychiatrist for treatment of major depressive disorder. A recommendation is needed for initiating an antidepressant for her

recent diagnosis. Her most recent vitals were HR 74 and BP 136/84. Her most recent labs were Na 142, K 4.6, CrCl 0.9, HbA1C 7.8%, LDL 96, HDL 52, TG 188. Hematology and LFTs are WNL.

Assessment: RD has several comorbidities to consider: chronic neuropathic pain, hypertension, cardiovascular (CVD) risk from hyperlipidemia, and insomnia. SNRIs like duloxetine can be considered to concurrently treat her depression and neuropathic pain. It is prescribed with caution in geriatric patients with hypertension due to the drug's hypertensive side effect, but low incidence (2%) is reported in comparison to other SNRIs. Duloxetine can be safely used by patients with high CVD risk, but sertraline is preferred. In this case, patient's labs and CVD risk do not warrant having to choose sertraline over duloxetine. Additionally, despite the patient having insomnia, mirtazapine should be avoided as this patient is obese and mirtazapine may cause further weight gain.

Plan: We recommend that the patient be started on duloxetine 20 mg once daily, with follow-up in 4-6 weeks before titrating the dose.

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