

SSRIs:

An Update for Home Care Clinicians

One out of seven community-dwelling older adults is prescribed an antidepressant drug (Gebara et al., 2015). Nationally, antidepressant use increased by almost 65% in recent decades (Pratt et al., 2017), and approximately 5% of the 17 million adults receiving antidepressant treatment are over age 50 (National Institute of Mental Health, 2019). As people age, they experience changes in pharmacokinetics (how the body absorbs, distributes, metabolizes, and eliminates drugs), and pharmacodynamics (the drug's effect on the body), creating higher risk for adverse drug effects. Thus, a cautious approach to prescribing antidepressant medications is warranted (Herron & Mitchell, 2018). Of the antidepressant drug classes, selective serotonin reuptake inhibitors (SSRIs) are the most well tolerated, cause the least number of side effects, and have been called the safest and first choice among antidepressants (Herron & Mitchell; Khanassov et al., 2018). They are commonly prescribed to help combat depression and some forms of anxiety in older adults (Garfield et al., 2014). Home care clinicians play a critical role in medication management and reconciliation, assessing patient knowledge of, adherence to, and responses to medications. Given the high frequency of antidepressant use among older adults, a full understanding of SSRIs, including benefits and risks, is important for home care clinicians.

Mechanism of Action and Indications

Depression has been linked in part to depleted concentrations of the neurotransmitters serotonin, norepinephrine, and dopamine (Hillhouse & Porter, 2015). Drugs such as the SSRIs that affect serotonin in the body are considered serotonergic. Serotonin is present in the brain, platelets, and gastrointestinal tract, but the exact mechanism by which serotonergic drugs work is not yet fully understood

(Salehi et al., 2019). We do know that SSRIs act by targeting and inhibiting serotonin transporter, which inhibits serotonin reuptake, thereby increasing the availability of serotonin to receptors in synapses (Garfield et al., 2014; Salehi et al.).

Side Effects and Adverse Events

Central and peripheral serotonin receptors are affected when SSRIs inhibit serotonin transporter, potentially resulting in both central and peripheral nervous system side effects. Although SSRIs are associated with fewer side effects than other antidepressants, nearly 40% of those taking SSRIs report experiencing at least one side effect. Older adults tend to suffer disproportionate numbers of adverse events and/or side effects than their younger counterparts (Garfield et al., 2014). Side effects from SSRIs can occur at any age, and vary from commonly established milder complaints like nausea, dry mouth, changes in bowels, and sexual dysfunction, to less frequent reactions that can be life threatening (Table 1). Older adults most commonly report weight gain, impaired concentration, attention issues, and falls while taking SSRIs. In addition, clinicians also should address covert symptoms such as syndrome of inappropriate antidiuretic hormone secretion, hyponatremia, serotonin syndrome, abnormal bleeding, and prolonged QT intervals (Garfield et al.). Given the vulnerable population of older adults with comorbidities and falls, the latter more covert side effects can be dangerous or even deadly, and are described below.

Fall Risk and Fractures

SSRIs can exhibit anticholinergic side effects including orthostatic hypotension and sedation (Herron & Mitchell, 2018). Both of these side effects can contribute to falls among older adults. Some researchers have reported on fall risk and

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resultant fractures related to older SSRI users, but study results vary greatly (Khanassov et al., 2018). However, data suggest that SSRIs have a significant impact on bone metabolism, and have been associated with decreased bone mineral density (Williams et al., 2018) that may contribute to fractures. In a meta-analysis, Khanassov et al. (2018) found a 1.67-fold increase in fracture risk among older adults using SSRIs compared with nonusers. These authors noted that fracture risk within 5 years of initiating SSRIs was 13.4% higher than nonusers, or 1 fracture in every 19 users. They also concluded that the increased fracture risk could be related to several SSRI side effects including orthostatic hypotension, dizziness, falls, and tachyphylaxis (drug tolerance). A limitation noted in the meta-analysis includes possible underestimation of fracture risk, based on how studies varied in their descriptions of control groups. Some studies combined those who were antidepressant-free with those who were on different types of antidepressants as long as they were not taking SSRIs (Khanassov et al.).

The American Geriatrics Society Beers Criteria® for Potentially Inappropriate Medications has been used by providers for decades (AGS, 2019).

In the 2019 updated version, SSRIs were added to the list of drugs to be used with caution among older adults. The rationale for inclusion in the list is the potential for SSRIs to exacerbate falls and fractures, especially when the patient is taking other central nervous system (CNS)-active drugs, and also due to the possibility of hyponatremia. Such CNS-active drugs include anesthetics, anti-convulsants, antiemetics, anti-Parkinson agents, CNS stimulants, muscle relaxants, narcotic and

nonnarcotic analgesics, and sedatives (Drugs.com, 2020), all of which can contribute to fall risk, especially when combined with SSRIs.

Syndrome of Inappropriate Antidiuretic Hormone and Hyponatremia

Syndrome of inappropriate antidiuretic hormone occurs when there is an excessive release of antidiuretic hormone that results in water retention and sodium depletion (U.S. Department of Health



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Table 1. Selective Serotonin Reuptake Inhibitors

Generic Name (Brand Name) Dosing Ranges ^a Reference	Indications and Usage	Common Adverse Reactions Reported in Clinical Trials	Additional Precautions That Require Monitoring
Citalopram (Celexa) 20–40 mg/day over age 60: 20 mg (Mylan, 2019)	Depression	Most common: nausea, dry mouth, somnolence, insomnia, sweating, tremors, diarrhea, ejaculation disorder, dyspepsia, fatigue, rhinitis Less reported: vomiting, anxiety, anorexia, abdominal pain, agitation, dysmenorrhea, impotence, sinusitis, fever, arthralgia, myalgia, decreased libido, yawning	Risk for: suicide, abnormal bleeding, hyponatremia, mania/hypomania, impaired cognition and motor function, QT prolongation
Escitalopram (Lexapro) 10–20 mg/day older adults: 10 mg (Lundbeck, 2018)	Major depression Social anxiety disorder (SAD) Generalized anxiety disorder Obsessive-compulsive disorder (OCD)	Most common: insomnia, diarrhea, dry mouth, somnolence, sweating, dizziness, constipation, fatigue, indigestion Less reported: QT prolongation	Risk for: suicide, abnormal bleeding, hyponatremia, seizures, diabetes, mania Other possible side effects: anxiety, agitation, panic attacks, irritability, hostility, akathisia (unpleasant restlessness), small decrease in heart rate
Fluoxetine (Prozac) 20–80 mg/day (Eli Lilly & Co., 2017)	Major depressive disorder (MDD) OCD Bulimia nervosa Panic disorder (PD)	Most common: nausea, headache, insomnia, nervousness, anxiety, somnolence, diarrhea, asthenia, anorexia, dry mouth, dizziness, tremors, sweating, flu syndrome, constipation Less reported: decreased libido, rash, flatulence, vomiting, yawn, pruritus, fever, vasodilation, weight loss, abnormal thinking, abnormal vision	Risk for: suicidal thoughts, serotonin syndrome, prolonged QT interval, allergic reactions, mania/hypomania, seizures, altered appetite and abnormal bleeding, angle-closure glaucoma, hyponatremia
Paroxetine Mesylate (Pexeva) 10–60 mg/day older adult: 10 mg start (Sebel Pharmaceuticals, 2017)	MDD OCD PD Generalized anxiety disorder	Most common: insomnia, somnolence, nausea, asthenia, abnormal ejaculation, dry mouth, nervousness, constipation, diarrhea, sweating, decreased libido, decreased appetite Less reported: chest pain, chills, palpitations, increased appetite, impaired concentration, abnormal dreams and others	Risk for: clinical worsening of depression, suicide, serotonin syndrome, angle-closure glaucoma, mania/hypomania, seizures, prolongation of QT interval (especially if on thioridazine), akathisia, hyponatremia, abnormal bleeding, bone fractures
Sertraline Hydrochloride (Zoloft) 25–200 mg/day (Pfizer, 2019)	MDD OCD PD Post-traumatic stress disorder SAD Premenstrual dysphoric disorder	Most common: nausea, diarrhea/loose stool, insomnia, dry mouth, dizziness, fatigue, somnolence, tremors, dyspepsia, hyperhidrosis, agitation, decreased appetite, decreases libido Less reported: palpitations, visual impairment, vomiting, erectile/ejaculation dysfunction	Risk for: suicide, serotonin syndrome, bleeding, hyponatremia, seizures, diabetes, mania/hypomania, angle-closure glaucoma, hyponatremia, QT prolongation

^aDosing ranges depend on the diagnosis, whether it is a starting or maintenance doses, age, and patient characteristics.

and Human Services, n.d.). The potential for hyponatremia is higher among older females, those with volume depletion, and when the hyponatremia is recurring rather than new (Eli Lilly & Co., 2017; Herron & Mitchell, 2018; Sebela Pharmaceuticals, 2017). When SSRIs are used concurrently with diuretics, especially among older adults, hyponatremia can occur resulting in patients who are asymptomatic in mild cases, to those with complaints of lethargy, muscle cramping, anorexia, and headaches in more severe cases (Herron & Mitchell). Therefore, the Beers List Criteria® suggests that sodium levels should be monitored when initiating SSRI use, and when altering doses (AGS, 2019).

Serotonin Syndrome

Serotonergic medications include amphetamines, antiemetics, certain opioids, over-the-counter cold medications, and antidepressants such as monoamine oxidase inhibitors, serotonin and norepinephrine reuptake inhibitors, and SSRIs (Volpi-Abadie et al., 2013). Use of serotonergic medications, such as the SSRIs, has been linked to a phenomenon called serotonin syndrome. Serotonin syndrome results from high levels of serotonin at both central and peripheral serotonin receptors and is more prevalent when SSRIs are used concurrently with other serotonergic agents (Volpi-Abadie et al.). The incidence of serotonin syndrome is unknown as it is likely underreported because symptoms range from mild to life threatening. Symptoms can include mental status changes (confusion, agitation, hypomania, delirium, hallucinations, coma); neuromuscular hyperactivity (rigidity, hyperreflexia, incoordination, myoclonus, tremor, seizures); autonomic dysfunction (tachycardia, dizziness, diaphoresis, diarrhea, flushing, fever/hyperthermia, shivering, and rapidly fluctuating vital signs with labile blood pressure); and/or gastrointestinal symptoms (nausea, vomiting, diarrhea; Eli Lilly & Co., 2017; Lundbeck, 2018; Volpi-Abadie et al.). Treatment for serotonin syndrome is supportive and includes discontinuing serotonergic drugs, stabilizing vital signs, and administering oxygen, intravenous fluids, benzodiazepines as needed for sedation, and if necessary, serotonin antagonists (Volpi-Abadie et al.).

Bleeding

There is an increased risk for upper gastrointestinal tract, vaginal, and nose bleeding (epistaxis) among



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SSRI users. Bleeding may present as purpura, ecchymoses, and/or hematomas (Lundbeck, 2018; Pfizer, 2019; Sebela Pharmaceuticals, 2017). Platelets must release serotonin in order for hemostasis to occur (Lundbeck). The SSRIs can inhibit serotonin reuptake by platelet transporters resulting in serotonin depletion, altered platelet function, and increased risk for hemorrhage (Herron & Mitchell, 2018). When patients simultaneously use SSRIs with nonsteroidal anti-inflammatory drugs, aspirin, or warfarin, the possibility for bleeding is potentiated (Lundbeck; Pfizer). Therefore, it is imperative to educate patients about these potential risks as well as signs and symptoms to report. Manufacturers also recommend pharmacologic “gastroprotection” to avoid gastrointestinal bleeding (Lundbeck; Pfizer; Sebela Pharmaceuticals).

Ventricular Arrhythmias

Electrocardiograms (ECGs) are used in part to measure ventricular repolarization and depolarization, and results are reported as the “QT interval.” Certain factors including older age, female sex, and use of certain drugs such as antiarrhythmics, antipsychotics, as well as some antibiotics and classes of antidepressants (such as SSRIs), can abnormally increase the QT interval and cause ventricular arrhythmias (Rochester et al., 2018). Two SSRIs (citalopram and escitalopram)

have been more commonly associated with QT interval prolongation, resulting in potentially serious ventricular arrhythmias. If citalopram is used for those 60 years or older, the Food and Drug Administration recommends a maximum daily dose of 20 mg (Rochester et al.). Conversely, sertraline is considered the safest SSRI alternative for people with cardiac risk factors, due to its lesser effect on the QT interval (Herron & Mitchell, 2018). Older adults using SSRIs require ECG monitoring when the medication is initiated, and then periodically thereafter, to assess for QT interval changes (Rochester et al.).

Drug Interactions and Contraindications

Assessing for drug interactions is an integral part of safe medication management. Older adults experience high rates of polypharmacy, making their risk of drug interactions higher. Home care providers require a full understanding of the potential for interactions, and must carefully assess medication lists and contraindications to advocate for patient safety. For example, monoamine oxidase inhibitors, also serotonergic in nature, are contraindicated when taking SSRIs due to the increased risk for serotonin syndrome (Eli Lilly & Co., 2017). It is important to educate patients about potential

side effects when the drug regimen changes from one serotonergic medication to another. When SSRIs are discontinued in lieu of a different regimen, drug plasma levels will take several weeks to decrease for older adults, so new drugs could cause an interaction despite the SSRIs having been discontinued (Eli Lilly & Co.). Another contraindication exists between SSRIs and the antipsychotic generic drug thioridazine. When used together, they potentiate the possibility for QT interval prolongation (Eli Lilly & Co.; Sebelo Pharmaceuticals, 2017).

Implications for Home Care Clinicians

The efficacy of antidepressant medication use and the safety of SSRIs are both well documented, including for use among older adults. However, it is important to weigh risk versus benefit for each individual when considering use of SSRIs (Taylor, 2015). In many ways, older people differ in their response to drug therapy. Unlike younger people, older adults may take longer than the typical 4 weeks to exhibit a noticeable response to their antidepressant treatment (Herron & Mitchell, 2018). Home care clinicians can be instrumental in educating patients about the need to adhere to the regimen, and to give the medications ample time to take effect, while depressive or other symptoms may persist. Conversely, it can take weeks for the drug to leave their system fully, making side effects last for up to weeks after medications have been discontinued due to the prolonged half-life that can occur with older adults (Eli Lilly & Co., 2017). It is also important to educate patients about the dangers of abruptly stopping an SSRI, and that they should be in contact with their prescriber should they plan to discontinue use of the drug.

It is well known that depressive episodes can recur, and that they can last for many years, sometimes requiring medication use for long periods (Khanassov et al., 2018). When conducting medication management, it is imperative that a review of potential side effects is completed, regardless of how long the drug has been in the patient's regimen. In the course of this assessment, it is worthy to note that ultimately proving causality between an SSRI and an adverse event can be very complicated because so many other factors may contribute (Taylor, 2015). For example, similar to the documented effects sometimes caused by SSRIs, depression itself can contribute to falls,

Sidebar 1. Case Study

Mr. H is an 88-year-old widow who lives with his daughter. His vital signs are within normal limits. He has a history of macular degeneration, hearing loss, hypertension, and mild obsessive-compulsive disorder for which he has not required treatment. His only medication is diltiazem extended release, 120 mg daily. He is alert and mildly forgetful. Over the past month, his daughter reported that he began having episodes of anxiety at night. According to his daughter, Mr. H gets out of bed and paces; he stands near his daughter's room and states that he is nervous and he will not get back into bed. He cannot report any known cause for his anxiety. In response, his physician ordered escitalopram 10 mg daily. Slowly, Mr. H's anxiety began to subside and by approximately 3 weeks into the regimen he was much calmer and was no longer pacing at night. However, shortly thereafter, he told his daughter that people were sitting in his room at night, that they were dressed formally as if going to a wedding, and that they were talking to him. Mr. H could describe the people in detail, and vehemently refuted that he could have been dreaming. As a result, the physician tapered Mr. H off of escitalopram and after several weeks initiated fluoxetine 20 mg. Sodium levels remained normal throughout. The hallucinations eventually stopped and his behavior became more appropriate with less anxiety noted. It is unknown whether the hallucinations were in some way related to the medication use, but it was important to decrease the dosage slowly to avoid harmful effects of abrupt discontinuation.

Table 2. Assistance for Medication Acquisition

Option	Service Provided	Additional Information
Patient Assistance Programs	Provide medications for free or at discounted price for those who can't afford them	Developed and run by pharmaceutical companies
National pharmacy chains	Offer reduced pricing or free medications to those who can't afford them	Examples include grocery stores and some big box stores
Medicare part D and Medicare Advantage Program	Provide drug plans for a fee; helpful in reducing drug costs	Recipients must meet eligibility requirements
Dispensary of Hope	Assist low-income individuals with comorbidities acquire medications	National Program

altered cognition, and other findings that could be mistaken for SSRI effects (Taylor). Additionally, age-related changes, comorbidities, polypharmacy, and functional and cognitive impairments can also lead to a variety of poor outcomes that may resemble drug side effects or adverse events. Therefore, comprehensive assessments, thorough history taking, and accurate medication reconciliation skills are crucial.

Physical assessment and history taking are instrumental in determining the possible presence of side effects. Although many of the SSRI effects may be considered mild, they can alter quality of life and outcomes for older people. Nausea, dry mouth, and bowel changes can affect nutrition, weight, and overall health and should not be taken lightly. Insomnia, nervousness, sweating, tremors, and other similar symptoms alter sleep, social functioning, sense of well-being and as such, can decrease life quality and health. Although the more life-threatening side effects warrant immediate attention and intervention, they are seen less frequently and so must still be on the forefront of assessment so as not be inadvertently missed.

Fall risk assessment is important when working with older adults in any setting. Given the many factors contributing to falls, home care clinicians must be expert at determining both modifiable and nonmodifiable fall risk factors. Knowing that SSRIs are on the Beers® list can help in developing appropriate plans of care. Educate patients to rise slowly, sit at the side of the bed before ambulating, and hydrate to avoid hypotension-related falls. Recommend and educate about assistive devices, grab bars, and durable medical equipment to also decrease fall risk.

Certain barriers can affect access to medications. Although prohibitive cost can be a barrier to medication adherence, several options are available to assist patients, and home care clini-

cians can be instrumental in relaying this information (Table 2). Transportation issues can also contribute to access barriers. Mail order prescriptions may help, and some pharmacies will deliver, creating viable options for people with functional limitations, or for those who cannot drive to pickup prescriptions.

Conclusions

Large numbers of community-dwelling older adults suffer from depression and/or anxiety, and are being treated in part with SSRI medications. These drugs are effective, safe, and have been known as the drug of choice for depression. However, they do pose a risk for mild-to-severe side effects and/or resulting adverse events, especially when combined with polypharmacy and comorbidities often present among older people. Home care clinicians are in a position to assess for, and educate about appropriate drug use, possible side effects, and important information to report to providers. ■

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