Geriatric depression: The use of antidepressants in the elderly

Depression is a common but undertreated condition in the elderly.

ABSTRACT: Depression in the elderly significantly affects patients, families, and communities. Awareness of predisposing and precipitating factors can help identify patients in need of screening with tools such as the Geriatric Depression Scale. After diagnosis, regular follow-up and active medication management are crucial to maximize treatment and remission. Selection of an antidepressant medication should be based on the best side effect profile and the lowest risk of drug-drug interaction. If remission is not achieved, then add-on treatments, including other drugs and psychotherapy, may be considered. In cases of severe, psychotic, or refractory depression in the elderly, electroconvulsive therapy is recommended.

epression is the most common mental health problem in the elderly1 and is associated with a significant burden of illness that affects patients, their families, and communities and takes an economic toll as well. Prevalence studies suggest that 14% to 20% of the elderly living in the community experience depressive symptoms,2 with higher rates among the elderly in hospital $(12\% \text{ to } 45\%)^3$ and even higher rates in long-term care facilities (an estimated 40%).4 Because of our aging population, it is expected that the number of seniors suffering from depression will increase. Symptoms include low mood; reduced interest, energy, and concentration; poor sleep and poor appetite; and preoccupation with health problems. Depression in the elderly is associated with functional decline that can require increased care or placement in a facility, family stress, a higher likelihood of comorbid physical illnesses, reduced recovery from illness (e.g., stroke), and premature death due to suicide and other causes.5 Suicide rates are high in the elderly, with an average of 1.3 suicides committed daily by Canadian seniors. According to a Statistics Canada report in 2005, the suicide rate for elderly men is almost twice that of the nation as a whole.⁶ Effectively lethal self-harm behaviors increase with age, with the most common means of suicide in older men being firearms and hanging, and in older women being self-poisoning and hanging.⁶

Fortunately, depression in the elderly can be treated successfully. However, it is necessary first to identify and diagnose depression, which can be challenging in this population owing to communication difficulties caused by hearing or cognitive impairment, other comorbidities with physical symptoms similar to those of depression, and the stigma associated with mental illness that can limit the self-reporting of depressive symptoms. There is also often a tendency for people to see their symptoms as part of the normal aging process, which they are not. Depression in the elderly still goes undertreated and untreated, owing in part to some of these issues.

Dr Wiese is a clinical instructor in the Department of Psychiatry at the University of British Columbia. She is also a psychiatrist with the UBC Hospital Mood Disorders Centre, and the Geriatric Psychiatry Outreach Team at Vancouver General Hospital.

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Assessment

An awareness of risk factors for depression in the elderly can guide screening. Predisposing risk factors for depression include:

- Female sex.
- · Widowed or divorced status.
- Previous depression.
- Brain changes due to vascular prob-
- Major physical and chronic disabling illnesses.
- Polypharmacy.
- · Excessive alcohol use.
- · Social disadvantage and low social support.
- · Caregiving responsibilities for person with a major disease (e.g., de-
- Personality type (e.g., relationship or dependence problems).

Precipitating risk factors for depression should also be considered. These include:

- Recent bereavement.
- Move from home to another place (e.g., nursing home).
- Adverse life events (e.g., loss, separation, financial crisis).
- · Chronic stress caused by declining health, family, or marital problems.
- · Social isolation.
- Persistent sleep difficulties.

Screening for depression should be undertaken for any recently bereaved individual with unusual symptoms (e.g., active suicidal ideation, guilt not related to the deceased, psychomotor retardation, mood congruent delusions, marked functional impairment more than 2 months after loss, or a reaction seemingly out of proportion to the loss). Screening should also be considered in cases involving bereavement effects continuing 3 to 6 months after the loss, social isolation, persistent complaints of memory difficulties, chronic disabling illness, recent major physical illness (e.g., within 3 months), persistent

sleep difficulties, significant somatic concerns or recent onset of anxiety, refusal to eat or neglect of personal care, recurrent or prolonged hospitalization, diagnosis of dementia, Parkinson disease, or stroke, and recent placement in a nursing home or other long-term care facility.1

The Geriatric Depression Scale (GDS) is a well-validated screening tool for depression in the elderly that comes in two common formats: the 30-item (long form) and 15-item (shortform) self-rating scale. The long-form uses an 11-point cutoff and the shortform uses a 7-point cutoff.^{7,8} The GDS is available free online in a variety of languages. Evidence suggests that while the GDS is a reliable screening tool for depression in the elderly with minimal cognitive impairment, its reliability decreases with increasing cognitive impairment.9 If there is dementia or significant cognitive impairment, then the Cornell Scale for Depression in Dementia (CSDD) is the gold standard.10 The CCSD relies on an interview with a family member or caregiver as well as with the patient, and is validated for use with nondemented and demented depressed elderly. No set Mini-Mental State Exam (MMSE) scores exist for when to use the CSDD.

When diagnosing depression in the elderly the criteria for a major depressive disorder set out in the DSM-IV-TR must be met.11 However, in the elderly minor depressive episodes are common (2 weeks or longer with fewer than five symptoms of depression) and are often associated with the same negative effects as major depression.¹² Diagnostic challenges in the elderly often include the absence of depressed mood, significant cognitive impairment, and high degrees of somatic or physical problems. Once criteria for depression are met, it is important to assess the severity of the depression, determine

whether there are any psychotic or catatonic symptoms, and complete a suicide risk assessment.13 A full assessment1 for depression in the elderly includes the following:

- · Review of diagnostic criteria according to DSM-IV-TR.
- Estimation of severity, including presence of psychotic or catatonic symptoms.
- · Suicide risk assessment.
- · Review of psychiatric comorbid ill-
- · Review of medical illnesses.
- · Personal and family history of mood disorder, as well as other psychiatric illnesses.
- · Review of current medications and allergies.
- Review of substance use.
- · Review of current stresses and life situation.
- Level of functioning/disability.
- Review of support system, family situation, and personal strengths.
- · Mental status examination, including an assessment of cognitive functioning.
- · Physical examination and laboratory investigations in order to identify any medical problems that could contribute to or mimic depressive symptoms (e.g., hypothyroidism and anemia, leading to TSH, B₁₂, and Hb testing being part of the workup).
- Review of collateral information when available.

Treatment

The current Canadian practice guidelines for the treatment of depression in the elderly were developed by the Canadian Coalition for Seniors' Mental Health (CCSMH) in 2006.1 They were created by experts in the field, are evidence-based, and include both pharmacological and nonpharmacological strategies.

Note that most depression studies have been conducted on younger pop-

Table. Commonly	y used antide	pressant medi	cations fo	r older adults.

Generic name	Trade name	Starting dose (mg/day)	Average dose (mg)	Maximum recommended dose (CPS) (mg)	Comments		
SSRIs							
Citalopram	Celexa	10	20–40	40			
Escitalopram	Cipralex	5	10–20	20			
Sertraline	Zoloft	25	50–150	200			
Other agents	•						
Buproprion	Wellbutrin	100	100 b.i.d.	150 b.i.d.	May cause seizures		
Mirtazapine	Remeron	15	30–45	45			
Moclobemide	Manerix	150	150–300 b.i.d.	300 mg b.i.d.	Do not combine with MAOB inhibitors or tricyclics		
Venlafaxine	Effexor	37.5	75–225	375*	May increase blood pressure		
Tricyclic antide	pressants			•			
Desipramine	Norpramin	10–25	50–150	300	Anticholinergic; may cause cardiovascular side effects; monitor blood levels		
Nortriptyline	Aventyl	10–25	40–100	200	Anticholinergic; may cause cardiovascular side effects; monitor blood levels		

^{*}For severe depression.

Adapted from guidelines of the Canadian Coalition for Seniors' Mental Health.1

ulations, and when mixed-aged groups have been studied older adults have been underrepresented. This limits the ability to generalize from these study findings when treating the elderly. Nonetheless, in recent years there is an increasing body of literature specific to the elderly (as referenced below), which helps guide the clinician in the appropriate prescription and use of antidepressants in this patient population.

When using antidepressant medication to treat the elderly, it is important to be aware that older adults have response rates similar to those of younger adults.14 Also, antidepressants have similar efficacy when used to treat elderly patients with and without multiple medical comorbidities.15 If older adults are unresponsive to low doses of antidepressants, higher doses may be required to achieve a therapeutic effect. Unfortunately, the failure to use effective doses in elderly patients is often the reason for a lack

of clinical response and referrals made to specialists for depression incorrectly diagnosed as "treatment resistant." 16

Principles of treatment

When selecting an antidepressant it is important to consider the elderly patient's previous response to treatment, the type of depression, the patient's other medical problems, the patient's other medications, and the potential risk of overdose. Psychotic depression will likely not respond to antidepressant monotherapy, while bipolar depression will require a mood stabilizer. Antidepressants are effective in treating depression in the face of medical illnesses, although caution is required so that antidepressant therapy does not worsen the medical condition or cause adverse events.17 For example, dementia, cardiovascular problems, diabetes, and Parkinson disease, which are common in the elderly, can worsen with highly anticholinergic drugs.¹⁸ Such drugs can cause postural hypotension

and cardiac conduction abnormalities. It is also important to minimize drugdrug interactions, especially given the number of medications elderly patients are often taking. Tricyclic antidepressants are lethal in overdose and are avoided for this reason.

Choice of antidepressant

Fortunately there are several antidepressants that have been shown to be efficacious in elderly patients being treated for a major depressive episode without psychotic features. In choosing an antidepressant it is recommended that selection be based on the best side effect profile and lowest risk of drug-drug interactions. For a list of commonly used antidepressants and associated doses for older adults, see the accompanying Table .

The selective serotonin reuptake inhibitors (SSRIs) and the newer antidepressants buproprion, mirtazapine, moclobemide, and venlafaxine (a selective norepinephrine reuptake inhibitor

or SNRI) are all relatively safe in the elderly. They have lower anticholinergic effects than older antidepressants and are thus well tolerated by patients with cardiovascular disease. Common side effects of SSRIs include nausea, dry mouth, insomnia, somnolence,

Of the SSRIs, fluoxetine is generally not recommended for use in the elderly because of its long half-life and prolonged side effects. Paroxetine is also typically not recommended for use in the elderly as it has the greatest anticholinergic effect of all the SSRIs,

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agitation, diarrhea, excessive sweating, and, less commonly, sexual dysfunction.17 Owing to renal functioning associated with aging, there is also an increased risk of elderly patients developing hyponatremia secondary to a syndrome of inappropriate antidiuretic hormone secretion. This is seen in approximately 10% of patients taking antidepressants, and is associated particularly with SSRIs and venlafaxine.19 It is important to check sodium levels 1 month after starting treatment on SSRIs, especially in patients taking other medications with a propensity to cause hyponatremia, such as diuretics. Of course it is also important to check sodium levels if symptoms of hyponatremia arise, such as fatigue, malaise, and delirium. There is also an increased risk of gastrointestinal bleeding associated with SSRIs, particularly in higher-risk individuals, such as those with peptic ulcer disease or those taking antiinflammatory medications.

similar to that of the tricyclics desipramine and nortriptyline.1 SSRIs considered to have the best safety profile in the elderly are citalogram, escitalopram, and sertraline. 16 These have the lowest potential for drug-drug interactions based on their cytochrome P-450 interactions. Venlafaxine, mirtazapine, and bupropion are also considered to have a good safety profile in terms of drug-drug interactions.16 SSRIs such as fluoxetine, paroxetine, and fluvoxamine have higher risks of drug-drug interactions.

Tricyclic antidepressants are no longer considered first-line agents for older adults given their potential for side effects, including postural hypotension, which can contribute to falls and fractures, cardiac conduction abnormalities, and anticholinergic effects. These last can include delirium, urinary retention, dry mouth, and constipation. Many medical conditions seen in the elderly, such as dementia, Parkinson disease, and cardiovascular

problems can be worsened by a tricyclic antidepressant. If a tricyclic is chosen as a second-line medication, then nortriptyline and desipramine are the best choices given that they are less anticholinergic.16 Also, it is recommended that an ECG and postural blood pressure reading be obtained before starting a patient on a tricyclic antidepressant and after increasing the dose.1 Tricyclic antidepressant blood levels should be monitored since tricyclics are associated with more toxicity and since blood levels can be high despite low doses because some patients can be slow metabolizers.

Given the side effect profile and high rates of drug-drug interactions, monoamine oxidase inhibitors (MAOIs) are not considered first- or even second-line agents for depression in the elderly.

Dosing

Once an antidepressant is selected for an older patient, the starting dose should be half that prescribed for a younger adult¹ in order to minimize side effects. Increased side effects from antidepressant use in the elderly are thought to be due to changes in hepatic metabolism with aging, concurrent medical conditions, and drugdrug interactions. In the past the recommendation was to "start low and go slow," although now evidence suggests that it may not be necessary to titrate upwards so slowly in all individuals. Instead, the goal should be to increase the dose regularly as tolerated at 1- to 2-week intervals in order to reach an average therapeutic dose more quickly,²⁰ with the CCSMH guidelines suggesting therapeutic dosing be reached within a month. Also, it is now recognized that while the average therapeutic dose is typically lower than that prescribed for younger adults because of the way aging affects hepatic metabolism,

there is much individual variability and some individuals will require a greater than average therapeutic dose.1 If there is no significant improvement after 2 to 4 weeks on an average therapeutic dose, further increases should be made until there is either a clinical improvement, intolerable side effects, or the maximum suggested dose is reached. Thus, it is important to schedule regular follow-up visits to monitor treatment response while assessing for side effects and titrating accordingly. It is also important at each visit to monitor for any worsening of depression, emergence of agitation or anxiety, as well as for suicide risk, especially in the early stages of treatment. There is no evidence of an increase in suicidal ideation due to antidepressant use in the elderly.²¹

Treatment to remission

According to the current CCSMH guidelines, if there is no improvement in depressive symptoms after 4 weeks or insufficient improvement in symptoms after 8 weeks on the maximum recommended or tolerated dose of an antidepressant, then the antidepressant should be changed. This may result in a loss of clinical improvement as the patient is weaned off the agent and started on another. Crosstitrating can be done—weaning the patient off the old antidepressant while introducing the new one although caution is needed to ensure that there are no interactions between the two antidepressants. For example, if fluoxetine is being discontinued, then a wash-out period of several weeks is recommended because of the drug's long half-life. Stopping some medications suddenly (particularly venlafaxine and paroxetine) can lead to a withdrawal syndrome that includes anxiety, insomnia, and flu-like symptoms. This can be prevented with gradual tapering.²² In general, a 7- to

10-day tapering period is recommended for all antidepressants.

If there is significant improvement but not full remission after 4 weeks on the optimized antidepressant, the recommendation is to wait another 4 weeks and then consider add-on treatment if remission is still not achieved.1 Add-on options include either an antidepressant of a different class, another agent such as lithium, or psychotherapy such as cognitivebehavioral therapy or interpersonal therapy. If a second antidepressant is added, monitor for the emergence of serotonin syndrome, which can arise if both medications are serotonergic.

Newer pharmacological approaches

Since the CCSMH guidelines document was published in 2006, newer antidepressant agents have become available including duloxetine and desvenlafaxine, both SNRIs. Placebocontrolled studies of duloxetine suggest that it is an effective treatment for depression in the elderly and generally well tolerated at daily doses of 60 mg.^{23,24} However, to date there is a lack of geriatric-specific research on desvenlafaxine and more studies are needed. Methylphenidate has also been used in the medically ill depressed elderly, with some evidence to suggest that it might be effective in treating depressive symptoms, fatigue, and apathy, although study methodologies have been poor.25

Atypical antipsychotics used as add-on therapy in the treatment of depression shows some promise. A recent post hoc pooled analysis of three placebo-controlled trials suggests efficacy for the use of adjuvant aripiprazole in older adults with an incomplete response to standard antidepressant treatment, both in terms of a significant reduction of depressive symptoms and improvement in remission rates.26 In an open-label trial of risperidone augmentation of patients who had failed to remit on a previous antidepressant, most patients reached remission, although when a placebo arm was introduced there was a nonsignificant delay in the time until relapse for the risperidone group versus the control group.²⁷ The latest 2009 CANMAT national practice guidelines for the treatment of major depressive disorder in adults28 recommend the use of atypical antipsychotic agents such as rispiridone, olanzapine, and aripiprazole as first-line add-on agents in the treatment of depression, while quetiapine is recommended as a second-line add-on agent owing to fewer studies. However, the CANMAT recommendations are based on studies of younger adults and are not intended for the elderly. The use of atypical antipsychotics poses particular problems in older adults given the risk of extrapyramidal symptoms and falls as well as sedation, weight gain, dyslipidemia, and diabetes. There is also a black box warning on atypical antipsychotics because of their association with an increased risk of death, largely due to cerebrovascular events, among elderly demented patients compared with placebo.^{29,30} Nonetheless, atypical antipsychotics may prove to be an effective treatment for severe or refractory depression in the elderly who fail to respond fully to other medications. Atypical antipsychotics at the lowest doses for symptom control are also recommended for the treatment of psychotic symptoms associated with depression. Overall, rates of recovery from psychotic depression in the elderly are low at 33% with medication alone.31

Electroconvulsive therapy

Electroconvulsive therapy (ECT) is recommended as a first-line treatment

for psychotic depression in the elderly,17 with a recovery rate of over 80% and a faster and fuller response compared to medication.¹⁶ ECT is also considered as an alternate treatment for severe depression, particularly in cases where a patient has failed to respond to two antidepressants or is acutely suicidal such that a quick

lowed by a thorough assessment can help guide the selection of an appropriate antidepressant medication. There are several factors to consider when selecting, adjusting, and changing antidepressants in the elderly. Together, these strategies can help promote the safe use of antidepressants in the elderly. Besides medica-

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improvement in symptoms is required for the patient's safety, or if the patient is unable to take medications owing to medical problems.¹⁷ ECT is a relatively safe, well-tolerated, and effective treatment for depression. In the elderly it has been associated with better treatment outcomes and fewer side effects than medications.³¹ In the case of treating psychotic and severe depression with ECT, another advantage is that maintenance treatment is typically with an antidepressant, thus avoiding the use of an antipsychotic medication and its potential side effects with long-term use.1

Summary

Depression in the elderly is a significant, common, and growing problem that requires treatment. It has serious implications for the patient, family, and community. Identification foltions, other therapies for depression that might be considered include various forms of psychotherapy and neurostimulation, with electroconvulsive therapy still being the gold standard for severe or psychotic depression.

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Competing interests

None declared.

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