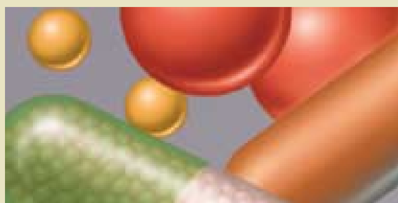
abstract



Anxiety in older patients, when excessive in degree and duration, can cause significant impairment and, if left untreated, may result in profound comorbidity—in particular, depression. Anxiety symptoms emerging in the older patient necessitate an extensive medical and psychosocial workup. There is a paucity of data for pharmacological treatment of anxiety disorders in older adults. In this review, we will discuss some of the research in the area of diagnosis and treatment of anxiety in older adults. We will also summarize some practice parameters common in our clinic when data are absent or lacking. The use of psychotherapies (such as cognitive behavioural therapy) and of medications such as the SSRIs, as well as benzodiazepines and other agents including the atypical antipsychotics, are discussed. The differential diagnosis of anxiety symptoms in the older patient, including careful attention to underlying medical and neurologic causes of anxiety, are emphasized.

Key words: *SSRIs, benzodiazepines, psychotherapy, anxiety, depression, dementia*

Diagnosis and Pharmacotherapy of Anxiety in Older Patients

Eric M. Morrow, MD, PhD, *Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA.*

William E. Falk, MD, *Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA.*

Anxiety is probably our most common emotion and has considerable adaptive value. It keeps us on our toes by enhancing our vigilance and serving as a warning signal for impending danger. It becomes pathological when excessive in degree and duration, or when it causes significant disruption in social or occupational functioning. Although anxiety disorders are the most common general category of psychiatric disorders afflicting older adults,[1] they remain among the least studied. Several authors have recently reviewed different aspects of this problem and have called for further research.[2–4] In this article, we will discuss some of the research in the area of diagnosis and treatment of anxiety in older adults. We will also summarize some practice parameters common in our clinic when data are absent or lacking.

The Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)[5] lists more than a dozen disorders in the anxiety category (Table 1). We will focus on several of the most common of them in our discussion of treatment.

New Onset Anxiety

In an older person, anxiety may present as a continuing part of a lifelong anxiety disorder. However, anxiety symptoms may occur for the first time, or significantly worsen, in an acute fashion in the aged. Although there are exceptions (which we will discuss below), primary anxiety disorders generally do not emerge *de novo* in the older population and should prompt the clinician to search for medical causes. Medical conditions such as arrhythmias, hyperthyroidism, pulmonary disease, anemias, or neurological disorders may present first with anxiety symptoms (Table 2). The psychological and somatic symptoms of these medical conditions may be attributed, erroneously, to primary psychiatric disorders. In addition, medications can produce anxiety symptoms, and withdrawal from medication or alcohol can also be a culprit (see Table 3).

The workup for anxiety disorders in older adults includes first a careful history obtained from the patient and, when possible, additional informants. Past medical and psychiatric history, family history, and mental status examination should also be obtained. Be sure to inquire about over-the-counter medication and alcohol usage histories. Any laboratory studies should be based on the findings of the clinical assessment. Useful measures include EKG, CBC, thyroid function, serum glucose, and vitamin B12.

With anxiety symptoms secondary to a generalized medical condition, the treatment for anxiety is to address the underlying medical problem. In short, we like to remember the mnemonic "MD, MD" (or you may prefer "Doctor, Doctor, I'm so anxious") to remember the differential diagnosis for new onset or worsening anxiety in an aged adult (M= Medical causes, D= Dementia, M= Medicines, D= Depression).

Anxiety symptoms may first emerge in seniors as a result of disorders such as depression, dementia, or substance

Table 1: Common Anxiety Disorders Designated by the Diagnostic and Statistical Manual of Mental Disorders

Generalized anxiety disorder
Panic disorder without agoraphobia
Panic disorder with agoraphobia
Social phobia
Simple phobia
Post-traumatic stress disorder
Obsessive compulsive disorder

abuse. Mood and anxiety disorder are frequently comorbid in older adults.[6] Treatment modalities for depression with anxiety will be discussed below; in addition, readers are referred to specific reviews on the topic of treating depression in the older population.[7]

Anxiety must be carefully discerned from agitation in a patient with mild cognitive impairment or dementia. Memory complaints are common in this patient population, but when they suggest progressive and impairing symptoms, a primary cognitive disorder should be considered. Making this distinction is often based on careful history and assessment of stressors, utilizing collateral sources where available. New onset anxiety in an older person should lead one to consider early cognitive impairment or dementia. At this time, a dementia workup may also be important.

Pharmacotherapy of Anxiety Disorders in Older Adults

Primary Anxiety Disorders

With persistent anxiety not due to an underlying medical condition, treatment could include medications, psychotherapies (particularly behaviour or cognitive-behaviour therapies [CBT]), combined treatments, or other psychosocial interventions such as supportive counselling.

Psychosocial interventions should not be undervalued, as anxiety in older adults is often secondary to acute stressors in the patient or spouse, and if addressed early and appropriately, may be short lived and without need of pharmacotherapies. Issues common in this patient population include coping with losses such as the death of a spouse, concerns about illness, and financial worries. A supportive early intervention can prevent the emergence of persistent symptoms. However, medication may still be necessary. With regard to the anxiety disorders listed in Table 1, we will focus on generalized anxiety disorder (GAD), panic disorder, and post-traumatic stress disorder (PTSD).

A series of trials targeting anxiety symptoms in older adults that have examined the efficacy of SSRIs,[8,9] buspirone,[10] and CBT have found each of these modalities to be effective. Based on available data from treatment trials in older adults and adapting trials on younger adults to seniors, pharmacotherapy recommendations involve the first-line use of an SSRI agent (particularly if depression is present). A benzodiazepine agent may be used in addition to an SSRI in cases where depression is not present. The use of benzodiazepines should be for specific indications, ideally time-limited and carefully monitored. Some alternative agents are discussed below, such as dual-agent antidepressants (i.e., venlafaxine), buspirone, gabapentin, and the atypical antipsychotics.

GAD is diagnosed when there is excessive anxiety or worry most days for six months or more, with associated motor tension, autonomic hyperactivity, and hyperarousal. GAD is common among older adults with estimates

Table 2: Medical Causes of Anxiety

Endocrine	Respiratory	Cardiovascular	Neurologic	Metabolic
Pheochromocytoma	Asthma	Anemia	Brain tumours (especially third ventricle)	Acidosis
Pancreatic carcinoma	Hyperventilation	Cerebral anoxia	Cerebral syphilis	Electrolyte abnormalities
Hypothyroidism	Hypoxia	Cerebral insufficiency	Cerebrovascular disorders	Hyperthermia
Hypoglycemia	Pneumonia	Congestive heart failure	Encephalopathies	
Hyperparathyroidism	Pneumothorax	Coronary insufficiency	Epilepsy	
Diabetes mellitus	Pulmonary edema	Dysrhythmias	Intracranial mass lesion	
Cushing's syndrome	Pulmonary embolus	Hyperdynamic beta-adrenergic state	Pain	
Carcinoid syndrome		Hypovolemia	Vertigo	
Adrenal tumours		Myocardial infarction		
Addison's disease				

Source: Adapted from Pollack et al., 2004.[22]

reaching as high as 7.3%.[11] It is essential to assess for an accompanying mood disorder as more than 50% of patients who have GAD will also be depressed.

Primary GAD may occasionally present for the first time in older adults,[1] but this should be considered the exception and a medical cause is more likely. Controlled treatment trials specifically targeting GAD in the older population are restricted to benzodiazepine trials[12–14] and psychotherapy trials.[15,16] Psychotherapies, particularly CBT, can be effective when adapted to the older population; however, the number of clinicians trained in this technique is limited. A series of trials targeting anxiety symptoms in older adults (without specification to GAD, but likely including GAD) have examined the efficacy of SSRIs[8] and buspirone[10] and have found these agents to vary in effectiveness. However, trials in younger adults with GAD have shown that SSRIs, venlafaxine, and buspirone are effective. Given scarce treatment data for GAD in aging adults, recommendations are based on experience and trial data in younger adults.

In our clinic, first-line treatment for GAD in older adults generally employs an SSRI agent (especially when there are associated depressive symptoms). At times, a benzodiazepine will be added or substituted depending on the efficacy of monotherapy with the SSRI. As summarized below, there are risks to the use of benzodiazepines in the older population, and data suggest that short-term use is preferable, thereby limiting their use in older patients with GAD.

Panic disorder involves recurrent episodes of acute, severe anxiety or fear accompanied by multiple somatic or cognitive symptoms. Required symptoms include hyperventilation, palpitations, sweating, tremor, fear of dying, or fear of losing control. These symptoms may be triggered or without cue and also may evolve into agoraphobia. Onset usually occurs in young adulthood and continues into old age. Some studies have suggested that panic in aging adults is less common at 1.0%.[11] Seniors' presentation may be slightly different than in younger adults, at least partially explaining the decreased prevalence of DSM-IV panic disorder. Treatment trials for panic disorder in aging adults are scant. One open-label trial of sertraline in older adults targeting panic disorder suggests efficacy and tolerability.[9] A trial of CBT in a population of seniors with anxiety (many with panic-like symptoms) also showed efficacy.[17]

PTSD presents similarly in older and younger patients, but there has been very little systematic study of this condition.[18] Central to the diagnosis is the development of characteristic symptoms after witnessing or experiencing events that involve actual or threatened serious injury or death. Symptoms involve a combination of three categories, including re-experiencing traumatic events in dreams, avoiding stimuli associated with the trauma, and numbing or hyperarousal. PTSD may emerge at any time in life, although this condition generally occurs in early adulthood. If PTSD symptoms emerge in aging adults in whom the trauma is remote, an underlying depression, dementia, or other medical cause should be investigated. Treatment recommendations for PTSD in older adults are extrapolated from younger populations and include psychiatric referral, SSRIs, and psychotherapy.

The Use of Psychotropic Agents for Anxiety in Aging Adults

As described above, there is a paucity of treatment studies targeted at anxiety in the aged. Recommendations for treatment therefore are based on studies in younger age groups. Nonetheless, one must take into account the altered pharmacokinetics and pharmacodynamics present in this group, as well as the high probability of drug-drug interactions; thus, the maxim "start low, go slow" is appropriate.

Selective Serotonin Reuptake Inhibitors

SSRIs (including fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram, and escitalopram [not available in Canada]) are currently the preferred agents for older patients with anxiety, particularly when depression is present. While no agent has proven efficacy with all anxiety disorders, they are considered to be equally effective. Each has potential advantages and disadvantages, and selection is based on their unique characteristics. For example, paroxetine may be more sedating than other agents, and could be helpful for sleep; however, its anticholinergic effect may be a problem in older patients. Citalopram may be preferred given its fewer drug-drug interactions.

Tricyclic antidepressants (particularly the tertiary amine agents such as amitriptyline and imipramine) are

Table 3: Medicines that May Cause Anxiety

Intoxicants
Acetylsalicylic acid
Analgesics
Antibiotics
Anticholinergics
Anticonvulsants
Antidepressants
Antihistamines
Antihypertensives
Anti-inflammatory agents
Antiparkinsonian agents
Caffeine
Chemotherapy
Cocaine
Digitalis
Neuroleptics
Steroids
Sympathomimetics
Thyroid supplements
Tobacco
Withdrawal
Ethanol
Narcotics
Sedative-hypnotics

Source: Adapted from Pollack et al., 2004.[22]

generally avoided given their propensity for causing anticholinergic effects and orthostasis. Nortriptyline has fewer side effects; however, this agent is reserved for when SSRIs and other newer agents have failed.

SSRIs used in the aging cause side effects similar to those seen in younger adults, including sedation, mania, gastrointestinal symptoms, sexual dysfunction, somatic symptoms, and even nervousness. Such SSRI side effects may be of short duration and dissipate as the medication trial is permitted to proceed. A good rule of thumb is to start at low doses, typically half of the starting dose in younger adults (e.g., citalopram 10mg or sertraline 25mg). Dosages may then be titrated upward slowly and carefully, until therapeutic benefit is attained or side effects emerge.

Venlafaxine

One study has examined the use of venlafaxine XR, a drug that inhibits both serotonin and norepinephrine reuptake, in older patients with anxiety.[9] Venlafaxine was somewhat effective in seniors (66% response rate, relative to 41% in placebo) and has a similar side effect profile to that of younger adults. A general concern about venlafaxine has been elevations in blood pressure, particularly when doses above 225mg daily are reached. As a consequence, special attention should be given to blood pressure monitoring if venlafaxine is used in the older population.

Benzodiazepines

Benzodiazepines are the most widely prescribed class of antianxiety drugs.[19] Studies demonstrating efficacy of benzodiazepines for anxiety disorders in this population are limited. Nonetheless, these drugs are routinely prescribed to the aged and may be associated with dangerous side effects if not carefully monitored. Some studies have correlated the use of benzodiazepines with falls and cognitive clouding in the older population.[20]

Short-acting agents that are metabolized solely by conjugation, which is relatively unaffected by age, are preferred. Examples include lorazepam, oxazepam, temazepam, and alprazolam. Longer-acting agents that undergo oxidative metabolism in the liver can have markedly prolonged half-lives when compared to younger age groups. Examples of the long-acting agents are diazepam, chlordiazepoxide, chlorazepate, and clonazepam. Thus, any side effects that occur in older patients can be longer-lasting and can include drowsiness, ataxia, depression, psychomotor or cognitive impairment, falls, and accidents. For benzodiazepines in general, there is concern about abuse and withdrawal; thus, indications should be quite specific and with a limited duration of treatment.

Buspirone

Buspirone, a serotonin 1A agonist, is indicated only for GAD but may also be used as an adjunct to other agents when mixed anxiety and depression is evident. It is generally well-tolerated in older patients, with no sedation or psychomotor impairment, as well as no evidence of cognitive impairment or ataxia. The pharmacokinetic properties are similar to those in younger patients, with minimal drug interactions and a lack of tachyphylaxis. Side effects that can occur include dizziness, headache, nausea, diarrhea, and restlessness. When initiating buspirone the clinician should start at 5mg twice a day, gradually increasing the dose as tolerated up to a total daily dosage of 60mg. The drug must be taken regularly to be effective, and evidence of any benefit may be delayed by several weeks.

Gabapentin

Gabapentin is a GABA-potentiating antiepileptic medicine that has been proposed to have efficacy in anxiety.[21] This use is currently off-label; gabapentin is at present not approved by Canada's Health Products and Food Branch (HPFB) (http://www.hc-sc.gc.ca/hpfb-dgpsa/) for the treatment of anxiety. As this medicine is generally well-tolerated and has few drug interactions, in theory it holds promise for anxiety in aging adults who cannot tolerate SSRI or benzodiazepine; however, more research is necessary.

Atypical or Second-Generation Antipsychotics

Neuroleptics may have some utility when administered in low doses to anxious, agitated, and/or demented patients in whom other modalities have not succeeded. As discussed above, whenever anxiety worsens severely or emerges for the first time in an older person, a medical cause should be sought, including dementia. Anxiety symptoms may occur early in dementia, either as part of the disorder or as a consequence of stresses associated with it. Counselling and other psychosocial interventions with the patient and caregivers are effective, but for severe, persisting symptoms, a second-generation antipsychotic may have utility.

All of these agents have side effects (e.g., weight gain, hyperlipidemia, hyperglycemia, diabetes, and tardive dyskinesia) and need to be prescribed with caution in older patients. Risperidone currently has a warning for older adults regarding its possible association with stroke, but this is not viewed as a contraindication to its use. Risperidone is a potent alpha-adrenergic blocker and can cause rapid drop in blood pressure if used acutely at too high a dose. Starting low and going slowly (to minimize risk of adverse events such as hypotension) is the rule with this drug as well as other agents in the class. Quetiapine also is associated with increases in orthostatic hypotension and should be used with caution and at low doses. Olanzapine may have some efficacy with anxiety and/or agitation but is associated with increased appetite, weight gain, and some anticholinergic properties.

Finally, other medicines that have been employed for younger age groups include beta-blockers and antihistamines. Antihistamines such as hydroxyzine should generally be avoided because of potential cognitive changes associated with anticholinergic effects. Beta-blockers have been used in younger adults, particularly for performance anxiety, but

these drugs are rarely used in older patients because of the risk of hypotension and bradycardia.

Conclusion

There is a paucity of data for medication treatment of anxiety disorders in older adults. However, clinical experience suggests that, when drugs are indicated, SSRIs and other newer agents (such as venlafaxine) are effective. Benzodiazepines (particularly short-acting agents with no active metabolites) can be used adjunctively and for short periods of time, but side effects should be carefully assessed. Atypical antipsychotics may be useful for treating the anxiety and agitation associated with dementing disorders, but they also have side effects that must be monitored. Newer anticonvulsants (such as neurontin) have only anecdotal data supporting their use. ◆

No competing financial interests declared.

References

1. Blazer D, George LK, Hughes D. The epidemiology of anxiety disorders: an age comparison. In: Solzman C, Lebowitz BD, eds. Anxiety in the elderly: treatment and research. New York: Springer, 1991:53–80.
2. Baykey AA, Levy JK, Fernandez F. Diagnosis and management of anxiety in the geriatric patient. Clin Geriatrics 1998;6:10–21.
3. Blazer DG. Generalized anxiety disorder and panic disorder in the elderly: a review. Harvard Rev Psychiatry 1997;5:18–27.
4. Lenze EJ, Pollock BG, Shear K, et al. Treatment considerations for anxiety in the elderly. CNS Spectrums 2003;8(Suppl. 3):S6–13.
5. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Washington, DC: American Psychiatric Association, 1994.
6. Beekman AT, de Beurs E, van Balkom AJ, et al. Anxiety and depression in later life: co-occurrence and communality of risk factors. Am J Psychiatry 2000;157:89–95.
7. Taylor WD, Doraiswamy PM. A systematic review of antidepressant placebo-controlled trials for geriatric depression: limitations of current data and directions for the future. Neuropsychopharmacol 2004;29:2272–7.
8. Wylie ME, Miller MD, Shear MK, et al. Fluvoxamine pharmacotherapy of anxiety disorders in later life: preliminary open-trial data. J Geriatr Psychiatry Neurol 2000;13:43–8.
9. Sheikh JI, Lauderdale SA, Cassidy EL. Efficacy of sertraline for panic disorder in older adults: a preliminary open-label trial. Am J Geriatr Psychiatry 2004;12:230.
10. Bohm C, Robinson DS, Gammans RE. Buspirone therapy for elderly patients with anxiety or depressive neurosis. J Clin Psychiatry 1990;51:309.
11. Beekman AT, Bremmer MA, Deeg DJ, et al. Anxiety disorders in later life: a report from the Longitudinal Aging Study Amsterdam. Int J Geriatr Psychiatry 1998;13:717–26.
12. Koepke JH, Gold RL, Linden ME, et al. Multicenter controlled study of oxazepam in anxious elderly outpatients. Psychosomatics 1982;23;641–5.
13. Bresolin N, Monza G, Scarpini E, et al. Treatment of anxiety with ketazolam in elderly patients. Clin Ther 1988;10:536–42.
14. Frattola L, Garreau M, Piolti R, et al. Comparison of the efficacy, safety and withdrawal of alpidem and alprazolam in anxious patients. Br J Psychiatry 1994;165:94–100.
15. Stanley MA, Beck JG, Novy DM, et al. Cognitive-behavioral treatment of late-life generalized anxiety disorder. J Consult Clin Psychol 2003;71:309–19.
16. Wetherell JL, Gatz M, Craske MG. Treatment of generalized anxiety disorder in older adults. J Consult Clin Psychol 2003;71:31–40.
17. Barrowclough C, King P, Colville J, et al. A randomized trial of the effectiveness of cognitive-behavioral therapy and supportive counseling for anxiety symptoms in older adults. J Consult Clin Psychol 2001;69:756–62.
18. Goenjian AK, Najarian LM, Pynoos RS, et al. Posttraumatic stress disorder in elderly and younger adults after the 1988 earthquake in Armenia. Am J Psychiatry 1994;151:895–901.
19. Gleason PP, Schulz R, Smith NL, et al. Correlates and prevalence of benzodiazepine use in community-dwelling elderly. J Gen Intern Med 1998;13:243–50.
20. Wang PS, Bohn RL, Glynn RJ, et al. Hazardous benzodiazepine regimens in the elderly: effects of half-life, dosage, and duration on risk of hip fracture. Am J Psychiatry 2001;158:892–8.
21. Hanlon JT, Horner RD, Schmader KE, et al. Benzodiazepine use and cognitive function among community-dwelling elderly. Clin Pharmacol Ther 1998;64:684–92.
22. Nemeroff CB. The role of GABA in the pathophysiology and treatment of anxiety disorders. Psychopharmacol Bull 2003;37:133–46.
23. Pollack MH, Otto MW, Bernstein JG, et al. Anxious patients. In: Stern TA, Fricchione GL, Cassem NH, et al., eds. Massachusetts General Hospital, Handbook of general hospital psychiatry, 5th ed. Philadelphia: Mosby, 2004: 175–201.