Key Words: : elderly, antidepressants, anxiolytics, atypical antipsychotics, anxiety disorders

Late-Life Anxiety Disorders

By Carl Salzman, MD

ABSTRACT *~ The prevalence, natural course, risk profile, and treatment of anxiety disorders in the elderly are remarkably understudied. Anxiety disorders are less prevalent in the elderly than in younger adults, but rates of subsyndromal anxiety disorders in elderly persons are nearly as high as in their younger cohorts. The most common late-life anxiety disorders are mixed anxiety-depression and generalized anxiety disorder. Though the benzodiazepines are widely used in this population and are considered relatively safe given appropriate dosing and safety monitoring, important liabilities remain with the use of these agents. Antidepressants also are widely used in elderly patients, but there are no randomized controlled anxiety disorder treatment trials in this population. Gabapentin and low-dose atypical antipsychotics are beginning to be used and studies of the atypical antipsychotics are ongoing. Until studies are completed, treatment of late-life anxiety will continue to be guided by extrapolating data from the general adult population.*
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INTRODUCTION

Even though it is well-recognized that the elderly represent the most rapidly growing segment of the population, the field of geriatric psychopharmacology is in many ways a new frontier. There is an abundance of studies of the epidemiology, diagnosis, and treatment of late-life depression. However, our understanding of anxiety and its treatment in the elderly remains in its infancy.

THE LATE-LIFE ANXIETY LITERATURE

The literature on late-life anxiety is very sparse, and what data are available can be difficult to interpret for several reasons. Older people are remarkably heterogeneous in terms of age, overall health, symptom patterns, comorbidities, and etiology of psychiatric disorders. The term 'elderly' is traditionally defined as a person aged 65 years and up, which is a range that can potentially span more than 4 decades of life. Clearly, a healthy and active 65 year old is much different clinically

Dr. Salzman is professor of psychiatry at the Harvard Medical School and director of Psychopharmacology at the Massachusetts Mental Health Center in Boston, MA.

To whom correspondence should be addressed: Carl Salzman, MD, professor of psychiatry, Harvard Medical School; Director of Psychopharmacology, Massachusetts Mental Health Center, 25 Shattuck Street, Boston, Massachusetts 02115; Tel: (617) 232-1113; FAX: (617) 730-9748; email: carl_salzman@hms.harvard.edu.

and neurobiologically than a frail, medically ill octogenarian who is living in a long-term care facility. The design and interpretation of clinical studies must take the heterogeneous nature of the population into consideration. Another element that hinders the interpretation of late-life psychopharmacology studies is an inordinately high placebo response rate. In depression studies, it is not uncommon to find placebo responses in excess of 40%. Moreover, there are virtually no data on remission in mood or anxiety disorders in the elderly population.

EPIDEMIOLOGY OF LATE-LIFE ANXIETY

Very little is known about the epidemiology of anxiety disorders in old age.[1] Although nearly one out of every four adults in the United States will have at least one episode of an anxiety disorder in their lifetime,[2] anxiety disorders are far less common in the elderly population than in younger adults.[1,3] These observations are validated by a prospective study of 286 community-living elderly persons in Germany that demonstrated lifetime prevalence rates of 6.6% for anxiety disorders. Interestingly, subsyndromal anxiety disorders were nearly threefold more common in this elderly population, with a lifetime prevalence rate of 18.5%.[4]

Most anxiety disorders in the elderly are chronic and first occur earlier in life.[3] The most common late-onset anxiety disorders are generalized anxiety disorder (GAD) and agoraphobia (without panic). GAD usually occurs secondary to major depression, and agoraphobia is typically secondary to a traumatic incident.[5-7] A first episode of obsessive compulsive disorder (OCD) also may occur in later years for women, but OCD in elderly men typically represents the persistence or recurrence of an earlier-onset disorder.[3] The prevalence of posttraumatic stress disorder (PTSD), panic disorder, and social anxiety disorder in the elderly is not known with precision, but is believed to be very low.[5,8]

As with major depression, old age, per se, is not a risk factor for anxiety disorders. However, anxiety disorders may be more common in elderly women than in men.[4] Other risk factors for the development of an anxiety disorder in late life include major depression, loss of a partner, social or residential isolation, and medical illness.[1] Depression may be a particularly significant risk factor for anxiety disorders in the elderly. Indeed mixed anxiety-depression is likely the most common presentation of mood and anxiety disorders in the elderly population.[1] Patients with mixed anxiety-depression present with features of both depression (eg, sadness, decreased appetite, anergia) and anxiety (eg, irritability, insomnia, muscle tension). In one study, the prevalence of anxiety disorders was assessed prospectively in a cohort of 182 depressed elderly patients, of whom 23% had a current anxiety disorder diagnosis and 35% had a lifetime history of anxiety disorders.[8] The most common current comorbid

anxiety disorder in this study was GAD (27.5%), followed by panic disorder (9.3%), specific phobias (8.8%), and social anxiety disorder (6.6%).

ANXIETY SYMPTOMS IN LATE-LIFE

There are several patterns of clinical presentation of anxiety symptoms in the elderly that differentiate this cohort from the general adult population. Many elderly persons exhibit subsyndromal, but none-the-less clinically significant, symptoms of both anxiety and depression. Medical illness and multiple medications can cause symptoms of anxiety and can hinder optimal patient management. For example, cardiopulmonary, cerebrovascular, neurologic, and endocrine diseases may be associated with significant symptoms of anxiety. In addition, medications, such as corticosteroids, levodopa, theophylline, caffeine, and decongestants, also can be anxiogenic.[1]

TREATMENT OF LATE-LIFE ANXIETY

The treatment of anxiety and anxiety disorders in the elderly is a remarkably understudied area. There are virtually no randomized, double-blind, placebo-controlled studies of the treatment of anxiety disorders in this population.

Benzodiazepines

The benzodiazepines, which are the most commonly prescribed class of psychotropic agents in the elderly, especially in elderly women,[9,10] are highly effective in the short-term treatment of anxiety. Short-acting agents (eg, lorazepam, oxazepam) are preferred in the elderly because of age-related changes in absorption and elimination. Given appropriate monitoring, low doses of short-acting benzodiazepines are believed to be reasonably safe in this population.[11]

Nevertheless, safety issues must be considered when using benzodiazepines in an elderly patient. The benzodiazepines are associated with dose-related unsteadiness, sedation, and an increased risk of falls and hip fractures in the elderly.[12-14] Benzodiazepines also impair psychomotor performance, and motor vehicle accidents involving their use in elderly persons is well-documented. Longer-acting benzodiazepines are particularly culpable in this regard.[15] The potential for abuse and dependence remains a salient issue for the benzodiazepines. Long-term users of benzodiazepines, particularly the shorter-acting agents, will experience rebound anxiety if treatment is tapered too rapidly. Memory impairment, which is a dose-related phenomenon, also is a concern. High-dose benzodiazepines may pose a problem with memory in the elderly. Use of the benzodiazepines in demented patients is controversial because they may exacerbate existing cognitive dysfunction.[16]

Antidepressants

Though there is increasing evidence from controlled studies for the safety and efficacy of antidepressants in elderly patients with depression,[17] there is very little data on the use of these agents in the treatment of late-life anxiety.[1] The antidepressants, especially SSRIs and venlafaxine, are also widely used in patients with mixed anxiety-depression. Mirtazapine, a tetracyclic antidepressant, is particularly useful for patients whose symptom profile includes insomnia.[18] Bupropion can be activating and may be anxiogenic in some elderly patients.[19]

Other Agents

There are virtually no published data on the use of other treatments in late-life anxiety. However, use of the atypical antipsychotic agents and gabapentin in geriatric patients with anxiety is increasing. The atypical antipsychotics are finding a niche in the treatment of late-life anxiety in very low doses, such as risperidone at 0.25 mg, olanzapine at 2.5 mg, quetiapine at 25 mg, and aripiprazole at 10 mg. Studies of atypical antipsychotics in late-life anxiety are underway, and the findings will help identify agents with desirable effects in this population (Table 1). In addition, some clinicians are using gabapentin in their anxious elderly patients because of its salutary effects on anxiety and agitation as well as its efficacy in common comorbid conditions (eg, chronic pain, insomnia).

AGITATION IN THE ELDERLY

Any discussion of anxiety in the elderly would be incomplete without consideration of agitation, which is an important and closely related symptom in this population. Elderly patients who are agitated often

TABLE 1

DESIRABLE CHARACTERISTICS OF AN ANTIPSYCHOTIC AGENT FOR USE IN TREATMENT OF LATE-LIFE ANXIETY

- No benzodiazepine abuse/dependence liability
- Lack of daytime sedation
- No cognitive impairment
- Minimal weight gain
- No effect on blood glucose levels
- No effect on serum lipid profile
- No effect on cardiac function
- Lack of orthostasis/unsteadiness
- Low risk of extrapyramidal symptoms and tardive dyskinesia
- Minimal drug-drug interactions

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exhibit motor restlessness, pacing, disturbed sleep, and aggressive or combative behavior.[20] Agitation is very common in elderly persons with dementia, and if untreated can lead to institutionalization. Among demented residents of long-term care facilities, agitation is associated with unsafe behaviors and disruption and distress for the patient, other residents, and staff. A number of different therapeutic strategies have been investigated for agitation in the elderly patient. Benzodiazepines are not rational choices for agitation in the context of dementia because of concern about excessive sedation, confusion, and disinhibition. Currently, atypical antipsychotic agents, which are as effective as the older agents, but better tolerated, are being increasingly used to treat agitation.[21-23] Although there are few randomized, controlled studies to inform the use of the atypical antipsychotics, very low doses are generally recommended to minimize the risk of extrapyramidal symptoms and other adverse effects.[22] Excessive daytime sedation, weight gain, and adverse effects on glucose tolerance and lipid profiles remain of concern with many of the atypical antipsychotics.

CONCLUSIONS

Anxiety in the elderly is a remarkably understudied area. Although prevalence rates are not know with precision, full syndromal anxiety disorders are less common in the elderly than in younger adults. In contrast, rates of subsyndromal anxiety disorders are believed to be much higher in the geriatric population, and mixed anxiety-depression is the most common presentation in this age group. There are currently no randomized, controlled studies of the pharmacological treatment of anxiety in the geriatric population. Until such studies are conducted, information needed to guide therapy in the elderly must be extrapolated from clinical experience and the findings of treatment studies in younger adults. In the future, treatment of late-life anxiety will likely include the antidepressants and a larger role for the atypical antipsychotics and novel agents, such as gabapentin. ✤

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