Depression in the elderly and very elderly, especially those in long-term care facilities, often is more difficult to treat than depression in young or middle-aged adults. Because this population may be more sensitive to the common adverse effects of many antidepressant drugs, particularly the anticholinergic side effects, administration of pharmacologic therapy for depression in the elderly requires careful consideration of the side effect profiles of the various classes of antidepressant medication.

(Clinical depression, although a serious public health problem in the elderly, is not a normal consequence of aging and is often underdiagnosed and undertreated in this population. Multiple pathways contribute to late-life depression, including neurobiological and psychological factors, multiple physical illnesses, as well as common social and economic problems. It is now accepted that the elderly, defined as individuals older than 65 years, actually constitute a very heterogeneous population cohort. Individuals older than 75 or 80 years are referred to as “old-old” compared with those aged 65 to 75 years, who are referred to as “young-old.” As the population continues to age, there is a growing group of people older than 90 years and even centenarians; these individuals may be termed the “oldest-old.” It is remarkable that so few controlled studies on the use of antidepressant drugs in patients aged 75 years or older have been conducted, because the oldest-old is the fastest growing age group in the world. Americans now are living well into their 80s, and it is no longer unusual for people to live into their 90s. Because many of the old-old and oldest-old live in long-term care facilities, it is also surprising that relatively few studies are available that describe elderly patients with depression living in long-term care or assisted-living facilities. This article briefly reviews the treatment of major and nonmajor depression in individuals older than 75 years, with particular reference to those living in assisted-care facilities. Three groups of antidepressants are considered: (1) tricyclic antidepressants (TCAs), (2) selective serotonin reuptake inhibitors (SSRIs), and (3) miscellaneous atypical antidepressants.

**PHARMACOTHERAPY OF MAJOR DEPRESSIVE DISORDER IN ELDERLY PATIENTS**

**Tricyclic Antidepressants**

The TCAs are effective medications for major depressive disorder in the elderly and very elderly. Blood levels necessary to achieve the therapeutic effect in the very elderly are the same as in younger adults, although most older people are more sensitive to the therapeutic as well as toxic effects of TCAs.

Reviews of TCA therapy in the elderly have been presented elsewhere. Only a few studies have investigated the benefits of pharmacologic therapy in patients older than 75 or 80 years. One of the most influential and important studies was conducted by Katz and colleagues, who reported on the clinical effects and pharmacokinetics of the TCA nortriptyline in 24 very elderly patients (mean age = 84 years) living in an institutional setting and characterized as having chronic illness and functional disability. Nortriptyline was effective in this population, and the investigators found no clinically significant differences in nortriptyline kinetics in the elderly patients compared with those found in younger and healthier patients.

Although the TCAs are effective as antidepressants, altered pharmacokinetics and adverse effects may interfere with the usefulness of TCAs in treating the very elderly patient with depression. Hydroxy metabolites of TCAs, which are potentially cardiotoxic to the very elderly, may be present at higher plasma levels in the elderly because the renal excretion of these metabolites is decreased by advanced age. It is possible, therefore, for elderly patients to develop cardiotoxic side effects from elevated hydroxy metabolite levels, even when plasma drug levels are within

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Presented at the closed roundtable “Treatment of Depression in Long-Term Care Patients,” Sept. 18–19, 1998, Boston, Mass. This roundtable was supported by SmithKline Beecham Pharmaceuticals.

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The most common adverse effects of SSRIs in the elderly are agitation and sedation. Because adverse effects may be more intense during the first several days of SSRI therapy, some elderly patients may discontinue the medication, although some elderly patients can take full therapeutic doses almost immediately. Drug interactions between the SSRIs and other compounds that share hepatic metabolism, although some elderly patients can take full therapeutic doses almost immediately. Drug interactions between the SSRIs and other compounds that share hepatic metabolism enzymes may be more common in the older age group because these patients tend to take several medications simultaneously. This is especially true during long-term maintenance antidepressant treatment because concurrent medications may change over time.
Atypical Antidepressants

The third general group of antidepressant drugs used in elderly patients with depression are the atypical antidepressants, including bupropion, venlafaxine, nefazodone, and mirtazapine. Although the number of elderly patients studied while taking each of these medications is significantly less than that for the TCAs and SSRIs, clinical experience suggests that each of these drugs is effective in the elderly.21,22 Prescribing principles are the same for atypical antidepressant drugs as for the TCAs and SSRIs, i.e., “start low and go slow.” None of these drugs have been studied in patients older than 75 years.

Each medication has advantages and disadvantages. Bupropion has no anticholinergic side effects and does not cause orthostatic hypotension, properties that are advantageous to the elderly.23 However, it tends to be activating, and very high doses are associated with a significantly greater risk of seizures than with other agents. Venlafaxine resembles a TCA in pharmacologic properties but lacks anticholinergic effects. It may be quite effective, but headache, nausea, and elevated blood pressure emphasize the need for caution when venlafaxine is given to very elderly patients. Nefazodone and mirtazapine are useful for bedtime sedation but may cause daytime drowsiness.

TREATMENT OF NONMAJOR DEPRESSION IN ELDERLY PATIENTS

Nonmajor depression in the elderly often goes unrecognized. Katz and colleagues23 conducted a study of 209 nursing home residents and found that 18% suffered from dysthymia. Another study, by Nobler and colleagues,24 reported a higher incidence of outpatient dysthymia in elderly patients (mean age = 67 years). Symptoms of nonmajor depression, which may interfere with the quality of life as much as major depression does, commonly include dysphoria, mixed anxiety, variable sadness, increased irritability, and increased social withdrawal. The diagnostic distinction between unhappiness and nonmajor depression may be difficult to determine because the patient may not be able to provide enough useful information to make the differentiation. Often, the best person to determine whether the patient’s level of unhappiness has reached clinically significant severity is the 24-hour caregiver.

Nonmajor depression may be treated without medication, using techniques such as expressive movement, group, reminiscence, problem-solving, and group-cognitive therapies.25–30 A recent study examined the effect of 8 weeks of planned socialization and leisure activities in 31 elderly nursing home residents (mean age = 78.7 years) with either minor depression or mild-to-moderate major depression. Approximately half of the patients were able to resume social interaction similar to their pre–nursing home pattern, suggesting that a psychosocial intervention enhancing socialization according to each patient’s choice had a positive therapeutic impact.31 It seems that each form of nonpharmacologic therapy has been successful in improving the quality of life of nursing home residents, suggesting that, to avoid unnecessary medical risks, patients suffering from minor depression should try nonpharmacologic therapy before undergoing drug treatment.32

My colleagues and I conducted a randomized, double-blind, placebo-controlled trial of paroxetine in elderly nursing home residents with nonmajor depression (A. Burrows, M.D., C. Salzman, M.D., A. Satlin, M.D., et al., unpublished data, 1999). The study design included a 1-week placebo run-in, 8 weeks of double-blind treatment with paroxetine or placebo, weekly monitoring of safety and global improvement or deterioration, and psychometric assessments performed at baseline and at weeks 4 and 8. The overall preliminary results showed a high placebo response and little difference between the 2 treatment groups. However, when response was originally defined according to evidence of specific rating scale improvements, paroxetine was significantly more effective than placebo. Our data support those of Nobler and colleagues,24 who reported that SSRI therapy is effective in 60% of elderly patients with dysthymia.

CONCLUSIONS

All antidepressant therapies seem to be effective in the treatment of elderly and very elderly patients with major depression in long-term care facilities. If drug selection is based on side effect profiles, the SSRIs offer the most favorable adverse effect profile. Regardless of which antidepressant is selected, dosing should start low and increase slowly to reduce the risks of adverse effects. It seems that psychotropic medication as well as nonpharmacologic therapies are effective for treating elderly patients with nonmajor depression.

Drug names: bupropion (Wellbutrin), citalopram (Celexa), fluoxetine (Prozac), fluvoxamine (Luvox), mirtazapine (Remeron), nefazodone (Serzone), nortriptyline (Pamelor and others), paroxetine (Paxil), sertraline (Zoloft), venlafaxine (Effexor).

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J Clin Psychiatry 1999;60 (suppl 20)