

Combined Psychotherapy and Pharmacotherapy for Late-Life Depression

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Despite the high prevalence and morbidity associated with late-life depression, this important disorder remains underrecognized and undertreated. There are a number of factors that complicate the diagnosis and treatment of depression in older adults: the presenting symptoms of depression in older adults often differ from those of middle-aged adults; depression in late life frequently occurs in the context of multiple medical or cognitive difficulties; and clinicians erroneously believe that depression is a natural, expected and therefore normal reaction to the myriad losses that are so common in the latter stages of life. It is precisely because of all these complications of late-life depression--medical, cognitive and psychosocial--that combined treatment approaches, using state-of-the-art pharmacologic and psychotherapeutic techniques, are the preferred management strategies (Alexopoulos et al., 2001).

Diagnostic Issues

One of the great difficulties in diagnosing clinical depression is the heterogeneity with which depression manifests among older individuals. The *DSM-IV-TR* criteria for depression were developed using younger subjects and do not always apply to older people. The most prevalent variant of depression in the elderly, subsyndromal depression, is not even mentioned in *DSM-IV-TR*. Older patients with depression are less likely than younger patients to report feeling sad or depressed. More commonly, older people with depression present with irritability, anxiety, somatic complaints, social withdrawal or a rapid change in functionality. They are less likely to report suicidal thoughts than their younger counterparts, although the rate of suicide is alarmingly high. In addition, late-onset depression may be a distinct subtype, with less likelihood of a family history of depression, more cognitive and neurosensory impairment, more of an association with cerebrovascular insults and white matter abnormalities, more chronicity, and less robust response to antidepressants than earlier-onset depression (Alexopoulos, 1996). Probably the most important differences between late-life depression and depression seen earlier in the life cycle are the associations of late-life depression with medical and cognitive impairments and with other adverse life events.

Comorbid Medical Illness

Older individuals often develop depression in the face of one or more general medical conditions (Reynolds and Kupfer, 1999). Such depressions are often unrecognized because: 1) older patients tend to discount psychological distress while embellishing somatic symptoms; 2) physicians often focus on biomedical issues; 3) symptoms of depression and general medical illness overlap; and 4) sometimes stigmatization and

reimbursement issues get in the way of diagnosis. Neglect may result in unnecessary pain and suffering, as well as increased medical morbidity and mortality. Several studies have shown that depression associated with medical conditions does respond to treatment (Lenze et al., 2001; Mulsant and Pollack, 1998).

Our recommendations are to: 1) keep a high index of suspicion for depressions in older patients with medical conditions known to be associated with increased rates of depression; 2) pay particular heed to psychological and cognitive red flags for depression, such as irritability, withdrawal, hopelessness, helplessness, pessimism, self-blame, and thoughts of death and dying; and 3) treat both the general medical condition and the depression promptly and vigorously.

Cognitive Dysfunction

The relationships between depression and cognitive functioning are complex and bidirectional. Depression often presents with difficulty concentrating and making decisions and, in an older person, may worsen already compromised cognitive function. In turn, many age-related cognitive disorders may be associated with depressive symptoms and syndromes, often early in the course of the cognitive disorders. Recently, a National Institute of Mental Health expert consensus panel developed draft diagnostic criteria for depression of Alzheimer's disease that emphasized: mild-to-moderate severity; less persistent and fewer symptoms needed for diagnosis; irritability and social isolation as the core features; gradual onset and progression of cognitive symptoms in conjunction with depressive symptoms; and the presence of language, gnostic and practice deficits (Olin et al., 2002). While much more systematic study of this syndrome's validity and response to treatment is needed, we recommend cautious yet vigorous treatment of depression, even when associated with pronounced cognitive impairment. The hope is to improve cognitive functioning and quality of life as well as to alleviate depression symptomatology.

Adverse Life Events

Depression in elderly patients is frequently associated with adverse life events. An unfortunate concomitant of aging is that the elderly are more likely to experience loss of loved ones, occupational functioning, health, hope and dreams, the ability to perform activities of daily living, and autonomy. Even when depression is precipitated or worsened by such adverse life events, it is absolutely imperative that the depression be considered a serious disorder warranting treatment. The outworn term "reactive depression" falsely connotes that major depression may be a normal reaction to a loss. The term has outlived its usefulness as it too often leads to neglect of true clinical depression among all age groups, especially the elderly. Regardless of whether there is an identifiable precipitant for the depression, we urge appropriate recognition, accurate diagnosis and prompt treatment.

Pharmacotherapy

[Table 1](#) summarizes a recent consensus of practicing geriatric psychiatrists, in which the selective serotonin reuptake inhibitors (SSRIs) or extended-release venlafaxine (Effexor XR) with psychotherapy were found to be the treatments of choice for late-life depression. Sustained-release bupropion (Wellbutrin SR) and mirtazapine (Remeron) were alternates, and electroconvulsive therapy should also be considered when depression is severe or has psychotic features. For minor depression present less than two weeks, education and watchful waiting are recommended. In the case of minor depression present for greater than two weeks and dysthymic disorder, the same combination of medication plus psychotherapy is recommended (Alexopoulos et al., 2001).

Most of the SSRIs have demonstrated efficacy in elderly people, including citalopram (Celexa), sertraline (Zoloft), paroxetine (Paxil) and fluoxetine (Prozac). Mirtazapine and the extended-release form of venlafaxine and sustained-release form of bupropion have also been found to be effective in late-life depression. The consensus recommendation is to continue an antidepressant three to six weeks before switching or augmenting. If no or minimal response is obtained, the consensus is to switch to extended-release venlafaxine (75 mg to 200 mg). For a first episode of depression with recovery following antidepressant therapy, one year of continual treatment is recommended. For two total episodes, at least two years of continual therapy are recommended, and for three or more episodes, at least three years of continual therapy are recommended.

Special considerations include concern about drug-drug interactions, especially in the aging population, where polypharmacy is routine. Citalopram and venlafaxine are the cleanest of the antidepressants in terms of inhibition of the cytochrome P450 enzyme system. One other notable concern is the fact that elderly inpatients on SSRIs and venlafaxine have been found at high risk of developing hyponatremia (39% in one study) and therefore should have sodium levels checked prior to starting medication and at regular intervals during therapy (Kirby et al., 2002). Other concerning side effects include serotonin syndrome, weight loss, sexual dysfunction, anticholinergic effects (most notable with paroxetine), agitation and insomnia. Sustained-release bupropion might be considered in patients for whom sexual side effects, excess daytime sedation or weight gain should be avoided; and mirtazapine in frail elderly patients for whom weight gain and sedation might be an advantage.

Psychotherapy

Psychotherapy is as effective as antidepressant medication for mild-to-moderate geriatric depression and as effective as psychotherapy for depression in younger adults (Robinson et al., 1990; Schneider and Olin, 1995). More than 25% of depressed older adults prefer to be treated with psychotherapy rather than with pharmacotherapy, and an additional 5% to 10% require psychotherapy in addition to antidepressant medication (Areán et al., 2001).

[Table 2](#) summarizes features of the most commonly used psychotherapeutic approaches with depressed older adults. Cognitive and behavioral psychotherapies and interpersonal therapy have the most empirical support (Bartels et al., 2002; Blazer, 2003). Other

interventions such as problem-solving therapy, brief psychodynamic therapy and life review have also proved efficacious in randomized clinical trials (Areán and Cook, 2002; Cuijpers, 1998; Engels and Vermey, 1997; Gatz et al., 1998; Pinguart and Sörensen, 2001).

Dialectical behavior therapy is a new approach designed for older depressed patients with comorbid personality disorders (Lynch et al., 2003). Family and caregiver interventions are also common (Cooke et al., 2001; Pusey and Richards, 2001; Sörensen et al., 2002). The effects of psychotherapy are typically larger for older adults with major depression as opposed to subsyndromal symptoms, for those treated in individual rather than group format, for those treated by therapists with both advanced degrees and geriatric experience, for those with no psychiatric comorbidity, and for those without cognitive impairment (Burckhardt, 1987; Engels and Vermey, 1997; Pinguart and Sörensen, 2001).

The combination of antidepressant medication and psychotherapy is superior to either alone, particularly in preventing relapse (Blanchard et al., 1999; Reynolds et al., 1999a, 1999b; Taylor et al., 1999). Research has begun on the dissemination of these results to the primary care setting where most older adults receive mental health care services.

Two recent clinical investigations with protocols that combine medication and psychotherapy show promise as models of collaborative care for depression in older primary care patients. They are the Prevention of Suicide in Primary Care Elderly-- Collaborative Trial (PROSPECT) (Mulsant et al., 2001) and Improving Mood-- Promoting Access to Collaborative Treatment (IMPACT) (Unützer et al., 2002).

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