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SPECIAL REPORT

Depression in Dementia: Diagnosis and Treatment

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The occurrence of neuropsychiatric symptoms in dementia patients has been well established (Rovner et al., 1990). Of patients with Alzheimer's disease (AD), 78% suffer depressive symptoms, 77% have agitation and 69% have psychotic symptoms, with over half experiencing all three symptoms (Tractenberg et al., 2003). The diagnosis and treatment of mood symptoms in this population remains a challenge for physicians (Harman et al., 2002). It is important to recognize and treat these neuropsychiatric symptoms, as they result in increased morbidity, mortality and health care costs (Janzing et al., 1999). Mandatory depression screening in nursing homes can improve treatment rates (Cohen et al., 2003).

Major depression and other, less severe forms of depression frequently form part of the clinical presentation of dementia. Depression with reversible cognitive impairment may be a prodrome for dementia rather than a separate and distinct disorder (Janzing et al., 1999).

Diagnostic Difficulties

Depression may be challenging to assess in a patient with dementia. In patients with AD, the presence of depression may range from 6% to 30%, depending on the diagnostic criteria employed (Cummings et al., 1995). The prevalence and course of depression in dementia are controversial, due to several confounding factors. Family members tend to report much greater levels of depression in patients than do clinicians.

Caregiver mood, patient's self-awareness of illness and

dementia severity appear unrelated to the prevalence of depression in dementia, but the presence of delusions is positively correlated with worse mood scores (Cummings et al., 1995). Clinically significant depression in dementia may be less common than previously reported, tending to remit within a year (Copeland et al., 2003).

In one study of seniors with dementia, 11.8% had major depression, compared to only 3.9% of nondemented seniors (Forsell and Winblad, 1998). Symptoms such as lack of energy, thinking/concentration difficulties, loss of interest and psychomotor disturbance were found more commonly in people who were demented than in those who were not.

Figure 1 shows various neuropsychiatric clusters in dementia. High level of disability is associated with major depression, in both demented and nondemented people.

Depressive symptoms can be present in AD in the absence of major depression. Symptoms of sadness, diurnal mood variation and insomnia present in depression alone differentiates from depression in dementia with almost 90% accuracy (Purandare et al., 2001). Symptoms such as irritability, retardation and weight loss were common to both depression and depression in dementia. A three-year study of seniors showed that those who converted to meet clinical criteria for AD had more symptoms of personality change, such as agitation, passivity, and mild symptoms of baseline depression, than those who did not progress to AD (Copeland et al., 2003). Personality changes, but not depressive symptoms, were associated with a more rapid increase in functional difficulty over time.

Major depressive disorder can be reliably diagnosed in patients with mild-to-moderate levels of cognitive impairment (Katz, 1998). Self-ratings of symptoms with the Geriatric Depression Scale (GDS) remain valid in patients with Mini-Mental State Examination (MMSE) scores of at least 15. Some rating scales are more inclusive than others for symptoms of depression in dementia (Schaub et al., 2003). Diagnostic dilemmas are more common in patients with intermediate symptom severity, rather than mild or severe cases. Interviewer scales such as the Hamilton Rating Scale for Depression (HAM-D) and the Cornell Scale for Dementia in Depression (CSDD) are the best established (Vida et al., 1994). The CSDD is the best diagnostic scale for detecting depression in dementia. Its optimal cutoff score in a recent study was 6/7 (sensitivity=91.7%, specificity=80%) in the mild dementia group and 12/13 (sensitivity=70%, specificity=87%) in the more advanced dementia group (Lam et al., 2004).

The clock-drawing test may be a useful way to identify

depressed patients with underlying AD (Herrmann et al., 1998). They typically have significantly lower scores on clock drawing, copying and reading than either patients without underlying AD or controls. Patients with depression do not differ significantly from controls on quantitative scores or qualitative errors on clock drawing.

In one study, approximately 25% of patients with dementia suffered from major depression and another 27% from minor depression (Ballard et al., 1996). Major depression was more common and severe in patients with vascular dementia than in patients with AD. In another study of 288 outpatients with dementia, a prevalence of 7.4% was found with HAM-D, 8% prevalence with the GDS and 6.3% with *DSM-IV* criteria (Brodaty and Luscombe, 1996). Clinically significant depression in dementia did not persist over 12-month follow-up. Depressive symptoms without depressed mood were common in patients with AD and multi-infarct dementia in another study (Reichman and Coyne, 1995). Major depression was found in 10.5% of patients with AD, in contrast to 29% of those with multi-infarct dementia. Rates of vegetative or subjective symptoms of depression were the same between AD patients with or without depressed mood or anhedonia. Presence of depression, lack of insight and personality changes do not seem to differ between vascular dementia and AD (Verhey et al., 1995).

Depressed mood has been reported to lead to a two- to threefold increased incidence of dementia, particularly AD. In a study of 1,070 elderly people living in the community, depressed mood at baseline was associated with an increased risk of incident dementia (relative risk=2.94) (Devanand et al., 1996).

In contrast, a comprehensive study of 140 patients older than 60 with depression showed that depression alone does not cause cognitive impairment (Butters et al., 2004). Half of the participants showed significant cognitive problems while depressed, but the other half did not. If significant cognitive problems exist in an elderly depressed person, they are likely permanent and may worsen over time.

Slowed information processing affecting all realms of cognition was a key finding supporting the notion that fronto-striatal dysfunction plays a key role in late-life depression. Risk factors include advanced age, low education, ventricular atrophy and depression severity. The vascular disease burden, age at onset of first depressive episode, apolipoprotein E genotype and serum anticholinergic activity did not correlate (Butters et al., 2004).

Treatment Options

In addition to pharmacological treatments (**Table 1**) and electroconvulsive therapy for more severe depression, a treatment plan for depression in dementia includes nonpharmacological therapies (**Table 2**) (Teri and Wagner, 1991; Teri et al., 1997). These are patient-focused interventions, as well as family or caregiver support. These interventions are very effective in milder depressions or when caregivers are depressed and should be considered first. Cognitive-behavioral therapy and pure behavior therapy for both patients and caregivers can be useful (Teri and Wagner, 1991; Teri et al., 1997). Pharmacological or nonpharmacological interventions do not totally eliminate depression in dementia symptoms, but they do decrease the symptom severity (Snowden et al., 2003). **Figure 2** lists an algorithmic approach to treatment.

Relatively few controlled studies have been done due to limitations of sample size and different defining criteria for depression in dementia and efficacy. Few placebo-controlled antidepressant trials have been conducted. Antidepressants are effective for major depression, but data for mild depression are limited. High placebo response rates are seen particularly with milder depression, but more efficacy is noted with higher drug-placebo differences in trials with more severe forms of depression (Lyketsos et al., 2003).

Only one placebo-controlled trial has been reported with a tricyclic antidepressant. There was significant benefit for both imipramine (Tofranil) and placebo in the treatment of major depression in AD, with no difference observed between the medication and placebo groups (Reifler et al., 1989). Two placebo-controlled trials of the selective serotonin reuptake inhibitor citalopram (Celexa) in elderly patients, with or without dementia, found significant improvements in depression and decreases in mood lability on citalopram (Gottfries et al., 1992; Nyth and Gottfries, 1990). Fluoxetine (Prozac) treatment did not differ significantly from placebo (Petraffa et al., 2001). This study also confirmed the presence of a placebo effect in the treatment of depression in AD. Sertraline (Zoloft) showed improvement in the CSDD scores and clinical global score in some studies (Lyketsos et al., 2003, 2000). Although moclobemide (Aurorix) has been shown to be safe, well tolerated and effective, it has limited clinical usefulness (Roth et al., 1996).

Antidepressant treatment often produces clinical improvement in 50% to 60% of patients with depression (Schneider and Olin, 1995), and side effects, particularly cardiovascular and anticholinergic, may be limiting (Moskowitz and Burns, 1986). Less improvement is noted with antidepressants in patients with white matter hyperintensities and lacunar infarcts (Simpson et al., 1998, 1997). The efficacy of ECT appears

particularly high in late-life depression (Flint and Rifat, 1998) and is safe for cardiac patients (Rice et al., 1994). No brain damage has been shown with ECT, but temporary cognitive problems can be frequent (Devanand et al., 1994; Scott, 1995).

A case series of 31 patients showed that ECT is effective, leading to improvements in both mood and cognition (Rao and Lyketsos, 2000). Multiple ECT treatments may be necessary before a significant improvement is achieved. Electroconvulsive therapy appears to be acceptable in terms of safety, but may need to be administered in lower doses and frequency than in nondemented patients.

Conclusion

In summary, depression in dementia is a common condition with a great impact on the quality of life of both patients and caregivers. It must be identified and treated promptly. Nonpharmacological and pharmacological therapies are helpful, but ECT may be needed in some cases. Depression in dementia is poorly understood in terms of prevalence and etiology, making it a challenge to conduct clinical trials and treat effectively.

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