

Depression in Dementia Patients: Issues and Challenges for a Physician

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Abstract

Depression and dementia share a complex and interesting relationship, with a possibility of biological linkages between the two disorders. Research has shown consistently increased prevalence of depression in patients suffering from dementia. As many as one fourth to half of dementia patients are likely to experience clinical depression during the course of illness. However, the onset of depressive symptoms is often misinterpreted as worsening of cognitive decline and hence, it remains under-diagnosed. The lack of a coherent account from patient, frequent overlap of symptoms, inadequate sensitization of physicians may enhance the diagnostic difficulty. Undetected depression adds to patient disability and caregiver burden. Early recognition and proper intervention will improve the patient outcomes including quality of life. Selective serotonin reuptake inhibitors, especially Sertraline and Citalopram, with a very gradual dose titration are likely to benefit. Certain behavioral interventions e.g involvement of patient in physical activity and pleasant activities has been found to be useful. All dementia cases should be routinely screened for depression and managed accordingly.

The phenomenon of demographic aging all over the world has been accompanied by a dramatic rise in the prevalence of depression and dementia. Both are common illnesses of the later life and share a very complex and interesting association. Depression is one of the early and most important non-cognitive manifestation of dementia. Often, there is a difficulty in determining whether depression or dementia is responsible for a particular cognitive or behavioral symptom. Presence of depression in dementia patients leads to poor functional outcomes. Further, there is growing evidence in favor of depression being a risk factor for subsequent development of dementia, which merit a closer study. It is, therefore, important that physicians are aware of this relationship in order to provide better clinical care to dementia patients.

Depression, along with apathy, is the most common psychiatric manifestation seen in dementia patients.¹ Existing literature suggests that 25-50% of the dementia patients will develop depression at some point over the course of their illness.^{2,3} Depressive symptoms have been found in up to two-thirds of dementia patients. Certain risk factors have been identified which may increase the risk of depression particularly in patients with Alzheimer's disease (AD), which include female gender, early onset of dementia, a past history of depression and a family history of mood disorder in first degree relatives.⁴ The natural history of depression over the course of AD has not been fully studied. It appears that depression may be the first symptom of AD and may be more common in mild to moderate dementia compared to severe dementia.⁵ Depressive symptoms tend to follow a fluctuating course over time. In approximately 60% to 70% of dementia patients, depressive symptoms disappear within six months, but they do recur within a year in as many as 85% of those patients.¹

Delineating the symptoms of depression in dementia patients can be quite a challenging task for the treating physician. There

is a considerable overlap between dementia and depressive symptoms and delineation of the cause of a particular behavior may be quite difficult. For example, although apathy is commonly associated with depression, but approximately 60% of dementia patients may have apathy without depression.⁶ Similarly, social isolation, loss of interest and concentration difficulties may also be a manifestation of cognitive decline, rather than depression. On the other hand, depression is also well recognized to cause memory difficulties, which generally resolve after treatment of depression, but subtle cognitive impairments may persist even after full recovery from depression especially in the elderly age group.

Researchers have debated as to what constitutes syndromal depression in dementia patients and where to set the threshold to define depression. Available studies differ in the instruments and criteria used to measure depression among dementia patients e.g Geriatric psychiatrists have mostly used the DSM-IV diagnostic criteria,⁷ Hamilton Depression Rating Scale⁸ or Geriatric Depression Scale,⁹ while studies initiated by dementia researchers have used Neuro-Psychiatric Inventory.¹⁰ A useful instrument for assessment and monitoring could be Cornell Scale for Depression in Dementia,¹¹ which uses a comprehensive semi-structured interviewing approach and integrates the patient and caregiver interviews to reach a composite clinician rating. In order to resolve the complexity of diagnosis and arrive at a consensus, the National Institute of Mental Health convened a workgroup for 'Depression of Alzheimer's Disease' (dAD), to develop provisional diagnostic criteria for diagnosing depression in AD.² The criteria are broadly similar to the DSM-IV criteria for major depression,⁷ but with a few significant changes. For a person to be diagnosed with depression in the presence of Alzheimer's disease, he or she must have either of the two symptoms over a two-week period:

- a. Depressed mood (sad, hopeless, discouraged or tearful) most of the day, nearly every day
- b. Decreased positive affect or pleasure in response to social contacts and usual activities along with a minimum of two of the following symptoms:

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- i. Social isolation or withdrawal
- ii. Disruption in appetite that is not related to another medical condition
- iii. Disruption in sleep
- iv. Agitation or slowed behavior
- v. Irritability
- vi. Fatigue or loss of energy
- vii. Feelings of worthlessness or hopelessness or guilt
- viii. Recurrent thoughts of death, suicide plans or a suicide attempt

Patients with depression in AD tend to be more anxious, agitated, delusional, or inattentive but have less guilt and self-deprecation. Recent, yet building, evidence from clinical, neuropathologic studies and PET scans have pointed towards the possibility that 'dementia of Alzheimer's disease' may be a unique clinical entity in itself which shares only some features with major depression.⁷

There can be several mechanisms through which depression and dementia are related. Depression may be understood as a 'psychological reaction' to the self-awareness of the dementing process in very early stages. It could be the result of the underlying neurological disease that caused dementia e.g. AD, Parkinson's disease, cerebrovascular disease etc. Certain medical conditions e.g. hypothyroidism, vitamin deficiencies may cause both dementia as well as depression and particular care must be taken to rule out these reversible causes. The various pharmacological treatments which dementia patient have been receiving may also induce depressive symptoms as an adverse effect. Interestingly, recent evidence from longitudinal cohort studies¹²⁻¹⁴ have found that depression, especially if severe or recurrent, is an independent risk factor for dementia. This adds to the evidence from an existing meta-analysis which had suggested that a history of depression may double the risk of subsequent dementia.¹⁵

Depression, when present with dementia, can adversely affect multiple areas of functioning in patients as well as caregivers. It has been associated with a greater decline in quality of life greater disability in activities of daily living, worsening of behavioral and psychological symptoms of dementia e.g. wandering, verbal and physical aggression and increased risk of mortality.¹⁶ Dementia caregivers also experience additional burden of care and there are increased chances of early institutionalization of dementia patients with comorbid depression. Although completed suicide seems to be relatively uncommon in elderly with dementia, suicidal thoughts or a sense of worthlessness are not uncommon in early stages.

When treating depression in healthy adult population, the clinician can choose from a range of interventions, from pharmacological to electroconvulsive therapy and cognitive behavioral therapies. However, the treatment of depression in dementia patients merits certain special considerations. The dementia patient is likely to be on multiple medications for dementia and/or comorbid physical illness. The safety considerations are of prime importance while using antidepressants in elderly dementia patients and utmost care has to be taken to prevent postural hypotension and other side effects, especially in case of tricyclic antidepressants. A careful and gradual dose titration of anti-depressant medication is required to minimize potential side effects. There are concerns that use of electroconvulsive therapy might exacerbate the

cognitive impairment and its use is supported with little evidence except when the patient's safety is at risk. Another important consideration is to realize the limitations of available treatments and set expectations at a realistic level. Providing information to caregivers e.g. psycho-educational sessions or referral to Alzheimer's society for support may be very helpful in reducing their distress. It is also extremely important to evaluate for any wishes of self-harm or suicidal ideation, particularly for patients in early stages of dementia. All patients with diagnostic dilemmas, severe depressive symptoms, risk of harm or management difficulty must be referred to a psychiatrist for expert management.

Selective Serotonin Reuptake Inhibitors (SSRIs) are preferred drugs for moderate or severe depression, in view of better adverse effect profile. So far, the available data from randomized controlled trials point to efficacy of sertraline and citalopram over placebo at least in the short term course, up to 12 weeks, making them reasonable initial drugs to treat depression in dementia.^{2,5} However, a note of caution is to be put since a more recent randomized controlled trial aiming at delayed outcome of sertraline, up to 24 weeks failed to show an antidepressant advantage over placebo.¹⁷ The treating physician should wait for at least 12 weeks to get a response before making a change of anti-depressant medication. In general, it is less often appropriate to move on to more complex treatments, such as combinations of antidepressants or lithium augmentation, when treating depression in the setting of dementia.

There are a few studies testing efficacy of behavioral interventions for mild depression in AD and the form of provision of pleasant activities, exercise training and caregiver problem solving skills have been superior to placebo.^{18,19} The treatment of depression in dementia involves a combination of medication, support, and gradual reconnection of the patient to activities and people he finds pleasurable. Following are some of simple steps which can be advised to family members caring for dementia:

- Schedule a predictable daily routine, using the patient's best time of day to undertake more difficult tasks e.g. bathing
- Make a list of activities, people or places that the person enjoys and schedule these things on a more frequent basis
- Help the person exercise regularly, particularly in the morning time
- Acknowledge the person's frustration or sadness, while continuing to express hope that he or she will feel better soon
- Find ways that the person can contribute to family life and recognize the contribution
- Provide reassurance that person is loved, respected and appreciated as part of the family

The outcome of the depression is variable depending on how well the patient responds to treatment. With improvement in depression, there is less behavioral disturbance and disability, but no improvement in cognition.²¹ In general, an organic brain disease is a relatively poor prognostic feature in late life depression, and the outcome for the patient and their family will also depend on the course of the dementia.

Conclusion

In conclusion, depression coexisting with dementia has emerged as a significant public health problem of the aging population, leading to increased health care utilization and

costs. There is an urgent need to sensitize the physicians who are managing a large proportion of dementia cases. It is highly recommended that all the dementia cases should be routinely screened for depression and managed accordingly. Early recognition and proper intervention will reduce the morbidity and mortality associated with depression in dementia and improve the patient outcomes. Lastly, it needs to be acknowledged that we are still striving to achieve better understanding of depression in relation to dementia, but we must make the best use of knowledge available to us so far.

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