Treatment Implications for Comorbid Diabetes Mellitus and Depression

January 18, 2013 | Major Depressive Disorder [1], Comorbidity In Psychiatry [2], Depression [3], Dysthymia [4], Metabolic Disorders [5]
By Shane M. Coleman, MD [6] and Wayne J. Katon, MD [7]

Diabetes mellitus and depression symptoms are associated with decreased self-care and less adherence to exercise, medications, smoking cessation, and eating a healthy diet.

Major depression and type 2 diabetes mellitus are common chronic illnesses within the general US population, with prevalence rates of approximately 5% to 10% and 11%, respectively. Moreover, depression and type 2 diabetes mellitus, individually, can be among the most disabling chronic disorders one can acquire, and when they occur comorbidly, they are even more detrimental. Together they exhibit a bidirectional relationship, with each disease an independent risk factor for development of the other.

In the presence of diabetes, the prevalence of depression increases to 15% to 30% depending on depression definition, population sample, and study type. In depressed cohorts, the risk of developing diabetes has been shown to be twice that of nondepressed persons. The bidirectional relationship between depression and diabetes is not limited to its effects on prevalence; instead, studies show that when these diseases are comorbid, they significantly amplify the cost, morbidity, and mortality expected from either one alone.

In the case of depression, changes in blood sugar levels have been linked directly to moods such as anger, anxiety, sadness, frustration, and even general well-being—common themes in depressed patients. Clinically, more than 70% of patients with diabetes have depressive episodes that last longer than 2 years. Dysthymia and double depression may also be more common in patients with diabetes. This was demonstrated in a large cohort of diabetic, primary care patients, well over half of whom had dysthymia. MDD is highly recurrent in diabetic patients—nearly 80% of depressed persons with diabetes experienced a relapse of symptoms, with an average relapse rate of nearly 1 episode every year.

Patient disability experienced in the home, workplace, or otherwise is exacerbated by the relationship between comorbid diabetes and depression. Studies that examined disability have shown not only that depression itself is one of the most disabling chronic conditions but also that the functional impairment it causes is substantially worse when it occurs in the context of another chronic disease, such as diabetes.

The course of diabetes becomes profoundly worse in depressed patients. Depression in diabetes has been associated with decreased self-care, including decreased adherence to exercise, medications, smoking cessation, and eating a healthy diet. Depression contributes to the pathophysiology of
diabetes by leading to greater body mass index, higher hemoglobin $A_1c$ ($HbA_1c$) levels, and increased medical comorbidity. It has also been associated with a myriad of adverse outcomes, including microvascular complications such as retinopathy, nephropathy, neuropathy, and sexual dysfunction, as well as the macrovascular complications of coronary artery and cerebrovascular disease.

Depression in diabetic patients is also a risk factor for dementia, hospitalization, and even death. In the case of dementia, diabetes and depression are independent risk factors for vascular and Alzheimer-type dementias, and comorbid they impart substantially more risk than either one alone. Effective treatment of depression and diabetes may be one of the most powerful interventions available for decreasing the prevalence of dementia. Treating depression in patients with diabetes and dementia may help slow the rate of functional and cognitive decline over time.

Not surprisingly, depression also contributes to decreased quality of life and increased costs of diabetes care. In one study of Medicare beneficiaries, the costs of the care for depressed versus nondepressed patients with diabetes was 4.5-fold higher. A second study of mixed-age patients with diabetes found that comorbid depression severity influenced costs as well; costs for severely depressed patients were 86% higher than those for patients with less severe depressive symptoms.9

**Diagnosis**

The diagnosis of depression in the context of diabetes and other chronic medical conditions can be challenging. Many of the symptoms of depression can overlap with a chronic disorder such as diabetes, and depression itself is associated with an increased likelihood of the patient experiencing diabetic symptoms. Examples of overlapping symptoms include fatigue or decreased energy, change in appetite or weight, difficulty in concentration, and sleep disturbances.

Some general concepts can be helpful when thinking about depression in diabetes. Dividing the symptoms of depression into somatic (energy, sleep, appetite/weight, concentration) and psychological (mood, interest, suicidal thoughts, guilt, worthlessness) is important. The psychological symptoms of depression have little overlap with the signs or symptoms of diabetes, which make them particularly specific to depression in this context.

This is supported by studies that used the Beck Depression Inventory (BDI) to identify which symptoms successfully differentiated between the depressed and nondepressed, medically ill patients. Study findings included 6 symptoms that were discriminatory: a sense of failure, loss of social interest, feelings of being punished, suicidal ideation, dissatisfaction, and indecisiveness. The somatic symptoms of depression are less specific to depression in patients with diabetes; however, that does not mean that they are without value. While the mere presence or absence of somatic symptoms is less helpful, there are many characteristics of these symptoms, such as severity, timing, etiology, and proportion, that can be useful. The more severe the somatic symptom, the more specific it is to depression.

These symptoms are also more specific when they develop in conjunction with at least 1 of the 2 cardinal symptoms of depression, so understanding the timing or onset of somatic symptoms is informative. Considering the etiology of the symptom, or whether the somatic symptom could be caused by diabetes can be helpful because symptoms unrelated to medical illness are more likely due to depression. And finally, if the somatic symptom is out of proportion to the illness, medication, or another relevant factor, it may be more likely due to depression.

Despite challenges associated with diagnosing depression in the medically ill, studies performed in ambulatory diabetic cohorts have been encouraging. In general, they have shown that common depression screening scales, including the BDI and Patient Health Questionnaire-9 (PHQ-9), retain both their sensitivity and specificity in identifying depression when administered in outpatient settings. Clinical tips and implications for treating depression in patients with diabetes

**Treatment**

Many studies have examined the effectiveness of treatment for depression in diabetic patients. This has included the examination of evidence-based psychotherapy; psychopharmacology; mixed-treatment modalities; and systems-based approaches, such as those using collaborative depression care models to treat depression in primary care. Cognitive-behavioral therapy (CBT) with added emphasis on diabetes self-management can be effective at treating depression and may also help reduce $HbA_1c$ levels.

Psychopharmacological approaches have proved effective for treating acute depressive episodes, for maintenance therapy for MDD, and for successfully preventing relapse of depressive episodes. Moreover, there is observational evidence that antidepressant use may increase the risk of type 2 diabetes mellitus. Collaborative depression care programs have successfully improved depression outcomes. However,
only multicondition collaborative care programs, such as TEAM-care, have demonstrated the ability to improve depression as well as diabetes-related measures such as blood pressure and HbA\textsubscript{1c} and low-density lipoprotein cholesterol levels.\textsuperscript{18}

Choice of psychopharmacological agents in the treatment of depression in diabetic patients deserves special attention because depression in these patients is complicated not only by the adverse effects of medication but also by the effects of diabetes. For instance, some SSRIs may cause weight gain, which will exacerbate insulin resistance and may contribute to sexual dysfunction, worsening a common, long-term complication of diabetes. SSRIs may also cause drug-drug interactions via their effects on the cytochrome P-450 (CYP) isoenzymes by interfering with the metabolism of diabetes medications. For example, fluoxetine, fluvoxamine, and sertraline may inhibit the CYP2C9 isoenzyme and affect the metabolism of the sulfonylureas tobutamide and glimepiride.

TCAs, while effective for treating depression in diabetes, have unique properties that limit their usefulness. First, TCAs may cause elevations in fasting blood glucose levels and they are more likely to cause weight gain than other, newer antidepressants. Second, many adverse effects associated with TCAs, such as orthostasis and arrhythmia, are particularly problematic when diabetes itself targets the nervous and cardiovascular systems.

Bupropion, in particular, possesses many qualities attractive for treatment of the diabetic patient, and it has been found to be efficacious for depression in this population.\textsuperscript{19} This drug is weight-neutral (or may even help diabetic patients lose weight); it is associated with less sexual dysfunction; it can be effective for smoking cessation (a common and costly comorbidity in depressed diabetic patients); and it has shown efficacy in treating neuropathic pain.\textsuperscript{16,19} However, bupropion is ineffective for treating co-occurring anxiety disorders. Venlafaxine and duloxetine, which have shown efficacy in treating depression and neuropathic pain, may also be useful in diabetic patients with depression.

CASE VIGNETTE

Mr M, a 54-year-old with diabetes and hypertension, was referred for evaluation by his primary care physician. During the interview, Mr M rated his mood as “fair,” but he is experiencing decreased interest in leisurely activities, such as hiking and cigar smoking, as well as decreased motivation for self-care, including eating a healthy diet and taking regular blood sugar readings. He describes frequent nighttime waking, with no more than 3 hours of uninterrupted sleep; normal appetite, with a recent 5-lb weight gain; normal concentration; and decreased energy. He denies hopelessness but endorses feelings of guilt and describes himself as a bad partner to his wife because he’s currently unable to work and no longer engages in physical activity with her. When asked if he ever has thoughts of hurting himself or others, he replies, “Yeah, sometime I think I’m no good and people might be better off without me.”

Mr M is clearly depressed; he has decreased interest, guilty thoughts, feelings of being ineffective, and intermittent suicidal ideation. He’s not sleeping well (possibly because of polydipsia) and has decreased energy as well as a recent 5-lb weight gain. Additional history about the duration of both his depression and diabetes may be helpful, as would specific symptoms that the patient attributes to his diabetes, including the severity of these symptoms. Knowing the time of onset of his decreased interest and somatic symptoms may be useful. Direct inquiry into whether the patient suffers from anxiety, sexual dysfunction, or neuropathy may also help guide treatment. We recommend administering the PHQ-9 and Montreal Cognitive Assessment during the initial patient evaluation. These examinations should be repeated regularly over time to track the patient’s progress and response to treatment. Additional history can be obtained from the patient’s primary care physician. Pending further history, CBT with an emphasis on diabetes self-care should be discussed as a possible option, as should treatment with bupropion, an SSRI, or a dual-acting agent.
Table

References: