Turkish Journal of Endocrinology and Metabolism, (2002) 3 : 95-100 **REVIEW**

Diabetes and Depression

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Approximately 30% of patients with diabetes experience comorbid depression. There is a significant association between depression and hyperglycemia in type 1 and type 2 diabetes. Also, the adverse consequences of depression in diabetics are the increased risk of the macro- and microvascular complications of diabetes. On the other hand, results from the studies suggest that effective management of depression improves glycemic control. Many newly diagnosed diabetics go through the typical stages of mourning. These are denial, anger, depression and acceptance. They may also show rebellion, anxiety, pathological dependency and regression. Often, individuals with depression do not realize that they are depressed. It is easy to attribute the symptoms of depression to the diabetes. On the basis of Beck Depression Inventory scores, cognitive symptoms are the most reliable means to separate diabetic depressed from diabetic non-depressed patients. In the diagnosis of depression; one should look for affective and cognitive symptoms, rather than the somatic-vegetative signs. Panic attacks may resemble hypoglycemic episodes and vice-versa. Physicians generally select among TCAs, SSRIs, and other newer antidepressant agents to treat depression, reserving monoamine oxidase inhibitors and electroconvulsive therapy largely for severe, unresponsive cases. Factors affecting the selection of an antidepressant for patients with diabetes include presenting symptoms, coexisting medical conditions, drug interactions and side-effect profiles.

Key words: Depression, diabetes

Diabetes mellitus is one of the most common chronic diseases. Diabetes throws many hormones and brain chemicals out of balance, and these changes may open a door to depression (1). Physical disease destabilizes one's homeostatic balance and causes emotional reaction. Every physical disease is a crisis. Illness provokes reactions like anxiety, guilt, feelings of loss and hopelessness (2). Among patients with type 1 diabetes at the Joslin Diabetes Center in Boston, the prevalence of depression is probably about 30% to 40% (3). The lifetime prevalence, that is, the percentage of patients with diabetes who, at some point in their lifetime, will have an episode of major depression-appears to be about 33% (4,5).

In the Epidemiologic Catchment Area Program survey conducted by researchers at Johns Hopkins University in Baltimore, Maryland; 3.481 community-dwelling adults were interviewed at baseline, and a 13-year follow-up was completed in 1.897 of these participants. This study showed that patients with a major depressive disorder had more than twice the risk of developing type 2 diabetes compared with patients without depression (6).

The mean age of onset of depression in diabetes is 22 years in type 1 diabetics (3). The age of onset of depression in the general population in the United States is 27-35 years (7). Depression precedes diabetic symptoms in type 2 diabetes, but the

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reverse is true for type 1 (8). It has been found that there is a direct correlation between severity of depressive symptoms, incidence of complaints of diabetes, and level of blood glucose in patients with type 1 diabetes (9).

Approximately 30% of patients with diabetes (types 1 and 2) experience comorbid depression (10). There is a significant association between depression and hyperglycemia in type 1 and type 2 diabetes (11). The likelihood of depression is nearly doubled in patients with diabetes (6). According to a research by Ryan Anderson et al, diabetes doubles the odds of depression (12).

Interestingly diabetic schizophrenic or manic depressive patients' glucose regulation does not seem to be affected by their psychiatric situation (13). Although women are twice as likely as men to experience depression, men suffer because they are less likely than women to seek help. For men, it's often masked by alcohol or drug abuse, which may seem more socially acceptable than seeking psychiatric help. In a study, men were more likely to report moderate to severe depression symptoms and women more moderate to severe anxiety symptoms (14). There was a significant link between depressions and poor glycaemic control, as measured by the HbA1c, in men but not in women. One in every five people with type 1 or 2 diabetes was depressed before they got diabetes (15).

The adverse consequences of depression in diabetics are the increased risk of the macro- and micro-vascular complications of diabetes (16,17). Results from the studies suggest that effective management of depression improves glycemic control (1,18-20).

Clinically significant anxiety is also known to have an adverse impact on glycemic control in diabetics (21). Organic brain syndrome, is the second most frequent psychiatric problem in diabetic patients (2).

According to one study, the initial onset of major depressivedisorder (MDD) seems to be independent of the onset of type 2 diabetes, but results remain equivocal for type 1 diabetes (22). However, in both type 1 and type 2 diabetes, diabetes-related psychological and physiological processes may be involved in the higher recurrence and longer duration of MDD and depressive symptomatology. MDD in diabetic individuals represents a multidetermined phenomenon resulting from interactions between biologic and psychosocial factors. This interaction may increase the probability of developing type 2 diabetes in otherwise healthy individuals.

Diabetics with major depression have a very high rate of recurrent depressive episodes within the following five years (23).

A depressed person may not have the energy or motivation to maintain good diabetic management. Depression is frequently associated with unhealthy appetite changes. The suicidal diabetic adolescent has constant access to potentially lethal doses of insulin (14).

One study found that children judged to have a "Type A" personality structure had an increased blood sugar elevation in response to stress. Children with a calmer disposition had a smaller glucose rise when stressed (24). A 1997 study suggested that type 1 patients with a history of a psychiatric illness might be at increased risk for developing diabetic retinopathy. Those patients with a psychiatric history were found to have a higher average HbA1c (25). Children whose relatives made more critical comments had significantly poorer glucose control. Interestingly enough, emotional over involvement between family members was not correlated with poor diabetic control (26). Diabetic adolescents had a higher incidence of suicidal ideation than expected. Not living in a two-parent home was associated with poorer long-term diabetes control (27). In a study from the University of California, Los Angeles, patients with higher scores on the Beck Depression Inventory (BDI) were more likely to experience complications of diabetes (28).

In psychosomatic medicine, it had been researched for long years whether there was a diabetes-specified personality type. Dunlar and Alexander searched for subconscious disagreements specific to diabetics and found out oral characteristics. But it is controversial whether these characteristics are premorbid or secondary to disease. These people experience decreasement in energy levels, chronic fatigue, irritability, depression and delay in psychosexual maturation (2).

Recent studies have suggested that effective treatment of depression can improve diabetic control. In a study by Lustman and colleagues, glucose levels were shown to improve as depression lifted (18).

Depressive symptom severity is associated with poorer diet and medication regimen adherence, functional impairment, and higher health care costs in primary care diabetic patients (29-31). Based on findings of an increased prevalence of diabetes among those with a major depressive disorder, "depression may have an impact biologically" that affects insulin usage (6).

In a 10-year prospective trial of 24 children with insulin-dependent diabetes mellitus, three factors were independently associated with the risk of retinopathy: duration of diabetes, duration of time with poor glycemic control and duration of time with symptoms of major depression (34).

There was a threefold increase in incidence of coronary disease in the diabetic patients with depression versus in those without depression (32).

There has been some speculation, that serotonin dysfunction may be a factor in both depression and lack of glycemic control. Preliminary evidence has shown that serotonin may increase response to insulin (33).

Making the diagnosis

On the basis of Beck Depression Inventory scores, cognitive symptoms are the most reliable means to separate diabetic depressed from diabetic non-depressed patients (35,36). In the diagnosis of depression; one should look for affective and cognitive symptoms, rather than the somatic-vegetative signs (2). Panic attacks may resemble hypoglycemic episodes and vice-versa (14).

Many newly diagnosed diabetics go through the typical stages of mourning. These are denial, anger, depression and acceptance (14). They may also show rebellion, anxiety, pathological dependency and regression (2). Often, individuals with depression do not realize that they are depressed. It is easy to attribute the symptoms of depression to the diabetes.

Symptoms of depression

These are based on the Diagnostic and Statistical Manual of the American Psychiatric Association, 4th Edition (DSM-4) (37). A clinician would diagnose depression if a patient had five or more of the following symptoms for at least two weeks:

- Depressed mood for most of the day
- Decreased pleasure in normal activities
- Difficulty sleeping or significantly increased need to sleep
- Weight loss or weight gain.
- Feelings of guilt or worthlessness
- Low energy level
- Difficulty making decisions or concentrating
- Suicidal thoughts
- Feeling agitated or sluggish nearly every day

Selection of antidepressant agents

Physicians generally select among TCAs, SSRIs, and other newer antidepressant agents to treat depression, reserving monoamine oxidase inhibitors and electro convulsive therapy largely for severe, unresponsive cases (38). Factors affecting the selection of an antidepressant for patients with diabetes include presenting symptoms, coexisting medical conditions, drug interactions (patients with diabetes typically take many medications), and side-effect profiles (38,39). The older tricyclic antidepressants can increase glucose levels in non-depressed diabetics (14).

TCAs have the potential for hyperglycemia, weight gain and orthostatic hypertension and other cardiovascular side effects. Drug interactions with other medications are another problem with TCAs (38). TCAs are well-known to lead to "sweets" cravings and weight gain (40,41). Also their effect to impair memory, worsens the patient's cooperation with the glycemic control instructions (40).

Since 1964, MAOIs are known to suddenly reduce plasma glucose to the degree of requiring emergency intravenous glucose (42), and so are not a good choice for the diabetic patient.

In the studies of antidepressants in diabetics, nortriptyline and fluoxetine effectively treated depression (1,18). There have been four studies on the use of fluoxetine in NIDDM patients (43-46). Treatment with fluoxetine also improved glycemic control and reduced severity of depression (1,46). The combination of cognitive–behavioral therapy (CBT) and supportive diabetes education proved to be effective in treating depression in patients with diabetes, and improved glycemic control (20). The antianxiety agent alprazolam was also found to improve glucose regulation (47).

Treatment of depression with selective serotonin reuptake inhibitors (SSRIs) and other newer classes

of antidepressants has not been associated with hyperglycemia in persons without diabetes (41). Although weight gain and sedation are not generally caused by the SSRIs and other newer antidepressants, some of them cause agitation, gastrointestinal distress, and sexual dysfunction. SSRIs are easier to administer and have fewer side effects, so they are more often used as the first line antidepressants. Decreased sexual desire may be a sensitive issue for some diabetics, especially those who have some sexual difficulty due to their diabetes. Often, treatment of the depression can result in much better sexual functioning. Bupropion, mirtazapine, and nefazodone do not usually cause sexual dysfunction. Bupropion is sometimes used in combination with an SSRI to alleviate sexual dysfunction (i.e., decreased libido, anorgasmia, delayed ejaculation). Drug interactions with SSRIs are not common, but this class of antidepressants interferes with the cytochrome P450 system (principally the 2D6 isozyme) and may interfere with the metabolism of other medications in patients (14,38). SSRIs may decrease fasting plasma glucose and induce weight loss in patients with diabetes (41). Even in patients who are not depressed, SSRIs may be useful in treating diabetic neuropathy (48).

Potential benefits of depression management in persons with diabetes (39)

- Depression relief, anxiolysis
- Restoration of normal sleep and eating habits
- Behavioral activation (e.g., increased physical, social, and occupational activities)
- Pain relief, improved pain tolerance
- Improved illness coping and general functioning
- Decreased somatic preoccupation
- Enhanced sexual functioning
- Improved treatment compliance and glycemic control

Psychotherapy

Cognitive psychotherapy is one of the methods that has demonstrated good results for depression (14,20). In this type of therapy, the individual identifies thought patterns associated with a depressive, hopeless outlook. Frequently these thought patterns are based on erroneous assumptions about self and others. The therapist helps the patient monitor such thoughts and to replace them with more effective positive ways of thinking. Cognitive therapy can also be helpful in non-depressed individuals who are having trouble with their diabetic management.

The importance of follow-up

Residual symptoms of depression after treatment predict recurrence (49). In general; it'is important that the patients be almost asymptomatic. The presence of diabetes complications and hyperglycemia predicts recurrence of depression following successful treatment, as well as diminished response to both psychotherapy and pharmacotherapy (23,49,50). About 60% of patients who are treated with anti-depressants can be expected to achieve a remission of depression, and approximately the same is true for psychotherapy (23). Diabetic patients have about one episode of depression annually and even after successful treatment, recurrence is really the norm rather than the exception (51).

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