Depressive Symptoms and Glycemic Control in Type 2 Diabetes Mellitus
Tip 2 Diyabetli Hastalarda Depresif Belirtiler ve Glisemik Kontrol

Feryal Çam ÇELİKEL, Ömer SAATÇIOĞLU*, Faruk KUTLUTÜRK**, Birgül CUMURCU, Bünyamin KISACIK**
Gaziosmanpaşa Üniversitesi Tıp Fakültesi Psikiyatri ve **İç Hastalıklar Anabilim Dalı, Tokat
*Bakırköy Ord. Prof.Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi, İstanbul, Türkiye

ABSTRACT
Objective: To determine whether the level of depressive symptoms is associated with poor glycemic control in type 2 diabetes patients.

Method: The sample was comprised of 83 outpatients (mean age 50.92±8.42 years). Participants were applied a structured clinical interview and the Montgomery Asberg Depression Rating Scale (MADRS). Metabolic control was measured by glycosylated hemoglobin A1c (HbA1c) levels.

Results: MADRS scores were not correlated with HbA1c levels (r = 0.065, p = 0.561). No relationship was found between higher levels of depression and longer duration of diabetes (r = 0.081, p = 0.468). A significant difference was observed in MADRS scores with regard to the different treatment regimens (F=5.84, df=3, p<0.001).

Conclusions: Our data showed no association between depressive symptoms and glycemic control. The lack of correlation between MADRS scores and HbA1c levels may be related to the restricted range of depression, the use of MADRS itself and may be due to the variability in sampling and the eligibility criteria.

Key words: Diabetes type 2, depressive symptoms, glycemic control

ÖZET
Amaç: Tip 2 diyabetli hastalarda depresif belirli düzeyinin glisemik kontrol ile ilişkisini araştırılmak.

Yöntem: Ayaktan tedavi gören 83 tip 2 diyabet hastasına (yaş ortalaması 50.92±8.42 yıl) yapılandırılmış psikiyatrik görüşme, Montgomery Asberg Depresyon Değerlendirme Ölçeği (MADÖ) uygulandı ve glikozillenmiş hemoglobin A1c (HbA1c) düzeyleri ölçüldü.

Bulgular: MADÖ puanları HbA1c düzeyleri ile ilişkili bulunmadı (r = 0.065, p = 0.561). Depresyon şiddetini ile diyabetin süresi arasında anlamlı bir ilişki belirmemiş (r = 0.061, p = 0.468). Farklı diyabet tedavileri alan hasta grupları arasında MADÖ puanları açısından anlamlı farklılık gözlendi (F=5.84, df=3, p<0.001).

Sonuç: Bulgularımızla göre, tip 2 diyabetli hastalardan oluşan bu örnekleme depresif belirtilerle glisemik kontrol arasında anlamlı bir ilişki göze gelmemiştir. (Nöropsikiyatri Arşivi 2007; 44: 134-8)

Anahtar Kelimeler: Tip 2 diyabet, depresif belirtiler, glisemik kontrol

Introduction

Maintenance of good glycemic control is the focus of diabetes therapy. Clinical factors that might affect prognosis are judged largely in relation to their effects on this parameter. It is a historical hypothesis that emotional disturbances possibly contribute to metabolic stability. Clinical and subclinical expressions of depression are present in more than 25% of patients with type 1 or type 2 diabetes (1-3). In spite of the wide literature, no consistent evidence exists regarding the association between depressive symptoms and poor glycemic control.

The role of depression in type 2 diabetes may primarily be through the adverse influence, such as affecting adherence to medical regimens (4-7). Besides, a psychiatric disorder may provoke biological changes in vulnerable individuals that eventuate in identifiable type 2 diabetes (7). It is pointed out that depression makes symptoms of poorly controlled diabetes less tolerable; thus, some persons with undiagnosed diabetes mellitus may become more symptomatic and seek medical care sometime after the onset of depression (4).

In order to improve diabetic outcome, reliable determination of both metabolic control and an existing psychiatric disorder is crucial. Glycosylated hemoglobin A1c (HbA1c) is a measurement reported as a percentage of total hemoglobin (8,9). Because the proportion of hemoglobin that is glycosylated is a function of the glucose concentration to which the erythrocytes are exposed, the measure correlates with the average blood glucose concentration over time. Since the half-life of the erythrocytes is approximately 120 days, HbA1c reflects the average level of glycemic control during that period (10).
In several previous studies, the association of depression, either by symptoms or the diagnosis, with glycemic control have been investigated (6,11-13). Patients with poorer metabolic control had significantly higher overall rates of diagnosable psychiatric illness than did patients in better metabolic control (4,5). Psychiatric illness may constitute a chronic stressor that leads, via direct metabolic or indirect behavioral pathways, to poorer glucose control. It is also possible that chronically unstable diabetes, as would be implied by repeatedly poor HbA1c, may potentiate psychiatric illness in particular patients. Poor glucose regulation per se may result in the increased reporting of psychiatric symptoms.

Studies documenting the impact of depression on glycemic control have varied in the methods of assessment, from self-reported questionnaire data to standardized psychiatric interview protocols (4,14,15). Self-report questionnaires provide only symptom endorsement. They do not allow clinical evaluation of the degree to which symptoms are organized into episodes, impaired functioning, or represent somatic manifestations of diabetes-related complications unrelated to mood syndromes. Thus, a study would benefit from a methodology in which the patient is evaluated by a structured psychiatric interview as well as being assessed by a scale, measuring depression. Among these scales, because of its reliance on cognitive features of major depression, Montgomery Asberg Depression Rating Scale is less likely to misdiagnose depression in patients with general medical illness (16).

In this research we aimed to conduct a cross-sectional study in a group of type 2 diabetic outpatients. The objectives are: 1) to determine the frequency of depressive symptoms in this sample, 2) to determine the relationship between depressive symptoms and metabolic control as measured by HbA1c.

Materials and Methods

Sample and Procedure

The sample was comprised of 83 outpatients, 67 women, 16 men, with a mean age of 51±8.42 (range of 23-70) years. All subjects were recruited from a single center, the outpatient clinic of the Department of Internal Medicine in Gaziosmanpasa University School of Medicine. Each subject, diagnosed as type 2 diabetes mellitus by an internist, was then evaluated by a psychiatrist. All patients who were invited to the study agreed to participate. After complete description of the study, written informed consent was obtained from each subject.

Measures

A detailed sociodemographic data form was used for each subject. Medical information regarding diabetes was recorded, and HbA1c values were used as metabolic control parameter. Participants were applied Structured Clinical Interview for DSM-IV-Clinical Version (SCID-I/CV) (17), Turkish version (18).

Depressive symptoms were explored by using Montgomery Asberg Depression Rating Scale (MADRS). MADRS is a 10-item checklist. Items are rated on scale of 0-6 with anchors at 2-point intervals. Scores on the MADRS range from 0 to 60.

Reliability for the total score in several studies ranged from 0.76 to 0.95 (19,20). The scale has been found valid and reliable in Turkish (21).

Statistical Analysis

Pearson’s correlations and chi-squared analyses were conducted to assess the relationships between independent variables and the depressive symptoms. The Independent-Samples T Test procedure was used to compare the means for two groups of cases. For a quantitative dependent variable by a single factor (independent) variable One-Way ANOVA procedure analyses were performed. All the statistical analyses were performed using SPSS, 13.0.

Results

Characteristics of the study sample

Selected characteristics of the study participants are shown in Table 1. The patient sample was predominantly women (80.7%), married (85.5%), house-wives (65.1%), and living in the city (85.5%). Thirty-two patients (38.6%) had only primary school education whereas only 7 patients (8.4%) were university graduates. Regarding the disease status, 72 patients (87%) had no complications of diabetes. Five (6%) patients had erectile dysfunction, and 3 patients (4%) had neuropathy. There were one patient each who had nephropathy, nephropathy plus neuropathy, and retinopathy plus erectile dysfunction. In the current sample of type 2 diabetes patients there were four main treatment regimen groups: 1. diet and exercise (n=6; 7.2%), 2. oral antidiabetics (n=36; 43.4%), 3. insulin (n=36; 43.4%), and 4. oral antidiabetics plus insulin (n=5; 6%).

Seventeen (20.5%) type 2 diabetic patients were diagnosed as major depressive disorder, and 59 patients (71%) had no psychiatric diagnosis at all. Four patients (4.8%) had the diagnosis of anxiety disorder, not otherwise specified, 2 (2.4%) had conversion disorder, and one patient (1.2%) had panic disorder.

Table 1. Characteristics of the study sample

<table>
<thead>
<tr>
<th>Measure</th>
<th>(mean ±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.92±8.42 (23-70)</td>
</tr>
<tr>
<td>MADRS score</td>
<td>11.15±9.23 (0.0-37)</td>
</tr>
<tr>
<td>HbA1c levels (%)</td>
<td>7.92±2.01</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>6.68±6.92 (0.3-26)</td>
</tr>
<tr>
<td>Diabetic complication</td>
<td></td>
</tr>
<tr>
<td>erectile dysfunction</td>
<td>5 (6)</td>
</tr>
<tr>
<td>retinopathy</td>
<td>3 (3.6)</td>
</tr>
<tr>
<td>nephropathy</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>nephropathy + neuropathy</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>retinopathy + erectile dysfunction</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Diabetic regulation</td>
<td></td>
</tr>
<tr>
<td>well (HbA1c ≤ 7)</td>
<td>41 (49.4)</td>
</tr>
<tr>
<td>moderate (HbA1c = 7-8)</td>
<td>32 (38.6)</td>
</tr>
<tr>
<td>poorer (HbA1c &gt;8)</td>
<td>10 (12)</td>
</tr>
<tr>
<td>Psychiatric history positive</td>
<td>24 (28.9)</td>
</tr>
</tbody>
</table>
Assessment of parameters of metabolic control

In this study, we used HbA1c as a measure for metabolic control. The mean HbA1c level of the study sample was 7.92±2.01. In addition, we recorded the internalist's evaluation for a general consideration of metabolic control. Generally, the range for (nondiabetic) normal subjects is 4.2% to 6.0%. Patients were sorted into three groups: first, a "well regulated" group exhibiting relatively "better" glucose control (HbA1c < 7), second, with only "moderate" glucose control (HbA1c = 7-8), and third a group having comparatively "poorer" glucose control (HbA1c > 8) (22). Forty-one (49%) patients were considered as well-regulated, 32 (39%) patients moderate, and 10 (12%) as poorer (Table 1).

Assessment of depressive symptoms

As shown in Table 2, depression levels (as measured by MADRS) showed no correlation with either HbA1c levels or duration of the disease. As shown in Table 3, the mean HbA1c levels were highest in the subgroup of patients on the treatment regimen of oral antidiabetics plus insulin. Yet, no statistically significant difference was found between four groups. Table III also displays the association between different treatment regimens and MADRS scores. Type 2 diabetes patients taking various treatment regimens differed significantly in their depression levels, as measured by MADRS (F=5.84, df=3, p<0.001). Patients with no drugs but only diet and exercise as well as those taking oral antidiabetics seemed to score higher on MADRS. Scores lowered significantly in the group of patients who were treated with insulin alone.

Discussion

Our data do not underline an association between the level of depressive symptoms and hyperglycemia. While many studies support that there is a link between poor metabolic control and depression, there are studies that deny this relationship. In de Groot’s study (8), type 2 diabetes patients with a lifetime history of major depression did not have significantly worse metabolic control than those with no history of psychiatric illness. In a study by Robinson et al. (14), in a combined sample of type 1 and type 2 adults, the investigators did not find significant differences in current glycemic control, as indexed by HbA1c, among normal controls and patients who were currently depressed cases. Our study is in accordance with Robinson et al.’s study except that we did not have a control group of healthy individuals for comparison. What we could show was that no relationship existed between the level of depressive symptoms and diabetes regulation in this group of type 2 diabetics. Similarly, in a recent study by Georgiades et al. (23), changes in depressive symptoms were observed not to be associated with changes in HbA1c or fasting glucose levels over a 1-year period in either patients with type 1 or type 2 diabetes.

Our sample seemed relatively free of comorbid psychiatric problems. Seventy-one percent of all cases had no psychiatric disorder at all. Only one fifth (20.5%) of our diabetic patients were diagnosed as depressives and this finding is reflected in the mean MADRS score of the total sample, which is 11.15±9.23. The majority (73.5%) were in a restricted range of mildly depressed as a global severity measure (16).

Variable findings from the studies may be attributed to sampling differences. In several studies (4,8,14), a combined group of type 1 and type 2 samples was used to conduct their analyses, with no separation by diabetes type. Nevertheless,
de Groot et al. (8) showed in their study that the relationship of glycemic control to major depression differed by diabetes type. Combining type 1 and type 2 patients into a single sample makes it difficult to understand the relationship of glycemic control to depression. Type 1 and type 2 diabetes are distinct diseases with differing etiologies, ages of onset, and treatment regimens. Given these differences, the relationship between glycemic control and depression may be expected to differ between diabetes types and even across diabetes treatment regimens (8).

In our study, only type 2 patients were recruited and among them a significant difference was observed in MADRS scores with regard to the different treatment types. However, unlike expected, MADRS was lowest in the group using insulin as a treatment regimen. In one study, insulin was thought to have the ability to move through the blood-brain barrier and enhance the transport of the amino acid tryptophan, promoting increased production and activity of serotonin (24). Although it is well beyond the aims and the scope of this study, insulin might have had a preventive effect on depressive symptoms in this group of patients. Another comment on this point might be linked with the sample itself. These patients were all followed up by a tertiary center, the outpatient clinic of a university hospital. Appropriate medical support may possibly be a more crucial factor than the disease severity in coping with type 2 diabetes in our patient group. A recent study to clarify the argument whether treatment regimen may be an important mediating factor in the relationship of major depression to glycemic control is performed by Surwit et al. (25). In that study, the authors hypothesized that complexity of self-care regimen rather than the type of diabetes, is more important in determining the relationship of depression to glycemic control and concluded that depressive symptoms are not correlated to glycemic control in patients taking fewer than three injections per day.

Meta-analysis methods have demonstrated the relationship of depression with poor glycemic control and an increased risk for diabetes complications (26-28). Our patient sample is relatively less physically ill (e.g., 87% of the sample had no diabetic complication at all). Likewise, the mean MADRS score of the sample is 11.15±9.23, which correlates with a global severity measure of mild depression (29). The lack of an association between depression levels with regard to the presence of diabetic complication in our patient sample might lead us to suspect that the severity of illness (i.e., the high incidence of diabetic complications) accounts for an increase in psychiatric illness. The traditional argument that depressive symptoms result from the hardships imposed by diabetes and its complications, is supported by these data. Nevertheless, further observations from longitudinal studies or from studies dating depression and diabetes onsets in type 2 diabetes are needed to clarify this point.

In their study, Robinson et al. (14) reported worsened postprandial blood glucose levels for patients with a past history of depressive illness. The correspondence of time and glycemic control is suggested as a potentially important indicator of an underlying mechanism that might be responsible for a relationship between psychiatric history and glycemic control. In our study, however, no association was shown between a positive psychiatric history and glycemic control. Similarly, in de Groot’s study, type 2 patients showed consistent glycemic control levels regardless of depression history status (8).

Most studies examining the relationship between depression and glycemic control have been studies with cross-sectional designs (4,14,30). Exceptionally, Lustman et al. (31) reported 5-year follow-up data for patients undergoing a randomized clinical trial of antidepressant treatment. These data documented worsened glycemic control in patients with recurrent major depression compared to baseline, yet comparison of glycemic status for nondepressed controls at baseline and follow-up was not presented. In another Lustman study (32), reduction in depressive symptoms had a positive effect (hypoglycemic) on blood glucose levels. The authors hypothesized that adherence with diabetes regimen accounted for the relationship between depressive symptoms and HbA1c, although small sample sizes prevented empirical validation of this hypothesis. Similarly, in a six-year longitudinal study by Roy et al. (33), depression was associated with both poor glycemic control in patients with type 1 diabetes.

The sample size of the current study places limitations on the generalizability of study findings, as well. Larger sample sizes would enable comparisons across various disease characteristics. Likewise, samples drawn from multiple diabetes treatment sites would further enhance the generalizability of study findings. In the current study, the sample was drawn from a single source. The lack of a control group is another limitation that should be mentioned for our study.

In spite of the growing literature, the direction of the relationship between depression and glycemic control remains unclear. Depression may lead to poor glycemic control or may be the result of failed efforts to improve blood glucose control. Longitudinal studies that track the course of disease, psychiatric comorbidity, and glycemic control at multiple points in time are needed to distinguish between these variables.

**Conclusions**

Depressive symptoms might be expected to affect the prognosis in diabetes and therefore be associated with poor metabolic control. Although data from observational studies as well as clinical trials support the depression-hyperglycemia association, this is not underlined by our data. The lack of correlation between MADRS scores and HbA1c levels may be related to the restricted range of depression, the use of MADRS itself (which is less likely to misdiagnose depression in patients with general medical illness), and may be due to variability in sampling and the eligibility criteria.
References


