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Psychiatric referral and glycemic control of Egyptian type 2 diabetes mellitus patients with depression

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ABSTRACT

Objective: To evaluate the relationship between psychiatric referral acceptance for fluoxetine treatment and glycemic control in type 2 diabetes mellitus (T2DM) Egyptian patients with depression.
Methods: Patients with T2DM who attended the diabetes outpatients clinic at Zagazig University Hospital, Egypt, between May 2013 and April 2015 and who scored ≥20 on screening with the Major Depression Inventory (MDI) ($n = 196$) were offered a psychiatric referral for fluoxetine treatment and monitoring. Decliners (56.1%) received time/attention matched care via diabetologist visits (attentional controls). Fluoxetine patients and controls were compared at the time of the offer (T1) and 8 weeks later (T2). Factors that significantly correlated with glycemic control were used in a linear regression analysis as the independent variables.
Results: Eighty-six patients (43.9%) accepted psychiatric referral. Most of them (97.7%) remained throughout the study adherent to fluoxetine (mean daily dose = 31.9 mg). At T2, these patients, in comparison to controls, showed a reduction from baseline in MDI, fasting plasma glucose and glycosylated hemoglobin (HbA1c) levels (P for all comparisons <.001). In the final model of a regression analysis, 65.9% of the variation in percentage change in HbA1c was explained by adherence to antidiabetics, psychiatric referral acceptance and Internalized Stigma of Mental Illness (ISMI) and MDI scores.
Conclusion: In T2DM patients with depression, psychiatric referral acceptance for fluoxetine treatment is a significant predictor of both depression and glycemic control improvements.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a global health crisis that threatens the economy of every country, particularly developing countries [1]. Depression is yet another major global health problem [2]. It will result in more years of life lost to disability than any other illness by the year 2030, as predicted by the World Health Organization [3]. The prevalence of these two serious conditions is rising at an alarming rate [4–6]. Moreover, most previous research has shown that diabetes and depression frequently occur together [7], though the rates of this comorbidity may vary widely between countries and between populations within countries [8]. The nature of the relationship between depression and diabetes is complex, but this comorbidity is most likely part of a bidirectional interaction with each of them, wherein one acts as an independent risk factor for the development of the other [9] and adversely affects their health-related outcomes [10,11]. In people with T2DM, the risk of developing depression is double that in nondiabetic medical people [12], and people with depression have a 37% increased risk of developing T2DM compared with those without depression [13]. The cooccurrence of depression with T2DM increases the burden of both illnesses [14]. Thus, in patients with T2DM, depression exhibits a more chronic and severe course [15,16]. Furthermore, depression in T2DM patients is associated with worse glycemic control [17,18], poorer self-care behaviors that are important to diabetes care [19,20] and more adverse outcomes, including increased functional impairment [21], decreased quality of life [22], decreased personal income [23], increased health care costs [24], increased diabetes-related complications [25] and increased cardiovascular and general mortality [26–28] compared with patients with depression or diabetes alone.

Conversely, it seems plausible that if depression could be treated in patients with comorbid diabetes, then these adverse outcomes would automatically be reversed, thereby resulting in improved glycemic control [29]. However, whether [30–31] treatment for depression can improve depressive symptoms in people with diabetes is controversial. Evidence concerning improvement in glycemic control through the treatment of depression is even more controversial [32]. Thus, in a well-designed integrated care, single-blind randomized controlled

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trial for depression in diabetes (mainly type 2), Katon et al. [33] found that enhanced depression care improved depression, but not glycemic control. Conversely, in a more recent randomized, double-blind, placebo-controlled study, pharmacological treatment of depression with an selective serotonin reuptake inhibitor (sertraline) significantly improved A1C levels compared with a placebo [34]. Inconsistent results of previous studies may be due to a variety of causes, such as sample heterogeneity (including type 1 diabetes mellitus, T2DM or even both in the same sample), differences in measurements (different clinical interviews and self-report questionnaires) and variation in study duration and treatment type.

Although the use of antidepressants in patients with diabetes has appeared to be rising over recent years, there are concerns that antidepressants may adversely affect glucose metabolism. A number of recent systematic reviews and metaanalyses have concluded that the use of antidepressants is associated with an increased risk of diabetes [35–37]. Additionally, the use of atypical antipsychotics as an adjunctive treatment for therapy-resistant depression is becoming increasingly common in clinical practice despite its further worsening of metabolic status [38]. Therefore, it is likely that some physicians might be reluctant to prescribe antidepressants to their depressed diabetes patients or even to refer them to specialized mental health professionals. Diabetes patients with depression are all the more likely to fear side effects and addiction to medication [10]. It is also possible that patients would refuse referral to psychiatric services perhaps to avoid being stigmatized by the label of mental illness [39].

Despite this social stigma, most of the literature is derived from studies conducted in developed countries. Data on the effects of offering treatment for depression in people with diabetes in a developing country, such as Egypt, are not well documented despite the fact that the number of adult patients with diabetes in Egypt is the highest in the Middle East and North Africa Region [40].

Furthermore, information on treatment adherence in diabetes patients with depression is limited, though there is some evidence that adherence to antidepressant treatment in people with long-term physical conditions and depression is increased with the referral to psychological treatment services [41]. This is important because, from the available literature, which is mostly American, there is indication that adherence to antidepressant treatment is associated with increased adherence to diabetes or other comorbid disease medication [42]. Consequently, adherence to antidepressants maximizes opportunity for improving outcomes such as glycemic control [43,44], which can be observed within only few weeks [45]. Therefore, in this study of T2DM Egyptian patients with depression, we wanted to evaluate the relationship between accepting psychiatric treatment and glycemic control. We hypothesized that, in a sample of Egyptian patients with comorbid T2DM and depression, the acceptance of psychiatric referral for treatment with fluoxetine for a period of 8 weeks would predict glycemic improvement.

2. Methods

An 8-week prospective study was undertaken at the out-patient clinic of the Diabetes Unit, Internal Medicine Department, Zagazig University Hospital (ZUH), Sharkia, Egypt. The ZUH is a tertiary health care facility with a catchment area of approximately 6 million people. Ethical approval for the study was obtained from the research ethics committee at the Faculty of Medicine, Zagazig University.

2.1. Study design and participants (Fig. 1)

For a period of 2 years from May 2013 to April 2015, consecutive patients with T2DM attending the diabetes out-patient clinic were approached for depression screening prior to study inclusion. Patients were screened if they provided a written informed consent to participate in the study. Refusal of possible referral to the psychiatric out-patient clinic, however, did not disqualify a patient from consenting to participate in the study. To be screened, patients had also to be over 20 years of age, have T2DM diagnosis according to the criteria of the American Diabetes Association [46] and be on oral hypoglycemic therapy for a minimum duration of 1 year; however, insulin users were excluded. Additionally, we did not include patients with advanced diabetic complications, such as blindness and amputation, or seriously ill patients with other medical conditions and females who were pregnant or lactating. Moreover, patients were not included if they had history of depression prior to the onset of diabetes; if they had past or current other significant psychiatric problems, substance use (other than tobacco-related) disorders and used psychiatric medication; or if they had a family history of depression.

Using the Arabic version of the Major Depression Inventory (MDI) [47], 620 patients were screened to determine their eligibility for study enrollment. One hundred ninety-six patients (31.6%) who were identified as depressed (with a score of ≥20 on MDI) and who fulfilled the other inclusion/exclusion criteria constituted the study sample. These patients were interviewed at baseline (T1) by a diabetologist. Towards the end of the interview, a psychiatric referral was offered. Patients who accepted the offer were asked to visit the psychiatric out-patient clinic once a week for 8 weeks to receive fluoxetine hydrochloride. In the weekly follow-ups, patients were monitored for compliance, adverse events and fluoxetine dose adjustment within the range 20–60 mg/day according to individual needs. Patients who refused psychiatric referral made weekly visits to the diabetes clinic for follow-up assessments. By receiving time/attention matched care via diabetologist visits, therefore, these patients served as "attentional controls". All study patients, whether they accepted or refused psychiatric referral, were maintained on their established oral hypoglycemic drugs until final assessment at week 8 (T2).

2.2. Assessments

2.2.1. Demographic and clinical data

These data were obtained with semistructured interviews. Measurements of height and weight were taken twice by trained research assistants while the subjects were in a barefoot standing position and dressed in light clothing. Means of these measurements were used to calculate the body mass index (BMI) as the weight in kilograms divided by the square of height in meters.

2.2.2. Major Depression Inventory

This Inventory was developed by Bech et al. [48] to measure symptoms of depression in accordance with the symptom guidelines defined by the WHO classification for unipolar depression (*International Statistical Classification of Diseases, 10th Revision*) and the American Psychiatric Association classification for major depression (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*). The original English language MDI has been translated into several languages. The Arabic version of the revised MDI was used here. It contains 10 items. However, items 8, 9 and 10 are divided into two subitems, "a" and "b". Only the higher scores of either "a" or "b" for each of these three items are included in the statistical analysis. Participants used a six-point Likert response format to indicate how frequently in the past 14 days each depressive symptom had occurred. The theoretical total score ranges from 0 (no depression) to 50 points (extreme depression). A score of ≥20 indicates the presence of depression of any degree, major and minor [49]. As we reported elsewhere, the MDI Arabic version is a reliable and valid instrument among Egyptian populations [47]. Cronbach's alpha value in the current study was .88.

2.2.3. Internalized Stigma of Mental Illness [50]

This widely used self-rated 29-item scale measures the subjective experience of stigma. Items are grouped into five subscales: Alienation, Stereotype Endorsement, Perceived Discrimination, Social Withdrawal and Stigma Resistance. Each item is rated on a four-point Likert scale