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Depressive symptoms and glycemic control in youth with type 2 diabetes participating in the TODAY clinical trial

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Summary

The relationship between depressive symptoms and glycemic control in youth with type 2 diabetes was assessed at baseline (n=682), 6, and/or 24 months (n=576). Neither baseline nor persistence of depressive symptoms was significantly associated with maintenance of glycemic control. Nevertheless, depressive symptoms were common, suggesting the importance of repeated screening.

Keywords

Adolescent; depressive symptoms; type 2 diabetes

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Materials developed and used for the TODAY standard diabetes education program and the intensive lifestyle intervention program are available to the public at https://today.bsc.gwu.edu/.

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1. Introduction

Depression is a mental health disorder often first evidenced in childhood or adolescence [1]. Type 2 diabetes (T2D), once considered an “adult” disease, is increasingly prevalent in this age group [2]. Although depression has been associated with poorer glycemic control in youth with type 1 diabetes [3] and in adults with type 2 diabetes [4], little is known about the course of depressive symptoms or their relationship to glycemic control in youth with type 2 diabetes. The TODAY (Treatment Options for type 2 Diabetes in Adolescents and Youth) study, the first longitudinal investigation of treatments for youth with type 2 diabetes, provides a unique opportunity to better understand the course of depressive symptoms over time and their relationship to glycemic control in this understudied population.

2. Methods

TODAY, a collaborative, multi-center randomized clinical trial (15 clinical centers and a data coordinating center), was funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health. The study design, objectives and primary outcomes have been previously reported [5]. An External Evaluation Committee convened by the NIDDK approved the protocol as did the individual Institutional Review Boards. All participants provided informed consent; minor children confirmed assent per local guidelines. Enrollment was May 2004 – February 2009 (total n=699). Eligible participants were 10–17 years of age, with type 2 diabetes <2 years and a BMI ≥85th percentile at diagnosis. Participants were followed for a minimum of two years.

All participants completed a pre-randomization run-in period to discontinue non-study diabetes treatments, achieve hemoglobin A1c (HbA1c) <8% on metformin only, and demonstrate adherence to the study protocol. After successful completion of run-in, participants were randomly assigned to treatment: metformin, metformin plus rosiglitazone, or metformin plus an intensive lifestyle intervention. Medical management occurred every 2 months in year 1 and quarterly thereafter; major outcomes were assessed at baseline, 6, and 24 months. Youth randomized to the metformin plus rosiglitazone arm had longer duration of sustained glycemic control when compared with those randomized to the other two treatment arms [5].

2.1 Assessment of Depressive Symptoms

At baseline, 6 and 24 months, participants ≤15 years completed the Child Depression Inventory (CDI) [6] and those ≥16 years completed the Beck Depression Inventory-II (BDI-II) [7]. These standardized self-report questionnaires assess the presence and severity of depressive symptoms. Clinically significant depressive symptoms were defined as: CDI score ≥13 [6]; BDI-II score ≥14 [7].

2.2 Assessment of Glycemic Control

Inadequate glycemic control (treatment failure) was defined as HbA1c ≥8% over 6 months or sustained metabolic decompensation requiring insulin [3].

2.3 Study Sample

Baseline data are reported for 682 of 699 youth (97.6%) randomized into the TODAY trial who completed an assessment of depressive symptoms at baseline (pre-randomization). Longitudinal data are reported for 576 who had measures of glycemic control plus an assessment of depressive symptoms at 6 or 24 months (360 at all 3 visits, 194 at baseline and 6 months only, 22 at baseline and 24 months only) before treatment failure. At baseline, presence of depressive symptoms in the longitudinal analysis sample of 576 was not different from the 106 with baseline data, but excluded from the analysis (14.4% versus 15.1%, respectively, p=0.8541).

2.4 Statistical Analyses

The present study reports on secondary analyses of the TODAY study data. Descriptive statistics (mean ± standard deviation or percentage) were calculated, and ANOVA for continuous variables (HbA1c values) and chi-square test for categorical variables (depressive symptoms) were conducted. The relationship between treatment failure (inadequate glycemic control) and longitudinal depressive symptoms was assessed using time-to-event survival methods (SAS PROC LIFEREG).

3. Results and Discussion

At baseline, average age was 13.9 (2.0) years, 65.5% female, 20.2% non-Hispanic White), and 41.3% lived in a household with an annual income <$25,000. Of the 14.5% reporting the presence of clinically significant depressive symptoms, 73.7% were female versus 64.2% of participants with no symptoms, but this was not significantly different. In the longitudinal analysis sample of 576 participants, 454 (78.8%) never had clinically significant depressive symptoms, 69 (12.0%) had symptoms present at 1 of the 3 visits studied, 44 (7.6%) had symptoms at 2 of the 3 visits, and 9 (1.6%) had symptoms present at all 3 visits. Of the 493 participants negative for depressive symptoms at baseline, 39 (7.9%) subsequently had evidence of clinically significant symptoms at 6 and/or at 24 months.

Survival analysis showed that clinically significant depressive symptoms at baseline did not predict adequacy of glycemic control (p=0.29). The longitudinal analysis sample of 576 was used to examine whether there was a cumulative effect of persistent presence of depressive symptoms during 2 years of follow-up. There was no relationship between treatment failure (inadequate glycemic control) and presence of depressive symptoms at baseline (p=0.46), or as number of visits reporting the presence of clinically significant depressive symptoms increased (p=0.64). Although we did not observe a relationship between clinically significant symptoms of depression and inadequate glycemic control in our youth, the long-term impact of depressive symptoms on comorbidities and disease progression in this cohort are unknown.

Participating in a clinical trial and experiencing the increased contact and intensified attention may have served to mitigate depressive symptoms as well as the impact of symptoms on glycemic control. For example, youth in two of the treatment arms received metformin, and its effect on weight and other aspects of functioning such as sleep and eating

could have confounded the relationship between glycemic control and depressive symptoms [8]. Further, although it would have been preferable to base the analysis on a definitive psychiatric diagnosis of depressive disorder resulting from clinical interview, study resources were limited to the more expedient assessment of depressive symptoms using standardized self-report instruments. Finally, diabetes distress (negative mood states and cognitions specific to having a chronic illness such as diabetes), which was not measured, may be more closely associated with glycemic control than the assessment of general depressive symptoms [9,10].

Nevertheless, clinically significant depressive symptoms emerged in 8% of the TODAY cohort who did not report clinically significant symptoms of depression upon entry into the study. These findings lend support to ADA recommendations to assess for depressive symptoms at regular intervals throughout the course of treatment and to refer for management of these symptoms as appropriate [11,12]. Further research examining the relation between depression and glycemic control in community samples of youth with type 2 diabetes is warranted.

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