MANAGEMENT OF DEPRESSION IN ADOLESCENTS WITH TYPE 2 DIABETES

ABSTRACT

Over the past 30 years, the incidence of type 2 diabetes mellitus continues to rise in the pediatric and adolescent population. The increased rates of depression in children with type 1 diabetes have long been established in literature. However, the association of type 2 diabetes and depression has only recently been acknowledged. The purpose of this article is to: 1) review the current literature to examine the incidence of depression and type 2 diabetes in adolescents, and 2) suggest approaches to identify and care for these patients.
INTRODUCTION

Type 2 diabetes mellitus (T2D) has quickly emerged as an epidemic in the pediatric and adolescent population over the past three decades. The Centers for Disease Control and Prevention projects that the incidence of T2D in youth will continue to rise with an estimated 5,000 new cases per year in the under 20-year-old population [1].

The treatment of T2D in a young person entails long-term lifestyle changes and a potentially difficult therapeutic regimen which may include significant lifestyle changes, glucose monitoring, and pharmacological intervention [2]. Traditionally an adult diagnosis, few studies focus on children with T2D. Treatment has been based on knowledge of adult studies or studies of children with type 1 diabetes mellitus (T1D) [3]. Moreover, the management of children and adolescents with T2D poses additional challenges in the form of emotional and psychological difficulties [4].

In 2013, the American Academy of Pediatrics (AAP) created guidelines for newly diagnosed T2D in children and adolescents to assist physicians in management of this condition [5]. These guidelines were developed in collaboration with the Pediatric Endocrine Society and the American Diabetes Association to produce comprehensive recommendations to improve clinical outcomes. These recommendations explicitly define important diabetes terms in the context of young patients, and outline the steps in management from initial diagnosis onward. Their recommendations include a screening schedule for comorbid depression; however, they lack guidance in managing comorbid depression in T2D adolescents.

There remains a need for a practical set of guidelines that physicians can use to better manage T2D patients with depression. This article seeks to review the current literature for management of comorbid T2D and depression in adolescents and considers recommendations for physicians caring for these patients. We will examine the incidence of depression in children with T2D and the effects of depression on their diabetes control.

We searched PubMed and Google Scholar electronic databases for English-language articles published between January 2000 and January 2017. References listed from included literature were reviewed to capture additional articles. Articles reporting information regarding adolescents or youth with T2D and depression were included in this review. This article focuses on depression secondary to T2D in adolescents, and literature was excluded that examined adult patients.

Incidence and Etiology of Depression in T2D

The comorbidity of T1D and depression in adolescents has long been recognized and described in literature [6]. Depression in adolescents with T1D has a prevalence rate for increased risk of depressive symptoms between 14 and 33% [7]. Moreover, the risk for depression further increases as adolescents with T1D develop into young adulthood [8]. Pediatricians have historically been better trained to recognize and address the depression that occurs in patients with T1D. Conversely, T2D was once referred to as adult-onset diabetes and until recently, there have been few studies on adolescents with T2D and little recognition of its comorbidities [9].

The 2012 Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study indicated that 14.8% of adolescents and youth had clinically significant depressive symptoms [8]. Compared to the estimated prevalence of 4-5% in the overall mid-to-late adolescent population, youth with T2D are at markedly greater risk for depression in this age group [10]. Studies of depression in youth with T2D found no significant differences in depression across racial or ethnic groups, ages, gender, or parent education level [4].

However, while studies have not found significant differences in depression rates across groups, the understanding of depression in T2D adolescents is complicated by other factors. T2D has emerged in the pediatric population as a consequence of a worldwide increase in obesity, and adolescents with T2D are predominantly overweight or obese [9]. Eighty-seven percent of participants in the TODAY study had a BMI greater than the 95th percentile [8]. Because there is a reciprocal link between depression and obesity, and T2D is also strongly associated with obesity, the relationship of T2D and depression is inherently confounded by weight [11].
Low socioeconomic status may also contribute to these two diseases. Greater than 25% of youth with diabetes in the TODAY study were from households in which no parent had a high school diploma [8]. Although largely unstudied in adolescents with T2D, studies in children with T1D have indicated that lower socioeconomic status is associated with poor glycemic control. Moreover, depression and the probability of depression increases as a patient’s glycemic control worsens [12]. The complex association of T2D with a multitude of risk factors for depression further complicates the management of patients.

**Effects of Comorbid Depression on T2D**

Major depression is a common mental disorder in young people in the United States and it is estimated that approximately 12.5% of the adolescent population experienced a major depressive episode in 2015 [13]. Depression in adolescents is associated with an increased rate of smoking, substance abuse, obesity, and serious social and educational impairments. It is also a major risk factor for suicide, which is the second leading cause of death in 10 to 24-year-olds [14]. Adolescents with T2D and comorbid depression are especially at risk for these social and psychological difficulties, subsequently making recognition of this disorder important [8].

The effect of depression on T2D in adolescents is twofold. Primarily, the high rate of depression in adolescents with T2D affects the adherence of these patients to a care plan. Achieving adherence is especially difficult in adolescent illness when it is accompanied by hopelessness or pessimism [15]. This low adherence increases medical complications and contributes to a poorer quality of life [16]. Moreover, adolescents with T2D and depression are susceptible to peer pressure to participate in social activities that may center around unhealthy eating or sedentary activities that do not align with the lifestyle modifications of a T2D management plan [5].

The physiological effect of depression on young people with T2D may also contribute to poorer glycemic control. A meta-analysis of the literature observed that depression in adults was significantly associated with hyperglycemia in patients with diabetes [17]. Although the physiological mechanism has not been rigorously researched, it has been suggested that the mental stress associated with depression dysregulates glucose levels directly through increased cortisol in addition to neglect of healthy lifestyle choices [18]. There is also some evidence that high levels of depressive symp-

toms in adolescents may be associated with the secondary development of T2D, especially for female patients [19].

Addressing depression, as well as other comorbidities, with T2D is particularly paramount for adolescents. While the pathophysiology of T2D in adolescents is similar to that of adults with insufficient insulin production from pancreatic beta-cells and insulin resistance, the comorbidities in young diabetes may be more aggressive than in adults [20]. Serious comorbidities are also seen earlier in the patient’s life because of the longer duration of the T2D and uncontrolled blood glucose [21]. Most notably, the early onset of T2D in youth has been associated with increased incidence of end-stage renal failure and death as compared with patients diagnosed with T2D as adults [22]. For adolescents diagnosed with T2D, glycemic control is fundamental to prevent or delay physical comorbidities [3]. However, first managing the adolescent’s psychological comorbidities may be necessary to achieve adequate glycemic control.

**SCREENING AND CHALLENGES**

The AAP recommends annual depression screening for children 11 to 21 years, while the United States Preventive Services Task Force (USPSTF) recommends that screening patients 12 to 18 years old. Because T2D is a risk factor for depression, screening for depression should be considered for all young people upon diagnosis of T2D, even if the child is younger than 11 years old. Scheduled depression screenings should be considered for at least the adolescent’s annual examinations and more often if there is physician suspicion of depression.

Screening tools should be selected based on the patient’s age, reading level, and time available to complete the screening [23]. The Beck Depression Inventory for Primary Care for adolescents 12 to 18 years old or the Children’s Depression Inventory for young patients seven to 17 years old are two common tools that may be used in a primary care setting [24]. These screening tools can also indicate the severity of the youth’s depressive symptoms.

The initial management of depression in adolescents with T2D should consider the treatment preferences of the patient and his or her family, the urgency and severity of the disease, and the availability of mental health services and specialists [25]. Prevention of a major depressive disorder is a primary goal. However, depression prevention programs are limited for adolescents, and psychological illness is
predominately identified only after depressive symptoms have emerged [26].

Because depression and T2D are both linked to obesity in adolescents, treatment of these patients is complicated [11, 27]. Depressed adolescents with T2D are typically sedentary and may be overwhelmed by a treatment plan that includes lifestyle modifications. For some patients, it may be necessary for physicians to address the adolescent’s depression before lifestyle modifications, such as diet or exercise, can be successfully implemented [28].

Adherence to treatment plans for adolescents with T2D and depression remains a significant barrier [29]. Furthermore, depression should always be considered in adolescents who have low adherence and present with a lack of motivation and loss of interest [16]. There is no simple intervention that will apply to every adolescent with comorbid medical illnesses, but family and peer support along with an organized and simplified care plan that the adolescent is able to self-manage may positively impact adherence [16, 30].

CONCLUSION AND OUTLOOK

This review of the literature highlights the incidence of depression in adolescent patients with T2D. While T2D is now more widely recognized in the pediatric and adolescent population, there is limited knowledge of the comorbid psychiatric problems seen in these patients. Although there is evidence linking T2D with higher rates of depression and consequential poor disease outcomes, there are no guidelines for addressing these in a comprehensive care plan. The clinical picture of depression in adolescents with T2D is complicated by underlying risk factors, such as socioeconomic status and obesity. A collaborative approach to care between the patient, the patient’s family, and physician is necessary to rapidly identify depression, educate and normalize the disease to the adolescent, and create a holistic management plan that addresses the psychologic and physical aspects of the comorbidities.

The information in this review may be used to raise awareness of depression in adolescents with T2D and to educate patients and their families. Additionally, the review identifies gaps in the literature for future clinical trials and research. While there has been substantial advances in treating T2D in adolescents and acknowledgment that mood disorders impact clinical outcomes, the exact etiology of depression in these patients remains complex and unclear. Further investigation is needed to identify treatments that address both T2D and depression, such as targeted diet and exercise treatments, or the efficacy of psychotherapy and support groups that enhance patient-centered care and promote adherence.

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CONFLICT OF INTEREST DISCLOSURES

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REFERENCES

1. Centers for Disease Control and Prevention. Diabetes Report Card 2014. Atlanta, GA: Centers for Disease Control and Prevention, US Dept of Health and Human Services; 2015. Available from: https://www.cdc.gov/diabetes/pdfs/library/diabetesreportcard2014.pdf.

2. Onge ES, Miller SA, Motycka C, DeBerry A. A review of the treatment of type 2 diabetes in children. J Pediatr Pharmacol Ther. 2015;20(1):4-16. DOI: https://dx.doi.org/10.5863/1551-6776-20.1.4. PubMed PMID: 25859165. PubMed Central PMCID: PMC4353199.

3. Smith JD, Mills E, Carlisle SE. Treatment of pediatric type 2 diabetes. Ann Pharmacother. 2016;50(9):768-77. DOI: https://dx.doi.org/10.1177/1060028016655179. PubMed PMID: 27307414.

4. Silverstein J, Cheng P, Ruedy KJ, Kollman C, Beck RW, Klingensmith GJ, et al. Depressive symptoms in youth with type 1 or type 2 diabetes: Results of the Pediatric Diabetes Consortium Screening Assessment of Depression in Diabetes Study. Diabetes Care. 2015;38(12):2341-3. DOI: https://dx.doi.org/10.2337/dc15-0982. PubMed PMID: 26459274.

5. Copeland KC, Silverstein J, Moore KR, Prazar GE, Raymer T, Shiffman RN, et al. Management of newly diagnosed type 2 Diabetes Mellitus (T2D) in children and adolescents. Pediatrics. 2013;131(2):364-82. DOI: https://dx.doi.org/10.1542/peds.2012-3494. PubMed PMID: 23359574.
6. Hood KK, Huestis S, Maher A, Butler D, Volkening L, Laffel LM. Depressive symptoms in children and adolescents with type 1 diabetes: Association with diabetes-specific characteristics. Diabetes Care. 2006;29(6):1389-91. DOI: https://dx.doi.org/10.2337/dc06-0087. PubMed PMID: 16732028.

7. Khandelwal S, Sengar GS, Sharma M, Choudhary S, Nagaraj N. Psychosocial illness in children with Type 1 Diabetes Mellitus: Prevalence, pattern and risk factors. J Clin Diagn Res. 2016;10(9):SC05-SC08. DOI: https://dx.doi.org/10.7860/JCDR/2016/21666.8549. PubMed PMID: 27790539. PubMed Central PMCID: PMC5072039.

8. Anderson BJ, Edelstein S, Abramson NW, Katz LE, Yasuda PM, Lavietes SJ, et al. Depressive symptoms and quality of life in adolescents with type 2 diabetes: Baseline data from the TODAY study. Diabetes Care. 2011;34(10):2205-7. DOI: https://dx.doi.org/10.2337/dc11-0431. PubMed PMID: 21836107. PubMed Central PMCID: PMC3177750.

9. Linder BL, Fradkin JE, Rodgers GP. The TODAY study: An NIH perspective on its implications for research. Diabetes Care. 2013;36(6):1775-6. DOI: https://dx.doi.org/10.2337/dc13-0707. PubMed PMID: 23704678. PubMed Central PMCID: PMC3661792.

10. Thapar A, Collishaw S, Pine DS, Thapar AK. Depression in adolescence. Lancet. 2012;379(9820):1056-67. DOI: https://dx.doi.org/10.1016/S0140-6736(11)60871-4. PubMed PMID: 22305766. PubMed Central PMCID: PMC3488279.

11. Luppinato F, de Wit LM, Bouvy PF, Stijnen T, Cuipers P, Penninx BW, et al. Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry. 2010;67(3):220-9. DOI: https://dx.doi.org/10.1001/archgenpsychiatry.2010.2. PubMed PMID: 20194822.

12. Hassan K, Loar R, Anderson BJ, Heptulla RA. The role of socioeconomic status, depression, quality of life, and glycemic control in type 1 diabetes mellitus. J Pediatr. 2006;149(4):526-31. DOI: https://dx.doi.org/10.1016/j.jpeds.2006.05.039. PubMed PMID: 17011326.

13. National Institute of Mental Health [Internet]. Major depression among adolescents [cited 2017]. Available from: https://www.nimh.nih.gov/health/statistics/prevalence/major-depression-among-adolescents.shtml.

14. Centers for Disease Control and Prevention. Ten leading causes of death and injury – 2015 [cited 2017]. Available from: https://www.cdc.gov/injury/wisqars/LeadingCauses.html.

15. Staton D. Achieving adolescent adherence to treatment of major depression. Adolesc Health Med Ther. 2010;1:73-85. DOI: https://dx.doi.org/10.2147/AHMT.S8791. PubMed PMID: 24600263. PubMed Central PMCID: PMC3915957.

16. Taddeo D, Egedy M, Frappier JY. Adherence to treatment in adolescents. Paediatr Child Health. 2008;13(1):19-24. PubMed PMID: 19119348. PubMed Central PMCID: PMC2528818.

17. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control: A meta-analytic review of the literature. Diabetes Care. 2000;23(7):934-42. PubMed PMID: 10895843.

18. Ranabir S, Reetu K. Stress and hormones. Indian J Endocrinol Metab. 2011;15(1):18-22. DOI: https://dx.doi.org/10.4103/2230-8210.77573. PubMed PMID: 21584161. PubMed Central PMCID: PMC3079864.

19. Suglia SF, Demmer RT, Wahi R, Keys KM, Koenen KC. Depressive symptoms during adolescence and young adulthood and the development of Type 2 Diabetes Mellitus. Am J Epidemiol. 2016;183(4):269-76. DOI: https://dx.doi.org/10.1093/aje/kwv149. PubMed PMID: 26838597. PubMed Central PMCID: PMC4753278.

20. Cree-Green M, Triolo TM, Nadeau KJ. Etiology of insulin resistance in youth with type 2 diabetes. Curr Diab Rep. 2013;13(1):81-8. DOI: https://dx.doi.org/10.1007/s11892-012-0341-0. PubMed PMID: 23135953. PubMed Central PMCID: PMC4296020.

21. Zeraatkar D, Nahari A, Wang PW, Kearsley E, Falzone N, Xu M, et al. Appraisal of clinical practice guidelines for management of paediatric type 2 diabetes mellitus using the AGREE II instrument: A systematic review protocol. Syst Rev. 2016;5(1):111. DOI: https://dx.doi.org/10.1186/s13643-016-0288-3. PubMed PMID: 27412255. PubMed Central PMCID: PMC4944246.

22. Dean HJ, Sellers EA. Comorbidities and microvascular complications of type 2 diabetes in children and adolescents. Pediatr Diabetes. 2007;8 Suppl 9:35-41. DOI: https://dx.doi.org/10.1111/j.1399-5448.2007.00340.x. PubMed PMID: 17991131.

23. U.S. Preventive Services Task Force. Screening for depression in children and adolescents: Recommendation Statement. Am Fam Physician. 2016;93(6):506-8. PubMed PMID: 26977836.
24. Beck AT, Guth D, Steer RA, Ball R. Screening for major depression disorders in medical inpatients with the Beck Depression Inventory for Primary Care. Behav Res Ther. 1997;35(8):785-91. PubMed PMID: 9256522.

25. Cheung AH, Kozloff N, Sacks D. Pediatric depression: An evidence-based update on treatment interventions. Curr Psychiatry Rep. 2013;15(8):381. DOI: https://dx.doi.org/10.1007/s11920-013-0381-4. PubMed PMID: 23881712. PubMed Central PMCID: PMC3744276.

26. Felnhofer A, Kothgassner OD, Klier C. How to prevent depression? Current directions and future challenges in children with chronic medical conditions. Psychiatr Danub. 2016;28(4):441-51. PubMed PMID: 27855438.

27. Goldfield GS, Moore C, Henderson K, Buchholz A, Obeid N, Flament MF. Body dissatisfaction, dietary restraint, depression, and weight status in adolescents. J Sch Health. 2010;80(4):186-92. DOI: https://dx.doi.org/10.1111/j.1746-1561.2009.00485.x. PubMed PMID: 20433644.

28. Hughes CW, Barnes S, Barnes C, Defina LF, Nakonezny P, Emslie GJ. Depressed Adolescents Treated with Exercise (DATE): A pilot randomized controlled trial to test feasibility and establish preliminary effect sizes. Ment Health Phys Act. 2013;6(2). DOI: https://dx.doi.org/10.1016/j.mhpa.2013.06.006. PubMed PMID: 24244220. PubMed Central PMCID: PMC3827851.

29. Katz LL, Anderson BJ, McKay SV, Izquierdo R, Casey TL, Higgins LA, et al. Correlates of medication adherence in the TODAY cohort of youth with type 2 diabetes. Diabetes Care. 2016;39(11):1956-1962. DOI: https://dx.doi.org/10.2337/dc15-2296. PubMed PMID: 27352955.

30. Hamilton J, Daneman D. Deteriorating diabetes control during adolescence: Physiological or psychosocial? J Pediatr Endocrinol Metab. 2002;15(2):115-26. PubMed PMID: 11874175.