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Hope and mealtime insulin boluses are associated with depressive symptoms and glycemic control in youth with type 1 diabetes mellitus

Alison K. Calkins-Smith¹, Arwen M. Marker², Mark A. Clements³, and Susana R. Patton⁴

¹Clinical Psychology Program, University of Kansas, 1415 Jayhawk Blvd., Lawrence, KS 66045

²Clinical Child Psychology Program, University of Kansas, 1000 Sunnyside Ave., Lawrence, KS 66045

³Pediatric Clinical Research Unit, Children's Mercy Hospital, 2401 Gillham Rd., Kansas City, MO 64108

⁴Division of Child Behavioral Health, University of Kansas Medical Center, 3901 Rainbow Blvd, MS 4004, Kansas City, KS 66160

Abstract

Adherence to treatment regimen is associated with improved glycemic control and is particularly problematic during adolescence for those with type 1 diabetes mellitus (T1DM). Both glycemic control and adherence may be negatively impacted by poor psychological outcomes in adolescence, such as depressive symptoms and low hopefulness. The purpose of this study was to examine associations between the mealtime insulin bolus score (BOLUS), a more robust proxy measure of adherence than frequency of blood glucose monitoring or self-report, with depressive symptoms, hope, and hemoglobin A1c (HbA1c). Ninety adolescents completed measures of hope (Children's Hope Scale) and depressive symptoms (Center for Epidemiologic Studies – Depression Scale), as well as lab-based measures of HbA1c and mealtime insulin bolus scores (BOLUS). Higher levels of hope were associated with lower levels of depressive symptoms, more frequent mealtime insulin boluses, and better glycemic control. Higher levels of BOLUS behavior were associated with lower depressive symptoms and better glycemic control. Both BOLUS behavior and hope independently and significantly impacted the relationship between depressive symptoms and HbA1c, suggesting a possible mediation. Since hope and BOLUS were each associated with the relationship between depressive symptoms and glycemic control, following confirmation of this relationship in a longitudinal study, clinics may consider measuring hope and BOLUS among youth with high depressive symptoms and further investigating BOLUS behavior and hope as potential intervention targets to improve glycemic control.

Keywords

Type 1 diabetes mellitus; adherence; bolus; hope

Introduction

Type 1 diabetes mellitus (T1DM) is one of the most common chronic illnesses in youth;¹ it involves complex and demanding treatment.² Daily management includes blood glucose checks, insulin administration, carbohydrate counting and monitoring dietary intake,² among other tasks. Adolescence represents a time of adjustment when youth begin to take on more tasks related to T1DM management. It also marks a high-risk period for deteriorations in T1DM self-management³ and glycemic control.⁴ Adolescents with T1DM may experience a number of acute physiological insults due to poor management, including ketoacidosis and hypoglycemia.⁵ They are similarly at increased risk for long-term complications such as heart disease and kidney failure.⁶

Patient engagement with the T1DM treatment regimen (a.k.a., “adherence”) is associated with improved glycemic control⁷ and is important in preventing long-term diabetes complications.^{8,9} Prior studies of patient engagement in diabetes management have used self-report measures (e.g., *Self-Care Inventory*¹⁰; *Diabetes Behavior Rating Scale*¹¹; *Barriers to Diabetes Adherence*¹²), structured interview (e.g., *Diabetes Self-Management Profile*¹³), or frequency of blood glucose monitoring (BGM) as proxy measures of adherence.¹⁴ These measures can be burdensome to complete¹¹ and subject to recall bias or inaccuracy.¹⁵ The mealtime insulin bolus score (BOLUS) has been proposed as a more robust proxy measure of adherence that uses objective data from insulin pump downloads to assess mealtime management behaviors, mitigating the need to rely on self-report.^{9,16,17} The BOLUS measure has previously been shown to be more strongly associated with current and future hemoglobin A1c (HbA1c) than BGM frequency,^{16,17} and to be superior to other methods of measuring adherence to insulin self-administration for youth with insulin pumps.⁹

Adolescents with T1DM also experience high rates of negative psychological outcomes^{18–21} that are associated with declines in adolescent adherence to self-management of T1DM.^{22–24} Depressive symptoms in adolescents with T1DM are associated with reduced scores on a modified Self-Care Inventory²⁵ and less frequent BGM.²⁶ Higher endorsement of depressive symptoms has been found to predict higher HbA1c values, and adherence has been shown to mediate the relationship between depression and glycemic control.²⁷ Therefore, one purpose of this study was to further examine associations between psychological outcomes, glycemic control, and adherence using the more robust mealtime insulin BOLUS proxy measure of adherence.

While numerous studies have investigated the relationship between depression and both adherence and glycemic control among youth with T1DM, few studies have investigated the impact of hope. Hope is defined as “a positive motivational state that is based on an interactively derived sense of successful agency (goal-directed energy) and of successful pathways (planning to meet goals)” [p. 287].²⁸ In two previous studies, hope was significantly associated with self-reported adherence, BGM, and HbA1c in youth.^{29,30} Van Allen et al. further found that frequency of BGM significantly mediated the relationships between hope and adherence/glycemic control.³⁰ Another study found that hope was positively associated with metabolic control and negatively associated with depression among adolescents and young adults with T1DM.³¹ However, no studies have evaluated the

relationship between hope and mealtime insulin BOLUS scores, or relationships between hope, depressive symptoms, mealtime insulin BOLUS scores, and glycemic control.

Importantly, all of the factors described above fit into Hilliard, Harris, and Weissberg-Benchell's proposed Diabetes Resilience Model.³² This model suggests that individual risks, such as depressive symptoms, predict diabetes health outcomes, such as HbA1c, and that this relationship is mediated by diabetes-specific behavioral competence (e.g. adherence behaviors) and diabetes-specific and non-specific protective factors (e.g. coping skills, hopefulness). Using this model, we hypothesized that hope and BOLUS may be protective factors that potentially mediate relationships between individual risk factors (e.g. depressive symptoms) and glycemic control.

Therefore, the purpose of the present study was to 1) assess relationships among glycemic control, hope, and adherence using the BOLUS measure of adherence, 2) investigate new relationships between these factors and depressive symptoms, and 3) examine hope and BOLUS as potential protective factors associated with depressive symptoms and glycemic control in adolescents with T1DM.

Methods

Participants

Families were eligible to participate in a larger study about child and family factors related to adherence if youths were 10-16 years old, diagnosed with T1DM for at least 6 months, and English speaking. Exclusion criteria included diagnosis of developmental delay (i.e., autism, cerebral palsy, or intellectual disability) or hospitalization within the last year for a psychological disorder. In the current analyses, we used the subset of youth from this larger sample who were on insulin pump therapy (i.e. continuous subcutaneous insulin infusion) and for whom we could calculate BOLUS scores. Those on a multiple daily injection treatment regimen were excluded.

Procedure

Families were recruited during diabetes clinic visits at two large metropolitan hospitals from April 2011-April 2012. Families that consented to participate signed both consent and assent forms. Youths completed study measures on an iPad, HbA1c was obtained from their medical chart, and insulin pump data were collected from device downloads. Additional demographic information was also extracted from the medical chart to characterize the sample. This study was approved by institutional review boards at both hospitals and families were compensated for study participation.

Measures

Youth Hope—The Children's Hope Scale (CHS)³³ is a six-item self-report measure used to assess level of hope in children aged 7 to 16 years. It uses a Likert scale ranging from 1 (none of the time) to 6 (all of the time), resulting in a total score ranging from 6 to 36 with higher scores reflecting greater overall hope. The CHS has documented internal and test-retest reliabilities as well as a valid two-factor structure.³³ The CHS's two factors (Agency

and Pathways) are each composed of three items. Example items include, “I am doing just as well as other kids my age” (agency) and “When I have a problem, I can come up with lots of ways to solve it” (pathways).

Youth Depression—The Center for Epidemiologic Studies – Depression Scale (CES-D)³⁴ is a 20-item questionnaire that assesses depressive symptoms and utilizes a 4-point Likert-type scale assessing frequency of symptoms from “None of the time” to “All of the time.” Scores range from 0 to 60 with higher scores indicating greater depressive symptoms. Scores over 16 indicate those at risk and scores over 21 suggest the possibility of major depression. This measure has been validated for use with children and adolescents.³⁵

Bolus Behavior (Adherence)—Mealtime insulin bolus scores (BOLUS) have been cited as a proxy measure of adherence in T1DM.^{9,16,17} BOLUS scores were calculated using youth’s insulin pump records. A point was given for each food-associated mealtime bolus occurring between 0600-1000, 1100-1500, and 1600-2200, for a possible 0-3 points per day. Daily BOLUS scores were averaged over a 14-day period to calculate an overall BOLUS score.

Glycated Hemoglobin (HbA1c)—HbA1c is a proxy measure of glycemic control that estimates average blood glucose levels over about 3 months.³⁶ HbA1c values from regular clinic visits were abstracted from the medical chart by the research team.

Statistical Analyses

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) Software Version 23 (IBM Corp. 2014, Armonk, NY). Pearson correlations were conducted to test associations between hope, depression, BOLUS, and HbA1c. We then examined hope and BOLUS as possible mediating factors (if confirmed by longitudinal analyses) and their impact on associations between depression and HbA1c using regressions with Sobel tests of significance.

Results

Participant Characteristics

Of the 139 families that consented/assented for the larger study, 90 youths with T1DM were on insulin pump therapy, completed study measures, and provided both HbA1c and insulin pump data. The majority of the participants were male ($N = 51$; 56.7%) and Caucasian ($N = 79$; 87.8%). Youths ranged in age from 10 years to almost 17 years ($M = 13.68$ years; $SD = 1.76$) and had been diagnosed with T1DM for an average of 6.01 years ($SD = 3.11$). Additional demographic characteristics are described in Table 1.

Descriptive Statistics

The average HbA1c of participants ($M = 9.04 \pm 2.12\%$ [75.30 mmol/mol]) was slightly elevated compared to a nationally representative sample of 6-17 year-olds with type 1 diabetes ($Range = 8.5\text{--}9.0\%$ [69.39-74.86 mmol/mol])⁴ and was above the recommended target range for adolescents ($<7.5\%$ [<58.46 mmol/mol]).³⁶ Youths’ average BOLUS score

was 2.11 ± 0.70 , suggesting that they dosed for about 2 meals per day. BOLUS scores did not appear to differ for youth who participated in the summer versus youth who participated during the school year ($p = 0.99$). Mean scores on the CHS were 27.12 ± 4.39 . Participants had a mean CES-D score of 12.69 ± 11.29 . Twenty-four youth (26.7%) scored equal to or greater than 16 on the CES-D indicating elevated depressive symptoms, and 15 (16.7%) scored above the clinical cutoff score of 21 for major depression.

Higher levels of hope were associated with lower levels of depressive symptoms, more frequent mealtime insulin boluses, and better glycemic control (i.e., lower HbA1c; see Table 2). Depressive symptoms were correlated with less frequent bolusing behavior and poorer glycemic control. Higher levels of bolus behavior were associated with better glycemic control. Increasing age was also associated with less frequent bolusing and worse glycemic control, and was thus included as a covariate in additional analyses. Due to significant correlations between variables of interest, multicollinearity statistics were examined for these variables prior to running regression analyses; all were in the normal range.

Potential Mediation (if confirmed by longitudinal data)

After controlling for age, regression analyses were used to examine whether mealtime insulin bolusing behavior may serve as a potential mediator of the relationship between depressive symptoms and HbA1c, if confirmed by longitudinal data. Results of these analyses revealed that BOLUS was associated with depressive symptoms ($\beta = -0.30$, $p = .004$) and HbA1c ($\beta = -0.49$, $p < .001$). Youth depressive symptoms were also independently associated with HbA1c ($\beta = 0.23$, $p = .019$). A regression analysis in which BOLUS and depressive symptoms were used to predict HbA1c was significant ($R^2 = 0.37$, $F [3, 86] = 16.82$, $p < .001$). The relation between depressive symptoms and HbA1c was no longer statistically significant ($\beta = 0.10$, $p = .30$) when controlling for the relation between BOLUS and HbA1c. A Sobel test of significance revealed that this effect was statistically significant ($t = 2.75$, $p = .006$).³⁷

Regression analyses controlling for age were additionally used to examine whether hope may serve as a potential mediator of the relationship between depressive symptoms and HbA1c, if confirmed by longitudinal data. Results of these analyses revealed that hope was associated with depressive symptoms ($\beta = -0.50$, $p < .001$) and HbA1c ($\beta = -0.39$, $p < .001$). Depressive symptoms were also independently associated with HbA1c ($\beta = 0.23$, $p = .019$). A regression analysis in which hope and depressive symptoms were used to predict HbA1c was significant ($R^2 = 0.27$, $F (3, 86) = 11.76$, $p = .001$). The relationship between depressive symptoms and HbA1c was no longer statistically significant ($\beta = 0.04$, $p = 0.68$) when controlling for the relationship between hope and HbA1c. A Sobel test of significance revealed that this effect was statistically significant ($t = 3.38$, $p < .001$).³⁷ These significant models are described in Figure 1 as one possible interpretation of these relationships; however, directionality cannot be inferred from this cross-sectional analysis. Regression analyses did not find hope to influence the relationship between BOLUS and HbA1c, or for bolusing behavior to impact the relationship between hope and glycemic control.

Discussion

This study aimed to provide additional information about the relationships between glycemic control, adherence, and depressive symptoms with two novel contributions: 1) the examination of BOLUS as the primary measure of adherence, and 2) the incorporation of hope, a variable that has been minimally researched in T1DM. Similar to previous research in T1DM and this age group, youth in this study demonstrated generally poor glycemic control.⁴ Twenty-six percent of youth in this sample also had elevated depressive symptoms, which matches recent findings that almost a third of youth with T1DM are expected to report depressive symptoms.¹⁸ Consistent with previous research, glycemic control was associated with adherence,²⁵ depressive symptoms,^{25,27} and hope.^{29–31} Children with greater depressive symptoms demonstrated worse glycemic control, but hope and BOLUS were two protective factors that suggest further investigation in longitudinal samples to determine if they are mediators of the relationship between depression and HbA1c.

BOLUS was significantly associated with the cross-sectional relationship between depressive symptoms and glycemic control. Our finding that adherence may mediate depressive symptoms and glycemic control if confirmed by longitudinal samples was consistent with previous research;²⁷ however, this study used a different measure of adherence (e.g., BOLUS), which has demonstrated a stronger relationship with HbA1c compared to BGM.¹⁶ Appropriate use of insulin is a key component of diabetes management and BOLUS likely assesses a component of treatment adherence that is more proximal to the outcome compared to BGM. For instance, children with poor glycemic control may check blood glucose frequently due to frequent highs/lows without treating, while appropriate insulin dosing before meals more directly influences glycemia. Interestingly, BOLUS did not impact the cross-sectional relationship between hope and glycemic control, although adherence as measured by BGM was found to mediate this relationship by Van Allen et al.³⁰ This discrepancy may be due to differences in the amount of variability in individual BOLUS scores versus BGM, and requires further research using independent samples. Alternatively, the relationship between hope and glycemic control may be better explained by factors that were not the focus of this study, such as self-efficacy, optimism, perceived social support, parenting strategies, or general well-being.^{29,30}

Hope was also significantly associated with the cross-sectional relationship between depressive symptoms and glycemic control. The construct of hope includes individual abilities to set goals, sustain motivation toward goals, and recruit supportive resources to reach goals.²⁸ This type of goal-directedness may be an essential component of diabetes management behaviors that are crucial to improving glycemic control. In one previous study of Brazilian adolescents, hope explained 9% of the variance in HbA1c and 30% of the variance in depressive symptoms, indicating that interventions targeting hopefulness may alter the impact of depressive symptoms on diabetes management up to 30%.³¹ However, this previous study did not measure adherence behavior. In other pediatric populations (e.g. children with cancer), research demonstrated that changes in hope partially mediated the effects of depression on quality of life.³⁸ Combined with findings from our current study, these results indicate that in youth with higher depressive symptoms, hope may be a key factor that can help to offset the impact of depressive symptoms on glycemic control.

Depression is common in youth with T1DM¹⁸ and there is positive evidence for treating depression in this population;³⁹ however, existing treatments do not always directly affect glycemic control. Including other factors, such as hope and bolus behavior, that can have a positive influence on glycemic control, may result in more positive outcomes in youth who are dealing with both T1DM and depressive symptoms. One clinical implication of these findings is the need for screening measures to assess both depressive symptoms and hopefulness in youth with T1DM. Although clinics have begun implementing annual depression screenings for youth with T1DM,⁴⁰ screeners for hope have not been implemented. By screening for hopefulness using validated measures (e.g. Snyder's Children's Hope Scale [1997], Hind's Hopefulness Scale for Adolescents [1999], Miller's Hope Scale [1988]), clinicians may be able to better identify adolescents who are most in need of intervention (e.g. those with elevated depressive symptoms and low hopefulness, for whom poorer glycemic control is expected) and adolescents who may be most receptive to treatment (e.g. depressed youth with high hopefulness). Currently, only a quarter of patients with diabetes and clinical-level depression are estimated to receive treatment,⁴¹ so additional screeners may help to tailor limited treatment resources to those most in need.

A second clinical implication is the importance of developing interventions aimed at increasing hope among T1DM youth with depressive symptoms. To the authors' knowledge, there are currently no interventions that specifically target hope in youth with T1DM. Limited hope-based interventions in the adult cancer literature show preliminary evidence for increasing hope by targeting effective goal-setting, problem-solving skills, pathways to motivation, and positive self-talk.⁴² Many of these intervention components are active ingredients in cognitive behavioral therapy, for which pilot interventions have been tested in depressed youth with T1DM, with some evidence for reducing depressive symptoms, stabilizing HbA1c, and increasing self-efficacy.^{39,43,44} Our findings support future research to further refine cognitive behavioral and motivational interviewing techniques aimed at increasing self-efficacy and agency for change, problem-solving, and goal setting as primary foci of interventions for youth with T1DM with higher depressive symptoms.

Strengths of the present study included: 1) the collection of data from a moderately large sample of parent/youth dyads, 2) use of the mealtime insulin BOLUS score, which has been shown to relate more strongly to current and future glycemic control than frequency of glucose monitoring, and 3) the examination of possible protective factors associated with depressive symptoms and glycemic control, which have not previously been analyzed together (e.g. hope and BOLUS). There are also limitations to this study that deserve comment. Findings from this study were cross-sectional so we cannot comment on mediation relationships over time. Future research is needed to establish whether these proposed protective factors serve as mediators in longitudinal data. While BOLUS scores provide a more robust measure of adherence than BGM,^{9,16,17} this measure captures the frequency of bolusing during discrete and typical mealtimes (e.g. morning, afternoon, evening) and does not assess if the insulin dose was appropriate or optimally timed. Future studies may consider linking pump data with other patient-reported outcomes, such as food diaries, to determine if the amount of insulin administered was appropriate to the carbohydrate content of meals and to determine the actual timing of boluses to food intake. This study examined a limited set of factors related to glycemic control in youth with

T1DM, so additional variables not included in this study could further explain these relationships (e.g., self-efficacy, optimism, perceived social support). Finally, the sample was primarily Non-Hispanic White and from the middle to upper socio-economic status, which may limit generalizability to youth from other racial, ethnic, and socio-economic backgrounds. Future research is needed to confirm these associations in more diverse populations.

Conclusions

Over a quarter of our sample exhibited elevated depressive symptoms, and higher levels of depressive symptoms were related to worse glycemic control, less frequent mealtime BOLUS, and lower hope. Since hope and BOLUS were each significantly associated with the cross-sectional relationship between depressive symptoms and glycemic control, future researchers should consider analyzing these factors in a longitudinal sample to confirm mediation. If supported, clinics may consider measuring hope and BOLUS among youth with higher depressive symptoms. The use of clinic screeners by providers who have routine contact with this patient population (e.g., physicians, nurses, and social workers) are needed to increase appropriate referrals to mental health services for psychological factors that negatively affect health outcomes. Future research may also focus on developing interventions that target hope and BOLUS, as well as depressive symptoms, so that researchers can evaluate whether modifying these potential protective factors can improve glycemic control during adolescence.

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Figure 1.

Table 1

Descriptive statistics of the study sample.

	Mean (SD) or Percent
Age (years)	13.68 (1.76)
Sex (male)	56.7%
Race/Ethnicity (Non-Hispanic White)	87.8%
Hollingshead Four-Factor Index of SES	3.71 (1.27)
5	28.9%
4	38.9%
3	17.8%
2	6.7%
1	4.4%
T1DM Duration (years)	6.01 (3.11)
HbA1c (%; mmol/mol)	9.04 (2.12); 75.30
In-Range (<7.5%; <58.46 mmol/mol)	27.8%
Uncontrolled Glycemia (≥9.0%; ≥74.86 mmol/mol)	44.4%
BOLUS (total score)	2.11 (0.70)
Hopefulness (CHS mean score)	27.12 (4.39)
Depressive Symptoms (CES-D total score)	12.69 (11.29)
Elevated Depressive Symptoms (≥16)	26.7%
At-Risk Depressive Symptoms (≥21)	16.7%

Table 2
Correlations between hope, depression, BOLUS, and HbA1c in youth with T1DM.

	Age	Hope	Depression	BOLUS	HbA1c
Age	–				
Hope	–0.03	–			
Depression	0.15	–0.51**	–		
BOLUS	–0.27*	0.26*	–0.33**	–	
HbA1c	0.37**	–0.40**	0.28*	–0.56***	–

*** $p < .001$;
* $p < .01$