Progress Report 2024 - ISPAD-JDRF Research Fellowship

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Project: Randomized Control Trial Evaluating the Impact of CGM Academy Education Curriculum Versus Standard Care on Glycemic Outcomes for Youth with Type 1 Diabetes

Duration: 01/02/2024 – 06/28/2024

ABSTRACT

Background: Youth with type 1 diabetes (T1D) are at increased risk for kidney failure, vision loss, heart disease, and premature mortality due to challenges with glycemic excursions. Continuous glucose monitoring (CGM) systems represent an important advance in diabetes technology with significant advantages over self-monitored blood glucose and have the potential to optimize glycemic management. Despite these advances, youth with T1D, including patients at Children's Hospital Los Angeles (CHLA), fail to achieve recommended glycemic targets, highlighting the opportunity for testing innovative diabetes education programs aimed at increased technology uptake such as the CGM Academy intervention, a curriculum developed in the United Kingdom (UK) that teaches strategies for teaching progressive dynamic glucose management for youth with T1D on CGM.

Aims: (A1) To determine the feasibility of the CHLA CGM Academy education curriculum to teach youth with T1D dynamic glucose management strategies. We hypothesize the CHLA CGM Academy curriculum will be well-accepted by participants. (A2) To evaluate the effect of the CHLA CGM Academy on the change from baseline to 6 months in glucose coefficient of variation (CV). We hypothesize participants in the CHLA CGM Academy will attain the same or better percentage change in CV as the standard diabetes education (SDE) group, while using fewer hours of diabetes education. (A3) To explore relationships between participants' glycemic outcomes with diabetes distress, diabetes family responsibilities, and number of hours of diabetes education.

Methods: A single institution, randomized controlled trial is proposed for youth with T1D ages 8-18 years who are eligible for CGM therapy. Youth (N=90) who are English- and Spanish-speaking will be randomized 1:1 to receive CHLA CGM Academy or SDE for a total of 4 weeks followed by a 6-month clinical review. Participants in the CGM Academy arm will have access to an online workbook and videos, in addition to in-depth virtual sessions with a diabetes care and education specialist to discuss dynamic glucose management strategies informed by CGM data. A subsample (n=16) of the CGM Academy arm will participate in focus groups at the end of study participation. All participants will complete measures on diabetes family responsibility and diabetes distress, and the study team will collect the number of hours of diabetes education at baseline, 4 weeks, and 6 months. The study team will collect demographic characteristics, diabetes history at baseline and 6 months, and glycemic metrics from chart review at weeks 1, 2, and 4, as well as at 6 months.

Analysis: To evaluate A1, we will report attrition rates, and thematic analysis on qualitative focus groups data. To evaluate A2, we will construct a 95% CI for the difference in change in glucose coefficient of variation to determine if change in the CGM Academy group is not inferior by more than our pre-specified non-inferiority margin to the change in the SDE group. To evaluate A3, we will use generalized linear models to explore the effect of covariates on change in glycemic metrics. To determine the time (baseline, 4 weeks, 6 months) and group (CGM vs SDE) effect on perceived diabetes distress and perceived diabetes family responsibility, we will use repeated measures ANOVA.

SPECIFIC AIMS

In 2022, there were 8.75 million people living with type 1 diabetes (T1D) globally—of them, 18% were younger than 20 years. T1D is one of the most common chronic diseases in childhood, putting those affected at risk for kidney failure, vision loss, heart disease, and premature mortality due to challenges with hypo- and hyperglycemia. Several landmark studies have shown that aggressive lowering of hemoglobin A1c (HbA1C)—considered the gold standard indicator for optimal glycemic management—is associated with fewer long-term complications. The Diabetes Control and Complications Trial (DCCT), involving 1,441 volunteers with T1D, and the follow-up Epidemiology of Diabetes Interventions Complications (EDIC) study demonstrated that intensive glycemic control reduces the risk of eye, kidney, and nerve diseases in addition to lowering the risk of nonfatal heart attack, stroke, or death from cardiovascular causes. Unfortunately, many therapy

intensifications aimed at lowering HbA1C levels increase the risk of hypoglycemia and frequent self-monitored blood glucose (SMBG) testing is seen as an important component of hypoglycemia avoidance strategies. However, SMBG testing has inherent limitations, including long between-test intervals especially at night, inconvenience, inaccuracy, invasiveness, and pain. As a result, most patients do not perform SMBG tests at the recommended frequency, and even those who do continue to have high rates of clinically significant hypoglycemia.

Continuous glucose monitoring (CGM) systems represent an important advance in diabetes technology with significant advantages over SMBG and the potential to optimize glycemic management. CGM relies on a subcutaneous, continuously worn electrochemical sensor that interrogates glucose concentrations in the interstitial fluid at 1- to 5-minute intervals. By providing real-time glucose concentration data throughout the day and night, CGM allows patients to base treatment decisions, such as insulin titration, on glucose concentration trends and offers programmable alerts that can prompt appropriate action in response to existing or impending glycemic variation. To attain more than 70% of glucose between 70 – 180mg/dL, also called time in range (TIR) with less than 4% time below 70mg/dL, youth and families must go beyond simple insulin corrections for hyperglycemia and set doses for hypoglycemia management. Despite the advances in CGM and insulin delivery systems in the last 5 years, youth with T1D often fail to achieve recommended glycemic targets. Many structured education programs for patients on CGMs have demonstrated improvements in diabetes-related outcomes such as TIR by providing youth and families with education on trend arrow adjustment, bolus timing, and review of CGM reports. However, lack of data on effective programs focused on teaching youth how to utilize CGM data for insulin adjustment results in significant gaps in diabetes evidence-based education.

The CGM Academy is an innovative curriculum encompassing strategies for teaching progressive dynamic glucose management for youth with T1D on CGM. Results from a clinical and cost-effectiveness comparison between face-to-face and virtual offerings of the CGM Academy in the UK highlighted better outcomes on the virtual modality, with higher TIR, lower delivery cost, and lower number of hypoglycemia episodes. Although the CGM Academy demonstrated promising results, the effects of such a structured virtual education curriculum are unknown in the United States. Furthermore, to achieve compliance with a virtual program in a diverse population with varying levels of socioeconomic status and racial and ethnic backgrounds, adaptation of the UK-developed curriculum is warranted.

For this proposal, we will perform a randomized controlled trial focused on process and patient-centered outcomes, while leveraging the collected UK data to operationalize a comprehensive virtual program, applicable to youth with T1D and families at CHLA.

Aim 1: Determine the feasibility of CHLA CGM Academy education curriculum to teach youth with T1D dynamic glucose management strategies. We hypothesize the CHLA CGM Academy curriculum will be well-accepted by participants.

Aim 2: Evaluate the effect of the CHLA CGM Academy on the change from baseline to 6 months in glucose CV. We hypothesize participants in the CHLA CGM Academy will attain the same or better percentage change in CV as the standard diabetes education group, while using fewer hours of diabetes education.

Aim 3: Explore relationships between participants' glycemic outcomes with diabetes distress, diabetes family responsibilities, and number of hours of diabetes education.

PROGRESS REPORT

Dr. Barber and the team have faced challenges in initiating data collection for this study, including the change in standard of care practice, the need to pivot eligibility criteria and the primary endpoint of the study, a delay in IRB submission and approval, and intervention development.

1. Current CHLA standard of practice: At the time of the ISPAD-JDRF submission, a new CGM device called Dexcom G7 received FDA approval. This new CGM is significantly smaller and provides patients, particularly young children, with improved device experience. Currently, all patients with a new T1D diagnosis are presented with the option of wearing CGM, which could impact the number of eligible patients for this study—the original inclusion criteria was greater than 6 months of T1D duration. Dr. Barber and her mentor decided to change the inclusion criteria to test the intervention with new T1D onsets only. With that, the primary endpoint of change in hemoglobin A1c (2 - 3 months mean glucose) would be compromised, as all new T1D onsets present improvement in A1c upon insulin treatment initiation. The new endpoint chosen is the glucose CV, derived from the CGM reading, which will allow for measurement of glucose variation during sensor wear. In order to understand the changes in CGM metrics—glucose time in range 70 - 180mg/dL, time below 70mg/dL, time above 180mg/dL, and CV—that happen in the first 6 months of diagnosis to inform the study sample size calculation, Dr. Barber proposed and conducted a 6-month chart review of all patients enrolled in the current standard education at CHLA, called the sensor class.

2. IRB submission: The chart review project was approved in September 2023 (IRB# CHLA-23-00221) and informed the sample size of 90 participants for the study. With the increase from 70 to 90 potential participants, Dr. Barber applied the grant funding to secure a part-time clinical research coordinator (CRC) 1 for this study. The bilingual CRC 1 started at the end of January 2024 and has been fundamental in all pre-intervention progress that took place over the last 6 months. Moreover, there was a review process with the IRB lasting over 100 days for this low-risk study. The study was finally approved on 02/29/2024 (IRB# CHLA-23-00298). We have not enrolled any patients to this study thus far as all materials to the virtual program must be vetted by various CHLA departments, including Marketing and Communications, Patient Family Education, and IRB. Additionally, a full-time PhD student, Milena de Lucca, joined Dr. Barber's research laboratory and will work on her projects as a research fellow until November 2024.
3. Intervention development: The CGM Academy intervention includes two types of materials that needed CHLA branding: an online workbook and the creation of educational videos. In the original intervention piloted in the UK, videos were recorded by the principal investigator John Pemberton, RD using videoconference software. Mr. Pemberton gave access to all materials to the CHLA team. Dr. Barber and the team secured a CHLA-approved vendor for the video making (WowHow) and initiated video development utilizing 2D video animations on April 4. We expect to receive 11 animated videos (Module 1 will have 6 videos, Module 2 will have 5 videos) by the end of July to begin study recruitment in early August 2024.

PROGRESS TOWARD REQUIREMENTS

Table 1. Training Objectives (TOs) & Training Activities

TO 1: Adapt the CGM Academy education curriculum to teach dynamic glucose management strategies to English- and Spanish-speaking youth with T1D. 1a) develop and finalize an intervention treatment manual and protocol; 1b) gain greater understanding of cutting edge, web-based and virtual intervention delivery advancements; and 1c) gain greater understanding of barriers to CGM uptake in youth with T1D and their families		
Training Activity	**Collaborator/Consultant**	**Status**
CGM Academy Training at CHLA (1-day session, virtual)	**John Pemberton, RD (Brigham Children's Hospital, UK), international collaborator**	Completed November 2023 (presented at the CHLA Endocrinology Education Conference)
Twice-monthly meetings: outline delivery of CGM Academy intervention and discuss barriers to delivery, fidelity measurement, and implementation in the clinical setting.	**Jennifer Baldwin, RN and Brenda Manzanarez, RD (diabetes education consultants)**	Hosted four meetings with nurse care manager (Baldwin) and dietitian (Manzanarez) in February 2024
TO 2: Develop skills to design and lead RCTs relevant to diabetes education and family-reported outcomes		
Training Activity	**Mentor/Institution**	**Status**
Monthly meetings: review protocol-specific issues related to design, randomization strategies, implementation, measurement, and dissemination.	**Jennifer Raymond, MD, MCR**	In progress. Completed 6 meetings to date.
Conference: National Pediatric Nurse Scientist Collaborative (NPNSC) Fly-In - This yearly meeting includes presentations by nurse researchers on topics related to clinical research and implementation science; opportunities for collaborations in multi-site investigations; and prime networking opportunities for junior investigators. Travel supported by CHLA.	**National Conference**	Meeting will take place September 2024. Dr. Barber attends the monthly calls as an associate NPNSC member.

Research Success Teams: Dr. Barber will continue to engage in Research Success Teams by attending the K-cohort meetings on the second Wednesday of the month and The Saban Research Institute (TSRI) seminar series.	**TSRI/CHLA**	Regular attendee for the Research Success Teams meetings.
TO 3: Continue training in research ethics		
Training Activity	**Mentor/Institution**	**Status**
CHLA IRB Committee Meeting: Will attend monthly IRB meetings as a voting member.	**CHLA IRB**	In progress. Completed 5 meetings to date.

PRESENTATIONS

Abstract submitted to the ISPAD 2024 conference on CGM chart review:

Title: Differences in Continuous Glucose Monitoring (CGM) Metrics in Minoritized Children with Newly Diagnosed Type 1 Diabetes (T1D)

Authors: Rebecca Barber, Troy Zeier, Jennifer K. Raymond, Lily C. Chao

Aim: Research supports early CGM initiation in children with T1D. We sought to assess characteristics, percentage of time of CGM wear, and changes in CGM metrics from baseline to 6 months in children with a new T1D diagnosis (T1Ddx) participating in a real-world CGM initiation program.

Methods: Children with a new T1Ddx from June 2022 to April 2023 were offered to start on CGM. CGM initiation included the provision of brand-specific handouts and attendance in a CGM class, with follow-up visits at 1 and 3 weeks, and 6 months post-T1Ddx. Baseline characteristics were collected via an electronic health record (EHR) review. Differences between baseline (at 30 days of CGM wear) and 6 months in HbA1c, CGM metrics[1] and percentage of time of CGM wear were collected via EHR and CGM software.

Results: Children (N=20) [(Mean±SD) 8.8±3.2 years old, 40% male, 70% POC, 60% publicly insured] had a median of 15 days between T1Ddx and the first sensor placement. At 30 days of CGM wear, children had: 97% CGM wear time, 66.6±17.8% TIR, 31.9±18.0% time above range (TAR), 1.5±0.7% TBR, and 33.4±6.7 CV. At 6 months of CGM wear, the percentage of time of CGM wear remained at 97% and 30% were on automated insulin delivery systems. Both white and POC children had significant decrease in HbA1c with decrease in TIR and increase in TAR. Children with private insurance had increases in TIR (65% vs. 69%, or an extra 57.6 minutes a day of TIR) with decreases in TAR (33% vs. 29%, or less than 57 minutes per day) , while children with public insurance decreased TIR (67% vs. 56%, or 2 hours and 38 minutes per day) with increased TAR (31% vs. 42%, or 2 hours and 38 minutes per day). Change in TBR and CV was not significant.

Conclusion: CGM usage did not differ by insurance or race with early CGM initiation. However, glycemic metrics at 6 months differed by insurance. Future studies must investigate tailored strategies for CGM initiation in publicly insured children.

[1] CGM metrics are mean percentage time in range 70 - 180mg/dL (TIR), percentage time greater than 180mg/dL (TAR), percentage time less than 70mg/dL (TBR), and percentage coefficient of variation (CV).