Smart Insulin Pens: A randomized, cross-over prospective interventional pilot study assessing the effect on glycemic control and diabetes related burdens

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General Study Information

Title of Project: Smart Insulin Pens: A randomized, cross-over prospective interventional pilot study assessing the effect on glycemic control and diabetes related burdens

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Research Question and Aims

Project summary: Managing diabetes requires a burdensome number of tasks leading to fatigue, distress, and poor compliance, which often worsens during adolescence. Despite availability of diabetes technology including hybrid closed-loop pumps, over half of adolescents and emerging adults with T1D choose to stay on insulin injections rather than insulin pumps. Adolescents choosing injections need to administer insulin four to five times per day. Every injection requires actively calculating the insulin dose based upon the current blood sugar, insulin sensitivity, and estimated carbohydrates that will be consumed. Furthermore, for optimal glycemic control, these calculations and ratios need to be adjusted frequently. To meet these targets, teenagers need to reliably perform these cumbersome calculations three to five times per day. This is a struggle for many busy adolescents, resulting in poor control and more frequent hospital admissions for diabetic ketoacidosis. Thus, there is a critical need to reduce the burden of diabetes cares for people with T1D using injections and improve outcomes during adolescence and young adulthood.
The InPen® is a smartpen that has been FDA approved for children with diabetes age seven years and older. The pen has many features that decrease the burden of diabetes cares. **We plan to randomize 30 adolescents and emerging adults (13-21 years) to either: 1. InPen® with continuous glucose monitors (CMG) or 2. the standard of care with traditional insulin injections and CGM for 90 days and assess glycemic control and overall improvement in diabetes-related psychological burdens in both teens and parent.**

We also plan on having around 30 parents participate in this study as well due to their participation with some of the questionnaires. This will bring our total to 60 participants.

Specific aims:

Specific Aim 1: To determine whether the InPen® alters the glycemic control and variability in adolescents and emerging adults with type 1 diabetes.

Hypothesis: InPen® use improves glucose time in range, decreases mean glucose levels, and standard deviation assess by CGM. In addition, we expect to see an improvement in the number of missed insulin injection and hemoglobin A1c level.

Specific Aim 2: To determine if InPen® use alters the perceived burden of diabetes cares, diabetes distress scores, transition readiness scores, and parental experience of child illness scale (11-13).

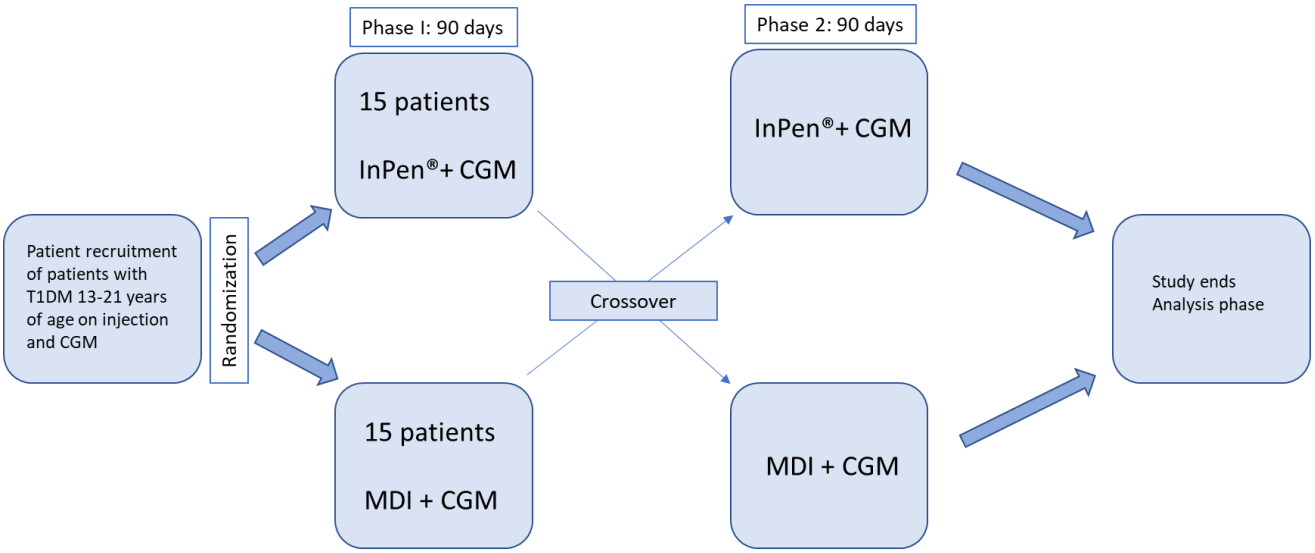
Hypothesis: InPen® use lessens the perceived burden of diabetes care, leading to decreased diabetes related distress in adolescent and improved parental experience in parent(s).

Study Design and Methods

Methods: *Describe in lay terms, completely detailing the research activities that will be conducted by Mayo Clinic staff under this protocol.*

Study Design:

We will perform a randomized, cross-over prospective interventional study. Half of the participants will be randomized to the InPen® and the other half will continue with their conventional insulin injection protocol. After 90 days, participants will switch to the second arm. Randomization will occur via block randomization. Teaching to use the InPen® will be done by Sarah Jackson, DO with supervision by Ana Creo, MD, which can be done by a telemedicine visit if it does not align with clinic visit. Participants will be followed for three months with hemoglobin A1c at the beginning and the end of the study. Data from the CGM and InPen® will be analyzed including time in glucose goal range (70-180 mg/dL), glucose standard deviation, percentage of time that is spent high (>180-250 mg/dL), very high(> 250 mg/dL), low(54-70 mg/dL) and very low(<54 mg/dL), along with total daily insulin dose. Data on missed insulin doses will be assessed via data from the InPen®. For participants randomized to traditional injections we will ask them to record missed insulin doses weekly. Participants should still adjust insulin doses at home, like they do at baseline. If insulin adjustments are made while in one arm of the study they should still continue that dosing when they cross over. We will also assess quality of life and fatigue related to technology with surveys prior to start of the study and at the end. Specifically, we will assess diabetes distress, transition readiness, and parental experience of childhood illness scales [11-13]. We will also utilize the insulin delivery satisfaction survey to assess how they view their current regimen and then how they view the effects of the InPen in managing their type 1 diabetes [14].



Research Materials:

Blood Tests: no blood shall be drawn for research purposes

Downloadable data from CGM site and InPen® data from app.

Recruitment of Subjects: Participants will be recruited from Mayo Clinic Pediatric Diabetes Clinic. All participants will be fully informed about the study and they (or the parents of adolescents) will sign an informed consent/assent form before participating.

Participants of the study will have the option to consent via telemedicine visit if they are unable to come into the clinic. We will plan to arrange a telemedicine visit to go over the consent form, giving them 30 minutes to make sure they are still wanting to participate in the study. The consent form will be sent through their portal via a secure link to ensure that it goes to the correct patient. This will be sent out the day prior to the video visit to ensure the parent and child have time to look at it on their own. Due to this study taking place in individuals 13-21 years of age we will also make sure that the parent or legal guardian is also present. We will also make sure that the teenager/young adult is also present for the video visit.

We will also be consenting one parent of each child due to them needing to fill out a survey on how their child is managing their type 1 diabetes.

Potential Risks: Participants will need to learn to administer insulin with the new device. There is the potential that if an adolescent was previously not taking all their recommended insulin with traditional injections and they then receive all the recommended insulin that they could have a low blood sugar. However, this is not a risk beyond day to day life as person living with diabetes.

Confidentiality: All materials collected will be used for research purposes only and confidentiality will be assured by use of identification codes. Electronic data will be kept in a secure database, which is only accessible to the study investigators.

Protection: Participants will be monitored routinely in the clinic and will have access to medical advice 24/7.

Benefits: Participants will be receiving the InPen® and remuneration. They will also be helping advance further diabetes technology in this specific age group.

Subject Information

Target accrual is the proposed total number of subjects to be included in this study at Mayo Clinic. A "Subject" may include medical records, images, or specimens generated at Mayo Clinic and/or received from external sources.

Study Participants: We aim to recruit 30 patients with type 1 diabetes between the ages of 13-21 years, who will be using the InPen® Type 1 diabetes will be defined as either a c peptide <1, one or more positive diabetes autoantibodies, or a clinical diagnosis with age of onset prior to puberty, based on chart review.

Patients are eligible if they currently receive insulin injections with a CGM. Given the nature of the study, patients will need to be able to read English and have access to a smart phone to participate. We will not exclude based on compliance or control.

Inclusion criteria:

- Individuals between the ages of 13 and 21 years.
- Patients with Type 1 diabetes for at least 6 months
- Defined as either a c peptide <1 , one or more positive diabetes autoantibodies, or a clinical diagnosis with age of onset prior to puberty
- Patients who currently receive insulin injections with a CGM.
- English speaking.
- Have access to a smart phone.
- Will also be recruiting parents/caregivers to fill out a study questionnaire during this study
- On an insulin to carbohydrate ratio

Exclusion criteria:

- Individuals less than 13
- Non-English speaking.
- No access to a smart phone.
- Intellectual disability that would impact their ability to utilize the technology
- Known pregnant women
- Taking chronic daily steroids (equivalent equal to or greater then 5mg of prednisone daily)

We will also recruit one parent for each child to participate in this study as well, estimate them to be less then 70s years of age. If a parent has two children who will be participating in this study then they will only have to consent one time. If we recruit no siblings we anticipate up to 30 adults, which will put are total study participants to 60.

For parent inclusion criteria they must have child with type 1 diabetes who is eligible for this study. We will want to make sure they can read English. They will be excluded from this study if they cannot read English and if their child does not have a diagnosis of type 1 diabetes.

Biospecimens

Collection of blood samples. When multiple groups are involved copy and paste the appropriate section below for example repeat section b when drawing blood from children and adults with cancer. Blood samples will be obtained as part participant's routine clinic visit and not part of the research visit.

a. **From healthy, non-pregnant, adult subjects who weigh at least 110 pounds**. For a minimal risk application, the amount of blood drawn from these subjects may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week.

Volume per blood draw: _0___ml

Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.) _____

b. **From other adults and children considering age, weight, and health of subject.** For a minimal risk application, the amount of blood drawn from these subjects may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period, and collection may not occur more frequently than 2 times per week.

Blood collected during this study will be limited to the glucose samples only (< 5 mL in total) and will not exceed 550 mL over a 12 week period (for adults) or 3 mL/kg body weight if body weight is <50 kg (for adolescents).

Prospective collection of biological specimens other than blood: _____none_____

Review of medical records, images, specimens

Check all that apply (data includes medical records, images, specimens).

☐ Only data that exists before the IRB submission date will be collected.

Date Range for Specimens and/or Review of Medical Records:
Examples: *01/01/1999 through 12/31/2015*, or all records through *mm/dd/yyyy*.

Note: The Date Range must include the period for collection of baseline data, as well as follow-up data, if applicable.

☒ The study involves data that exist at the time of IRB submission **and** data that will be generated after IRB submission. Include this activity in the Methods section.
Examples

- The study plans to conduct a retrospective chart review and ask subjects to complete a questionnaire.
- The study plans to include subjects previously diagnosed with a specific disease and add newly diagnosed subjects in the future.

☐ The study will use data that have been collected under another IRB protocol. Include in the Methods section and enter the IRB number from which the research material will be obtained. *When appropriate, note when subjects have provided consent for future use of their data and/or specimens as described in this protocol*.

Enter one IRB number per line, add more lines as needed

☐ Data ☐ Specimens ☐ Data & Specimens _____

☐ Data ☐ Specimens ☐ Data & Specimens _____

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Data Analysis

Power analyses may not be appropriate if this is a feasibility or pilot study, but end-point analysis plans are always appropriate even if only exploratory. Provide all information requested below, or provide justification if not including all of the information.

Power Statement:
Not needed

Data Analysis Plan:
Measurements and paired differences will be summarized using descriptive statistics. Data will be inspected for normality, and transformation applied, or nonparametric test used if necessary. All statistical tests will be two-sided with significance threshold of alpha=0.05. Paired t-tests will be used to compare glycemic curves within subjects.

1. Maahs, D.M., et al., *Epidemiology of type 1 diabetes.* Endocrinol Metab Clin North Am, 2010. **39**(3): p. 481-97.
2. Sherr, J.L., et al., *Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries.* Diabetologia, 2016. **59**(1): p. 87-91.
3. Sherr, J.L., et al., *Use of insulin pump therapy in children and adolescents with type 1 diabetes and its impact on metabolic control: comparison of results from three large, transatlantic paediatric registries.* Diabetologia, 2016. **59**(1): p. 87-91.
4. Dybdal, D., et al., *Increasing risk of psychiatric morbidity after childhood onset type 1 diabetes: a population-based cohort study.* Diabetologia, 2018. **61**(4): p. 831-838.
5. Hagger, V., et al., *Diabetes Distress Among Adolescents with Type 1 Diabetes: a Systematic Review.* Current Diabetes Reports, 2016. **16**(1).
6. Lasaite, L., et al., *Diabetes distress in males and females with type 1 diabetes in adolescence and emerging adulthood.* Journal of Diabetes and Its Complications, 2016. **30**(8): p. 1500-1505.
7. Wentzell, K., J.A. Vessey, and L.M.B. Laffel, *How Do the Challenges of Emerging Adulthood Inform our Understanding of Diabetes Distress? An Integrative Review.* Current Diabetes Reports, 2020. **20**(6).
8. Creo, A.L., et al., *Brain functions and cognition on transient insulin deprivation in type 1 diabetes.* JCI Insight, 2021.
9. Sangave, N.A., T.D. Aungst, and D.K. Patel, *Smart Connected Insulin Pens, Caps, and Attachments: A Review of the Future of Diabetes Technology.* Diabetes Spectr, 2019. **32**(4): p. 378-384.
10. Adolfsson, P., et al., *Increased Time in Range and Fewer Missed Bolus Injections After Introduction of a Smart Connected Insulin Pen.* Diabetes Technol Ther, 2020. **22**(10): p. 709-718.
11. Bonner, M.J., et al., *Development and validation of the parent experience of child illness.* J Pediatr Psychol, 2006. **31**(3): p. 310-21.
12. Schmitt, A., et al., *How to assess diabetes distress: comparison of the Problem Areas in Diabetes Scale (PAID) and the Diabetes Distress Scale (DDS).* Diabetic Medicine, 2016. **33**(6): p. 835-843.
13. Wood, D.L., et al., *The Transition Readiness Assessment Questionnaire (TRAQ): its factor structure, reliability, and validity.* Acad Pediatr, 2014. **14**(4): p. 415-22.
14. Polonsky, W.H., et al., *Development of a New Measure for Assessing Insulin Delivery Device Satisfaction in Patients with Type 1 and Type 2 Diabetes.* Diabetes Technology & Therapeutics, 2015. **17**(11): p. 773-779.


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