Original Article

Feasibility and acceptability of ambulatory glucose profile in children with Type 1 diabetes mellitus: A pilot study

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ABSTRACT

Background: Insulin administration and self-monitoring of blood glucose (SMBG) are pillars in the management of diabetes in children. Introduction of continuous glucose monitoring (CGM) has made it possible to understand the glycemic profiles which are not picked up by SMBG. Recent advent of flash glucose monitoring with inbuilt software to obtain ambulatory glucose profile (AGP) has emerged as a novel method to study glycemic patterns in adults with Type I diabetes. However, the use of AGP in children is yet to be explored. **Methods:** AGP was used in 46 children with Type 1 diabetes mellitus. Feasibility was measured regarding data and sensor failure. Acceptability was measured using a questionnaire. **Results:** Forty-six children (22 girls and 24 boys) with a mean age of 10.07 years and mean diabetes duration of 3.4 years were included in the study. In this cohort, for 30 (65.21%) subjects, the sensor remained *in situ* for a complete duration of 14 days. Except for minor discomfort, AGP was well accepted by most of the children and their parents. **Conclusion:** AGP is a feasible option for monitoring glycemic status in children with diabetes with a high rate of acceptance.

Key words: Continuous glucose monitoring, flash glucose monitoring, glucose sensor

Introduction

The mainstay of managing children with Type 1 diabetes mellitus (T1DM) is insulin administration and glycemic monitoring. Conventionally, glycemic monitoring is by measurement of self-monitoring of blood glucose (SMBG) involving multiple pricks to the child. The limitations of these pricks include pain and a point-in-time assessment without evaluation of the complete glycemic profile before making insulin adjustments. The importance of glycemic variability in determining the quality of life and long-term complications has been evaluated in several studies.[1-4]

Introduction of continuous glucose monitoring (CGM) by measuring interstitial fluid glucose has overcome the deficits in SMBG by providing an overview of the glycemic profiles in patients. However, most of the existing CGM devices still need to be frequently calibrated, using a minimum of 2–5 daily monitored capillary blood glucose, which is painful for children and distressing for the parents.[5-6] The other disadvantages include sensor replacement every 3–5 days and false alarms (when used with continuous subcutaneous insulin infusion, thus affecting compliance as demonstrated by pediatric studies on CGM).[7-9]

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The recent introduction of flash glucose monitoring (FGM) using the factory-calibrated meter has emerged as a novel method to study glycemic patterns in patients with Type I diabetes. FGM does not require finger prick calibration. The data are extrapolated using the inbuilt software to summarize the glycemic variability over 2 weeks. The glucose profile obtained using this system is called ambulatory glucose profile (AGP). The usefulness of AGP in adults has been studied and guidelines have been recommended by experts in the field.[10,11] To date, there are no studies looking into the feasibility of this tool in children. This pilot study was undertaken to assess the feasibility and acceptance of AGP in children with T1DM.

Methods

The data for this study were obtained from 46 children (1–18 years) of both sexes with T1DM from two health centers in South India for 3 months from August 2015 to October 2015. Written informed consent was obtained from participants and their parents or guardians, after clearance from the Institutional Ethics Board. Children with localized skin disorders were excluded.

A standardized pro forma was used to collect demographic and clinical data. Clinical data included age of the patient, duration of diabetes, weight, height, current insulin regimen, and hemoglobin A1C level.

The participants and their parents were briefed about AGP system (FreeStyle Libre Flash Glucose Monitoring System-Abbott). The system includes a sensor (shelf life of 2 weeks after application) and a reader which when flashed against the sensor provides a record of glucose values every 15 min. Data from the reader are downloaded to a computer and the inbuilt software summarizes the data and provides numerical and graphic display of patterns. The sensors were inserted by diabetes educators or clinicians who are trained to perform the procedure. Instructions were given to keep a written log of events of meals, exercise, and hypoglycemic symptoms in a standardized diary. SMBG was monitored as was their practice and during symptomatic hypoglycemia. The study participants continued their current insulin regimen during the study period. Dose adjustments, when indicated, were performed by the participants as they would routinely do based on their SMBG. After 14 days (or earlier if the sensor got detached), participants returned to the hospital for removal of the sensor.

Glucose profile for each patient obtained after 14 days includes the following three parts: Statistical summary, visual display, and daily views.

Feasibility measures

Feasibility was measured in terms of:

- Sensor failures (sensor detachment, attached but no data, and difficulty with insertion)
- Data failures (no input and gaps in data or graph).

Acceptability measures

Acceptability was measured by asking the children (8 years and older) and/or the parents (children younger than 8 years) about their experiences and noting their responses in the questionnaire, which was prepared based on the existing literature on acceptability studies on CGM.[12,13]

Results

Forty-six children (22 girls and 24 boys) were enrolled in this study. Mean age of the participants was 10.07 years and mean duration of diabetes was 3.4 years. About 51.06% of the children were on split mix regimen using regular and Neutral Protamine Hagedorn insulin, while 45.6% of the children were on basal bolus regimen, using analogs (lispro or aspart and glargine or levemir). Demographic features of the cohort are listed in Table 1. AGP recording of a patient is illustrated in Figure 1.

Feasibility

In this cohort, for 30 (65.21%) subjects, the sensor remained *in situ* for a complete duration of 14 days. Interestingly, all children between the age group of 2–5 years managed to keep their sensors *in situ* for 2 weeks. Average duration of sensor wear for the cohort was 9.3 days (range: 2–14 days). There was no difficulty in inserting the sensors. In seven boys and nine girls, sensor lasted for <2 weeks. Spontaneous detachment of sensor occurred within 14 days in 15.2% of the subjects. The sensor was *in situ,* but stopped recording within 14 days for 13% of the subjects. Three children (6.52%) got it

Table 1: Demographic characteristics of the study participants (*n*=46)

Demographic characteristics	Observations
Age (years) (mean±SD)	10.07±4.85
Gender, *n* (%)	
Female	22 (47.82)
Male	24 (52.17)
BMI (kg/m^2) (mean±SD)	17.50±4.07
Diabetes duration (years) (mean±SD)	3.40±3.26
HbA1c (%) (mean±SD)	10.06±1.98
Age at diagnosis (years) (mean±SD)	6.82±3.92
Insulin regimen, *n* (%)	
Split mix	24 (51.06)
Basal bolus	21 (45.65)
Continuous subcutaneous insulin infusion	1 (2.12)

BMI: Body mass index, HbA1c: Hemoglobin A1c, SD: Standard deviation

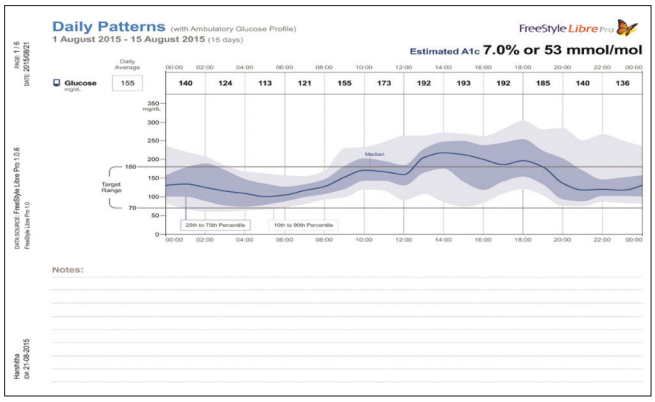

Figure 1: Ambulatory glucose profile of a study participant

removed because of pain at the insertion site. In this cohort, gaps in data were not noticed in any recordings. The distribution of age groups and duration of AGP are shown in Table 2.

Acceptability

In this study, acceptability of using AGP was assessed using a questionnaire. About 60% of the participants were willing to use AGP sensor again. Only five subjects complained of pain while wearing the sensor. Among those in whom the sensor lasted <2 weeks (n = 16), four of them rejected wearing it again. One child developed a pustule at the insertion site.

Discussion

This study evaluated the feasibility and acceptability of AGP in children with diabetes. The results of the present study are encouraging that a painless modality of glucose monitoring can be offered to children. The device is different from the existing CGM devices as it does not require calibration using SMBG, and hence, inaccuracies due to errors in the external blood glucose monitoring device could be eliminated. Moreover, wear time of this sensor is longer (14 days) than any other existing glucose monitoring system, thus providing robust data to look at the glycemic patterns. The average duration of sensor wear of 9.3 days among children is promising since this duration is longer than what is achieved with the existing CGM sensors. Earlier study on prolonged CGM in young and older children using the existing device had a mean wear of 6 days in the first 4 weeks with a declining duration of wear over 6 months.[9,14] Experts have recommended a minimum of 12 days record to study glycemic variability.[15] In this study, thirty subjects completed 14 days sensor wear period.

We did not observe a specific age limit to use AGP, since all the participants (n = 6) in the age group of

Table 2: Distribution of age groups and mean study duration

Age (years)	Total number of subjects (n)	Mean duration of ambulatory glucose profile (days)	Subjects completing 14 days of sensor wear n (%)
1-2	2	6	0 (0)
2-5	6	14	6 (100)
5-10	14	11.28	9 (64.28)
10-18	24	11.58	15 (62.50)
1-18 (all)	46	9.31	30 (65.21)

2–5 years managed to complete the total duration of 14 days suggesting that AGP could be feasible even in the very young age. Better feasibility seen in the younger age group could be related to parental supervision as these children were mostly at home (and at school for a very short period in a day) and their physical activity is restricted to the premises of their residences. The youngest subject (aged 1 year) in this cohort managed to keep AGP for 5 days. It has been reported that CGM has been used even in very low birth weight neonates to recognize hypoglycemia, thus providing more clinical indications for the use of FGM in future.[16-18]

In the present study, spontaneous detachment of the sensor device was seen in 15.2% of the subjects. Most of these children are more than 5 years of age. We speculate that this could be related to vigorous or violent movement of the arm (as children in this age group tend to be physically very active), contact sports, and sweating, which may lead to loosening of the glue. In cases where sensor was attached, but no data recorded (13%), it could have been slippage of the probe. The complaint of mild pain and discomfort while wearing the sensor was reported in only five children. This could be attributed to foreign body sensation. Only one subject with poorly controlled glycemic status had local reaction of pustule at the removal of sensor which healed in a couple of days without additional therapy. These results are comparable with other studies looking into the use of CGM in children. Wong *et al*. reported that the top reason to stop wearing CGM devices was discomfort while wearing it followed by problems with the adhesive holding the sensor on the skin, interference with sports, activities, and skin reactions from the CGM sensor.[19] However, we did not encounter the other issues such as difficulty with sensor insertion and CGM malfunction which were mentioned in their study.

The most common reason for children's refusal to wear the sensor again was perceived restriction of activity. Restriction of physical activity could be partly related to parental anxiety or over protection of children during sensor wear period because of fear of sensor detachment.

Five girls ($n = 5$) who refused to wear again were aged above 10 years and cited social reason of not wanting to disclose their diabetes status to their school friends. This could be overcome by changing sensor site to an area which avoids exposure and by wearing clothes with sleeves covering the upper arm. We used the posterior aspect of arm as suggested in the product manual. In our youngest patient who was aged 1 year, it was applied on the abdomen and sensor data were retrieved well without gaps. Though it lasted for only 5 days, the profile helped educating parents and making insulin adjustments.

Most (58.6%) parents and children accepted the sensor since it eliminated pricks to their children. Moreover, they could visualize event-related (food, activity, and insulin administration) glycemic patterns throughout the day. In a comprehensive review of CGM, it was noted that there was a low level of acceptance due to frequent sensor reinsertion and distracting alarms.[5] This is overcome by this sensor which can be worn for 2 weeks at a stretch, therefore making it more acceptable to children and their parents.

In our study, we assessed the glycemic profile by recalling patients at the end of 2 weeks. However, if the patient has access to the "reader," AGP can emerge as a replacement to SMBG. Using the reader, parents can check real-time glycemic trends and can make necessary adjustments.

Accuracy of AGP using FGM has been evaluated in studies involving adults as subjects and is comparable to capillary and venous blood glucose measurements which are used conventionally.[20] It has also been shown that the accuracy of this system remains stable over 14 days. Evaluation of accuracy of AGP in children has been undertaken and is presently under consideration for publication.

The study included a small number of subjects. The other factors which could affect the duration of sensor wear such as magnitude of physical activity, atmospheric temperature, and humidity were not studied. The assessment of intensity of physical activity in children for 14 days may be extremely difficult and inaccurate at natural home setting. Even though the thought of avoiding pricks to the child may be appealing to the parents of young children, considering the present cost and discomfort of foreign body sensation, AGP can be suggested for use in children intermittently, with the aim of studying glycemic variability. It has been agreed that AGP would aid in recognizing glycemic patterns and make specific modifications to the therapy in adults.[21] However, larger studies looking into the feasibility and acceptability of AGP in children are warranted.

Conclusion

AGP is a feasible option for monitoring glycemic status in children with diabetes with a high rate of acceptance because it is relatively painless and provides a visual display of patterns for 2 weeks.

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Conflicts of interest

There are no conflicts of interest.

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