

Continuous Glucose Monitoring for the Detection of Hypoglycemia in Patients With Diabetes of the Exocrine Pancreas

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Abstract

Background: Detailed evaluations of hypoglycemia and associated indices based on continuous glucose monitoring (CGM) are limited in patients with diabetes of the exocrine pancreas. Our study sought to evaluate the frequency and pattern of hypoglycemic events and to investigate hypoglycemia-specific indices in this population.

Methods: This was a cross-sectional study comprising 83 participants with diabetes of the exocrine pancreas. CGM and self-monitoring of blood glucose (SMBG) were performed on all participants for a minimum period of 72 hours. The frequency and pattern of hypoglycemic events, as well as hypoglycemia-related indices, were evaluated.

Results: Hypoglycemia was detected in 90.4% of patients using CGM and 38.5% of patients using SMBG. Nocturnal hypoglycemic events were more frequent (1.9 episodes/patient) and prolonged (142 minutes) compared with day-time events (1.1 episodes/patient; 82.8 minutes, $P < 0.05$). The mean low blood glucose index was 2.1, and glycemic risk assessment diabetes equation hypoglycemia was 9.1%. The mean time spent below (TSB) <70 mg/dL was 9.2%, and TSB <54 mg/dL was 3.7%. The mean area under curve (AUC) <70 mg/dL was 1.7 ± 2.5 mg/dL/hour and AUC <54 mg/dL was 0.6 ± 1.3 mg/dL/hour. All of the CGM-derived hypoglycemic indices were significantly more deranged at night compared with during the day ($P < 0.05$).

Conclusion: Patients with diabetes of the exocrine pancreas have a high frequency of hypoglycemic episodes that are predominantly nocturnal. CGM is superior to SMBG in the detection of nocturnal and asymptomatic hypoglycemic episodes. CGM-derived hypoglycemic indices are beneficial in estimating the risk of hypoglycemia.

Keywords

continuous glucose monitoring, hypoglycemia, hypoglycemic indices, diabetes of the exocrine pancreas

Introduction

Diabetes of the exocrine pancreas is associated with brittle glycemic control and an increased risk of hypoglycemia. The glycemic profile is typically characterized by hyperglycemic peaks interspersed with recurrent hypoglycemic episodes.¹ Pancreatic inflammation and damage is associated with the loss of β -cells, α -cells (glucagon), and δ -cells (somatostatin), as well as pancreatic-polypeptide (PP) cells of the pancreatic islets. This results in defective counter-regulation and brittle glycemic control, typically characterized by wide fluctuations in blood glucose levels.^{1,2} Malabsorption and variable nutrient absorption from the intestine further exacerbate the risk of hypoglycemia and contributes to extensive fluctuations in blood glucose levels. Repeated episodes of

mild asymptomatic hypoglycemia are a risk factor for hypoglycemic unawareness, a state that is associated with significant morbidity.^{1,3-6} Furthermore, recurrent hypoglycemic

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episodes increase the challenges associated with attaining tight glycemic control.

A high rate of hypoglycemia was observed in patients with diabetes of the exocrine pancreas by self-monitoring of blood glucose (SMBG).⁷⁻¹¹ Hypoglycemia is particularly challenging post-pancreatic resection, contributing to both morbidity and mortality in this patient population.¹² SMBG detects discrete capillary blood glucose levels and can be useful in detecting and managing symptomatic hypoglycemia; however, nocturnal hypoglycemia is frequently missed by SMBG. An additional shortcoming of SMBG is that it fails to provide meaningful information on different aspects of hypoglycemia.^{13,14} In contrast, continuous glucose monitoring (CGM) can provide integrated information on different aspects of daytime and nocturnal hypoglycemia, permitting a more detailed analysis. Such information will provide valuable insights for the planning of preventative strategies pertaining to hypoglycemia.¹³⁻¹⁵ Limited evidence suggests that hypoglycemic events identified by CGM were more frequent than those identified by SMBG in patients with diabetes of the exocrine pancreas and that use of CGM significantly reduced the incidence of hypoglycemia.¹⁶⁻¹⁸

Detailed evaluations of hypoglycemic events and other hypoglycemia-specific indices based on CGM are limited in patients with diabetes of the exocrine pancreas. These hypoglycemia-specific measures could be useful as an adjunct to glycated hemoglobin (HbA1c) for better overall assessment of glycemic status in patients with diabetes of the exocrine pancreas. They could also provide information regarding the burden of hypoglycemia in this patient population. Further, more in-depth knowledge of the various aspects of hypoglycemia and its indices will assist in the planning of preventative strategies. As well, such knowledge may provide novel insights into therapeutic regimens designed to reduce hypoglycemia. Prevention of recurrent hypoglycemic episodes will improve the overall quality of life and could contribute to a reduction in hypoglycemia-associated morbidity and mortality. Therefore, this study sought to use CGM to evaluate the frequency and pattern of hypoglycemic events and to estimate various hypoglycemia-specific indices in a large cohort with diabetes of the exocrine pancreas.

Methods

Subject Selection

Patients aged between 18 and 65 years who had been diagnosed with diabetes of the exocrine pancreas for at least 3 months and who were on self-adjusting insulin and under regular follow-up were eligible for this study. Diabetes of the exocrine pancreas includes the following: (1) post-pancreatic diabetes mellitus (PPDM), (2) pancreatic cancer-related diabetes (PCRD), and (3) cystic fibrosis-related diabetes (CFRD) as per American Diabetes Association (ADA). The diagnosis of PPDM is based on the presence of diabetes in the background of acute or

chronic pancreatitis regardless of the timing of diabetes onset.¹⁹ The diagnosis of fibrocalculous pancreatic diabetes (FCPD) was made on the basis of the previously defined criteria.²⁰ Alcohol-induced pancreatitis was defined as follows: (1) presence of alcohol consumption as described by the Alcohol Use Disorders Identification Test (AUDIT), whereby a score higher than eight was considered to be abnormal and (2) absence of other identifiable causes of pancreatitis.²¹ The diagnosis of autoimmune pancreatitis requires the fulfillment of at least one of the following criteria: (1) pancreatic histopathological findings; (2) imaging; (3) serology (immunoglobulin [Ig]G4, IgG, antinuclear antibodies); (4) other organ involvement; and (5) response to steroid therapy.²² Patients diagnosed with FCPD, diabetes secondary to alcohol-induced pancreatitis, and autoimmune pancreatitis were considered as patients with PPDM. Eligible patients were identified from the registry of our endocrine clinic and were invited to participate in this study over the phone. Patients were further screened for eligibility when they reported to the endocrine clinic at the Vydehi Institute of Medical Sciences and Research Centre, Bangalore. Exclusion criteria consisted of (1) patients on oral antidiabetic drugs; (2) those not on insulin; (3) those with a history of severe hypoglycemia in the preceding 3 months; (4) those on glucocorticoids; (5) use of beta-blockers; (6) HbA1c <6% or >12%; (7) those with undue fear of technical systems, alcohol, and/or drug misuse; and (8) patients with major psychological/psychiatric problems. After screening, a total of 92 patients were included in the final cohort. The study protocol was approved by the ethical committee of the Vydehi Institute of Medical Sciences and Research Centre, and the study conforms with the Good Clinical Practice provisions of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Clinical and Laboratory Evaluation

We collected information on the duration of diabetes, steatorrhea, and abdominal pain; history of hypoglycemic episodes; enzyme replacement therapy; pancreatic surgeries; initial and current treatment; details of insulin therapy, and the most recent HbA1c measurement. All patients underwent anthropometric assessment of height, weight, and body mass index (BMI).

Following a ten-hour overnight fast, fasting blood samples were drawn from patients with FCPD for estimation of the levels of fasting plasma glucose (FPG), HbA1c, the fasting lipid profile, and serum creatinine. Plasma glucose concentration was estimated using the hexokinase enzymatic reference method. HbA1c level was estimated by the high-performance liquid chromatography method using a BIORAD D10 analyzer (Bio-Rad, NY, USA). Enzymatic methods were used to determine serum total cholesterol and triglyceride concentrations. High-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein (LDL) levels were estimated using the direct measure polymer poly-anion method. The remaining tests were performed using a fully automated Beckman

Coulter DXC 860i autoanalyzer (Beckman Coulter Inc., CA, USA).

CGM Monitoring

Following determination of eligibility, the CGM system Medtronic iPro2 (Medtronic, USA), was inserted in all eligible patients by a trained professional. Patients were advised to remain hospitalized for a minimum period of three days. Bedside glucose monitoring (SMBG) was performed at frequent intervals (prebreakfast, prelunch, predinner, two hours after dinner, midnight 3a.m and whenever the patient develops symptoms of hypoglycemia) using an Accucheck Instant blood glucose meter (Abbott Diabetes Care, Alameda, CA, USA). Patients and nursing staff were instructed on recording events of hypoglycemia (symptomatic and asymptomatic), insulin doses, and physical activity, as well as maintenance of a food diary. The plasma glucose concentrations were maintained within the preprandial target range of 90-130mg/dL and with two-hour postprandial values below 180mg/dL. At the follow-up visit, adverse events including severe hypoglycemia, device-related issues, and any other notable adverse events, regardless of cause, were identified and reported. The final analysis included only those patients with a minimum of 72 hours of CGM data.

Measures of Glycemic Variability and Hypoglycemia

CGM-derived metrics of glycemic variability and hypoglycemia were estimated using the GlyCulator 2 (<https://apps.konsta.com/pl/app/glyculator>). The following parameters of glycemic variability were estimated: (1) SD of the mean of the sensor values; (2) mean amplitude of glycemic excursion (MAGE); (3) continuous overall net glycemic action (CONGA); (4) *M* value, and (5) coefficient of variance (%CV). Hypoglycemic indices derived from CGM included (1) low blood glucose index (LBGI), (2) area under curve the (AUC) <70mg/dL, (3) AUC <54mg/dL, (4) time spent below (TSB) <70mg/dL, (5) glycemic risk assessment diabetes equation (GRADE) hypoglycemia, (6) number of hypoglycemic events, (7) number of prolonged hypoglycemic events (>120minutes), and (8) mean duration of hypoglycemic event.

Sample Size

Sample size was estimated considering the low blood glucose index as an outcome. Assuming the expected SD of 0.82, to estimate a mean with 95% confidence and a precision of 0.2, the required sample size was 68.

Statistical Analysis

Assumption of normality was assessed. Descriptive statistics were reported as mean with SD for normally distributed

Table 1. Baseline Characteristics of the Study Group.

Parameters	Mean \pm SD
Age (years)	35.0 \pm 8.2
Gender	
Male (<i>n</i>)	47
Female (<i>n</i>)	36
BMI (kg/m ²)	18.9 \pm 2.8
Duration of diabetes (years)	5 (1, 8)
FPG (mg/dL)	191.8 \pm 79.3
HbA1c %	9.5 \pm 1.6
Serum creatinine (mg/dL)	0.7 \pm 0.3
Total cholesterol (mg/dL)	166.1 \pm 41.3
TG (mg/dL)	154.2 \pm 85.4
HDL (mg/dL)	41.7 \pm 9.4
LDL (mg/dL)	97.4 \pm 35.4

Data are represented by mean \pm SD for normally distributed continuous variables, while variables that were non-normal were reported as mean and SD along with median with interquartile range to understand the distribution of each variables.

BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides.

continuous variables, variables that were non-normal were reported with mean and SD along with median with 25th and 75th percentiles to understand the distribution of each variable. Categorical variables were reported as numbers and percentages. Comparison of hypoglycemic outcomes between night and day was performed using the Wilcoxon Signed-Rank test. *P* value of less than 5% was considered statistically significant. All the analyses were performed using SPSS version 25.0.

Results

Baseline Characteristics

Demographic information and biochemical measurements of the study group are presented in Table 1. A total of 92 patients met the eligibility criteria for enrolment in the study and completed the CGM procedure. Nine patients (six females and three males) were withdrawn from the study due to sensor displacement and technical issues. The final cohort was composed of 83 patients with diabetes of the exocrine pancreas. The distribution was as follows: 51.81% of patients (*n* = 43) were diagnosed with FCPD, 33.73% (*n* = 28) of patients had alcoholic pancreatitis, 8.43% (*n* = 7) had post-pancreatic resection (*n* = 5 patients underwent resection secondary to pancreatic malignancy, while *n* = 2 patients underwent resection owing to chronic intractable pain secondary to chronic pancreatitis), 4.82% (*n* = 4) had pancreatic cancer, and 1.21% (*n*=1) had pancreatitis attributed to an autoimmune etiology. Overall, 74 patients were diagnosed with PPDM, nine patients had PCRD, while none had CFRD. Among the study population, 56.6% of the patients were

Table 2. Hypoglycemic Outcomes.

Parameters	WHOLE (n = 83)	NIGHT	DAY	P value*
LBG1	2.1 ± 2.7 1 (0.4-2.4)	2.3 ± 3.8 0.9 (0.2-2)	1.3 ± 2.0* 0.7 (0.1-1.5)	0.011
AUC <70mg/dL	1.70 ± 2.5 0.7 (0.3-1.7)	1.9 ± 3.2 0.6 (0-1.7)	1.0 ± 1.7* 0.5 (0-1.5)	0.031
AUC <54mg/dL	0.6 ± 1.3 0 (0-0.7)	0.7 ± 1.6 0 (0-0.1)	0.2 ± 0.50* 0 (0-0)	0.003
Time spent below 70mg/dL %	9.2 ± 10.4 4.4 (2-13.7)	10.4 ± 13.6 5.5 (0-13.3)	5.8 ± 7.6* 2.5 (0-10)	0.003
Time spent below 54mg/dL %	3.7 ± 6.5 0 (0-5.2)	3.6 ± 9.4 0 (0-1.3)	1.7 ± 3.4 0 (0-1.1)	0.077
GRADE _ hypoglycemia	9.1 ± 11.0 5.1 (1.4-12.8)	13.1 ± 19.4 4.4 (0.6-14.2)	5.9 ± 8.6* 1.8 (0.1-8.4)	<0.001
No. of hypoglycemic events	2.9 ± 2.7 2.0 (1.0-4.5)	1.9 ± 2.4 1 (0-3)	1.1 ± 1.2* 1 (0-1)	<0.001
Mean duration of hypoglycemic event (min)	177.3 ± 143.5 157.8 (63.9-227.3)	142 ± 157.8 135.5 (0-164.5)	82.8 ± 83.4* 54.8 (0-148.3)	<0.001

Data are represented by mean ± SD for normally distributed continuous variables, while variables that were non-normal were reported as mean and SD along with median with interquartile range to understand the distribution of each variables. P value < 0.05 was considered significant.

*P value between day and night parameters.

AUC, area under curve; GRADE, glycemic risk assessment diabetes equation score; LBG1, low blood glucose index.

males. The mean age of the participants was 35 ± 8.2 years, and the duration of diabetes was 5.1 years. The mean BMI was 18.9 ± 2.8 kg/m². The mean HbA1c value of the participants was 9.5 ± 1.6%, and the patients required approximately 0.6 U of insulin per kg of body weight administered daily by multiple subcutaneous injections. No ketoacidosis was reported during the hospital stay.

Hypoglycemic Outcomes

Data from CGM revealed that 75 patients had at least one hypoglycemic event. Among these, 29.3% of patients (n = 22) developed symptoms, while 70.7% (n = 53) were asymptomatic. Level 1 hypoglycemia (blood glucose <70mg/dL and >54mg/dL) was observed in 40.9% of patients, while level 2 hypoglycemia (blood glucose <54mg/dL; did not require external assistance for recovery) was recorded in 42.1% of patients. Data from SMBG revealed that 32 (38.5%) patients had at least one hypoglycemic episode. Of these, 68.7% developed symptoms (n = 22), while the remainder (31.3%, n = 10) were asymptomatic. Severe hypoglycemia was reported by six patients, one of whom had two episodes of severe hypoglycemia.

CGM recorded a mean number of 2.9 hypoglycemic episodes per patient (Table 2). Approximately 62 patients (74.7%) had at least one nocturnal hypoglycemic episode (12 am – 6 am) detected by CGM, 80.6% (n = 50) of whom did not develop any symptoms. SMBG recorded nocturnal hypoglycemic episodes in 22 patients (26.5%), 45.4% of whom (n = 10) were asymptomatic. The mean number of recorded hypoglycemic episodes was significantly higher during the

night than during the day (1.9 vs 1.1, P < 0.001). Similarly, the mean duration of hypoglycemic episodes recorded by CGM was significantly higher at night than during the day (142 minutes vs 82.8 minutes, P < 0.001). The period between 3 and 6AM was the most common time for nocturnal hypoglycemia. A typical CGM graph depicting hypoglycemia in patients with diabetes of the exocrine pancreas is shown in Figure 1.

Measures of Glycemic Variability and Hypoglycemic Indices as Determined by CGM

The baseline CGM-derived measures of glycemic variability are provided in Table 3. The mean cohort values of MAGE, SD, and %CV were 138.9 ± 57.7mg/dL, 57.3 ± 24.3 mg/dL, and 30 ± 11.4%, respectively. The mean CGM-derived 24-hour glucose concentration was 193.3 ± 56.9 mg/dL. In general, significant differences were observed between daytime and nocturnal CGM-derived hypoglycemic events and indices. The mean TSB <70mg/dL was 9.2%, and <54mg/dL was 3.7% (Table 2). The mean TSB <70mg/dL was significantly higher during the night in comparison with during the day (10.4% vs 5.8%, P < 0.05). Although TSB <54mg/dL was numerically higher during the night (3.6%) than during the day (1.7%), the result was not statistically significant (P = 0.07). The mean AUC <70mg/dL at night (1.9 ± 3.2) was significantly higher than during the day (1.0 ± 1.7, P = 0.03). Similarly, the mean AUC <54mg/dL was significantly higher during night (0.7 ± 1.6) than during the day time (0.2 ± 0.5, P < 0.05). The mean LBG1 and GRADE hypoglycemia were also significantly higher at

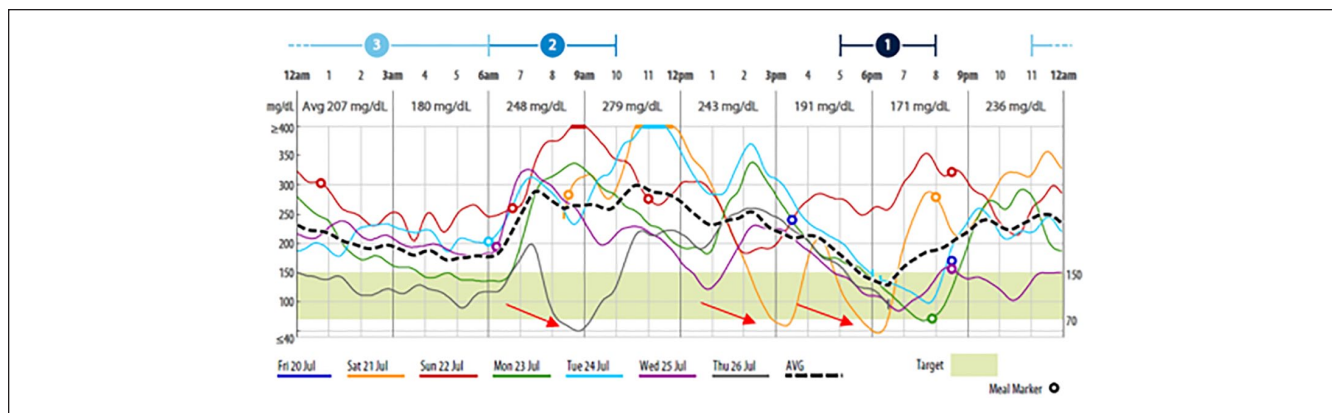


Figure 1. A typical CGM graph of patient with diabetes of the exocrine pancreas. Dotted black lines represent integrated CGM curve; red arrows represent hypoglycemia. CGM, continuous glucose monitoring.

Table 3. Baseline CGM-Derived Glycemic Parameters.

Parameters	Whole (n = 83)
Mean	193.3 ± 56.9; 184.3 (159.3-222.5)
Median	188.4 ± 60.1; 180 (147.5-220.0)
SD	57.3 ± 24.3; 55.3 (37-79.7)
CV %	30 ± 11.4; 27.2 (20.5-38.2)
LBGI	2.1 ± 2.7; 1 (0.4-2.4)
HBGI	13.5 ± 10.3; 11.2 (5.6-18.1)
M100	268.1 ± 108.1; 252.9 (202.1-330)
J Index	68 ± 36.8; 63.5 (39.1-93.3)
GRADE	12.9 ± 6.6; 11.6 (8.6-16.4)
MAGE	138.9 ± 57.7; 132.3 (89.6-186.2)
MODD	60.6 ± 28.5; 53.4 (40.3-82.5)
CONGA_6hrs	45.8 ± 20.5; 42.7 (30.3-59.5)

Data are represented by mean ± SD for normally distributed continuous variables, while variables that were non-normal were reported as mean and SD along with median with interquartile range to understand the distribution of each variables.

CGM, continuous glucose monitoring; CONGA_6hrs, continuous overall net glycemic action at four hours; CV, coefficient of variation; eA1c, estimated glycated haemoglobin; GRADE, glycemic risk assessment diabetes equation score; HBGI, high blood glucose index; J index, measure of quality of glycemic control; LBGI, low blood glucose index; M100 (mg/dL), weighted average of glucose values; MAGE, mean amplitude of glycemic excursions; MODD, absolute means of daily differences.

night (2.3 ± 3.8 and 13.1 ± 19.4 , respectively) than during the day (1.3 ± 2.0 and 5.9 ± 8.6 , respectively; $P < 0.05$).

Discussion

The present study represents an important expansion of our prior work on CGM-derived measures of glycemic variability in patients with T2D and FCPD.²³ In this study, we used CGM to assess hypoglycemic events and hypoglycemia-associated indices in patients with diabetes of the exocrine pancreas. We found that the majority of patients experienced hypoglycemic events with significant alterations in hypoglycemic indices.

As well, nocturnal hypoglycemic events and indices were more prevalent and unstable than those observed during the day. To our knowledge, this is the first study to evaluate various hypoglycemic indices in a large cohort with diabetes of the exocrine pancreas.

Diabetes of the exocrine pancreas is characterized by glycemic variability and instability with broad fluctuations in plasma glucose.¹ In tropical countries, the forms of diabetes of the exocrine pancreas that are most commonly observed include chronic alcoholic pancreatitis and FCPD. A high frequency of hypoglycemia has been demonstrated in patients with diabetes of the exocrine pancreas using SMBG. Studies in patients that had developed diabetes secondary to pancreatic resection reported incidences of hypoglycemia detected by SMBG in the majority of their patients.⁸⁻¹¹ In a study involving patients who underwent pancreatectomy, severe hypoglycemia was reported in 41% of patients, and non-severe hypoglycemia was reported in 79% of patients,⁸ while a separate study reported symptomatic hypoglycemia in 50% of their patients.¹⁰ In a retrospective analysis of patients with PPDM (secondary to alcoholism, biliary tract disease, and idiopathic etiology), hypoglycemia was detected by SMBG in 78% of patients treated with insulin.⁷ A similar observation was reported in patients with diabetes secondary to hereditary pancreatitis.²⁴

Detailed evaluations of hypoglycemia using CGM in patients with diabetes of the exocrine pancreas are limited thus far. In our study, CGM revealed that the majority of the patients (90.4%) with diabetes of the exocrine pancreas experienced at least one hypoglycemic event. These findings are consistent with those reported by a previous study involving 60 patients with diabetes of the exocrine pancreas, in which hypoglycemic events detected with CGM were five times higher than those detected with SMBG.¹⁷ As well, it has been shown that CGM contributes to a reduction in the number of hypoglycemic episodes through improved glycemic control.^{17,25-27} In a prior study, usage of CGM was associated with a 44% reduction in hypoglycemic events in patients with

T1D.²⁵ Similarly, the use of CGM led to a reduction in hypoglycemic events in patients with diabetes post-pancreatic resection.¹⁸

Hypoglycemic indices are useful in estimating the risk of hypoglycemia. They also assist in assessing the overall quality of glycemic control. LBGI is an indicator of risk for severe hypoglycemia in patients with diabetes, and the highest risk was seen in patients with LBGI >5.²⁸ In our study, the mean LBGI was 2.1, while a subset of patients with HbA1c <8.5% had a mean LBGI of 5.2. In a study involving 50 patients with T1D on continuous subcutaneous insulin infusion therapy, LBGI was 3.49 with an HbA1c of 7.5%.²⁹ In another study composed of patients with T1D, LBGI was 5.7 in patients with an HbA1c of <7.2, while in patients with HbA1c >9.2%, LBGI was 2.2.³⁰ GRADE hypoglycemia is an indicator of the degree of hypoglycemic risk, and it has been suggested that values >5 are associated with a higher risk of hypoglycemia.³¹ The GRADE hypoglycemia value of 9.1 observed in this study is consistent with a value of 8.4 reported by a study composed of patients with T1D.³² TSB represents the duration of hypoglycemia, while AUC <70 mg/dL represents hypoglycemic exposure; in normal individuals, both are close to zero. Although there are no recommended cut-off values for TSB and AUC <70 mg/dL, our study results are similar to those reported in a study composed of patients with T1D.³³ Our findings suggest that patients with diabetes of the exocrine pancreas have greater instability in hypoglycemic indices than has been previously reported in patients with T1D. This instability in hypoglycemic indices could be attributed to higher glycemic variability, exocrine insufficiency, malabsorption, and deficient counter-regulatory glucagon response in this population.^{34,35}

Information derived from CGM is of vital importance in improving glycemic control and planning preventative strategies which include education of the patient (regarding diet, exercise, dose adjustments, self-monitoring of glucose), use of long-acting insulins (degludec, glargine) and flexible dosing, and individualized glycemic goals, help in reducing the incidence of hypoglycemia and its associated morbidity. Furthermore, CGM-derived hypoglycemic indices will guide the clinician in assessing the patient-specific risk of hypoglycemia and could help in monitoring the response to therapy.

Our study has a few limitations. First, the majority of the patients in our study belonged to the PPDM (chronic) group, and we excluded patients diagnosed with postacute pancreatitis diabetes mellitus which is the most common subtype of diabetes of the exocrine pancreas.³⁶ In addition, there were limited patients belonging to the PCRD group and none in the CFRD group. Further CGM-based studies might be required to assess hypoglycemic indices in PCRD and CFRD categories. Second, it is possible that the interstitial glucose readings obtained by CGM were lower compared with capillary blood glucose levels, which could have resulted in over-reporting of hypoglycemic events.^{37,38} Lastly, hypoglycemic indices were assessed during hospital admission, and it is

therefore possible that they do not reflect hypoglycemia that occurs at home. Further prospective studies are required to validate our findings in nonhospitalized patients on a stable treatment regimen.

Conclusion

Patients with diabetes of the exocrine pancreas have a high frequency of hypoglycemic episodes that predominantly occur at night. CGM is superior to SMBG in the detection of nocturnal and asymptomatic hypoglycemic episodes. CGM-derived hypoglycemic indices are beneficial in estimating the risk of hypoglycemia.

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