Rev. Fac. Med. Hum. 2022; 22(4):893-899.
DOI: 10.25176/RFMH.v22i4.5046
ISSN Versión Online: 2308-0531
Facultad de Medicina Humana URP

CLINICAL CASE

DECREASING HYPOGLYCEMIA UNAWARENESS IN A PATIENT WITH TYPE 1 DIABETES MELLITUS AFTER CONTINUOUS GLUCOSE MONITORING: TOOLS FOR SELF-CARE

DISMINUCIÓN DE HIPOGLICEMIA ASINTOMÁTICA EN UNA PACIENTE CON DIABETES MELLITUS TIPO 1 LUEGO DEL MONITOREO CONTINUO DE GLUCOSA: HERRAMIENTAS PARA EL EMPODERAMIENTO.

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ABSTRACT

Diabetes mellitus is a public health problem that causes early and late complications. Continuous glucose monitoring (CGM) has become the main technological tool for real-time glycemic control and has the potential to prevent complications. However, its use has not spread in low- and middle-income countries.

We present the experience in the management of a patient with type 1 diabetes with hypoglycemia unawareness in whom the use of real-time CGM achieved both: less hypoglycemic episodes and optimization of insulin regimen. The benefit of real-time CGM in addition to the use of analog insulins and diabetes education resulted in better metabolic control. CGM is a useful tool to consider in patients with hypoglycemia unawareness and to minimize the risk of complications in the future.

Keywords: Diabetes mellitus type 1; Technology; Education; Blood Glucose Self-Monitoring; Hypoglycemia. (Source: MeSH NLM)

RESUMEN

La diabetes mellitus es un problema de salud que ocasiona complicaciones tempranas y tardías. El monitoreo continuo de glucosa (MCG) se ha convertido en la principal herramienta tecnológica para el control glicémico en tiempo real y evitar las potenciales complicaciones. Sin embargo, su uso no se ha extendido en países de medianos y bajos ingresos. Se presenta la experiencia en el manejo de una paciente adulta con diabetes tipo 1 con hipoglicemias asintomáticas recurrentes en quien el uso del MCG en tiempo real permitió reducir los episodios de hipoglicemias y optimizar la insulino terapia. La aplicación del MCG sumado al uso de insulinas análogas y educación en el manejo de la enfermedad resultó en un mejor control metabólico. El MCG, especialmente incorporando un sistema de alarma, es una herramienta útil a considerar en pacientes con hipoglicemia frecuente para minimizar el riesgo de complicaciones a futuro.

Palabras claves: Diabetes Mellitus Tipo 1; Tecnología; Automonitorización de la Glucosa sanguínea; Hipoglucemia. (Fuente: DeCS - Bireme)

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Cite as: Perez-Cavero SH, Manrique-Hurtado H, Leey-Casella J. Decreasing hypoglycemia unawareness in a patient with type 1 diabetes mellitus after continuous glucose monitoring: tools for self-care. Rev Fac Med Hum. 2022;22(4):893-899.
doi:10.25176/RFMH.v22i4.5046

Journal home page: http://revistas.urp.edu.pe/index.php/RFMH

INTRODUCTION

Type 1 diabetes mellitus (DM1) represents between 5 to 10% of all diabetes cases and is a condition where beta cells are destroyed by an autoimmune phenomenon. The prevalence and incidence of DM1 are approximately 5.6 and 15 cases per 100,000 inhabitants, respectively, worldwide[1], with the number of new cases in children and young people during the COVID-19 pandemic being alarming[2].

In Peru, the incidence is low, with approximately one case per 100,000 inhabitants in children under 15 years of age[3], but it is increasing. Recently, the National Institute of Child Health in Peru reported a greater number of new cases per year between 2011 and 2018 [4]. Patients with DM1 have greater difficulty in reaching glycated hemoglobin (HbA1c) goals and thus be able to reduce complications. Fear of hypoglycemia and poor adherence to treatment in these patients greatly affect good glycemic control. In parallel, hypoglycemia increases mortality and cardiovascular risk [5].

Self-monitoring is essential for the control of DM1; however, the cost of fingerstick glucose monitoring and the discomfort and pain associated with it limits its use. In developed countries, the use of continuous glucose monitoring (CGM) has become the main technological tool for real-time glycemic control. In Peru, there is a previous report on the use of CGM in an adult [6] and a retrospective study of 28 patients between children and adults [7].

In this report, we describe the case of a patient with DM1 with poor metabolic control and recurrent hypoglycemia in whom the use of real-time CGM reduced hypoglycemic episodes, improved quality of life, and reached the appropriate dose of insulin.

DESCRIPTION OF THE CLINICAL CASE

A 39-year-old female patient from the northern region of Peru, with a personal history of two previous abortions and DM1 since she was 23 years of age, with a report of an episode of diabetic ketoacidosis currently undergoing treatment with insulin therapy. On the first visit, the patient is evaluated by teleconsultation due to confinement due to the COVID-19 pandemic. Capillary glucose was measured 1 or 2 times a day, 50-70% of the time with a value less than 70 mg/dl, several of the episodes were asymptomatic. She suffered from almost daily episodes of hypoglycemia either day and/or night, with documented symptoms up to approximately 35mg/dl of capillary glucose, some of them were severe nocturnal hypoglycemia that required the assistance of another family member with glucose reaching up to 23 mg/dl.

He has a history of an arm fracture due to severe hypoglycemia with loss of consciousness. His height is 163 cm and weight 49 Kg (BMI 18.4 Kg/m2), body mass index is usually less than 20 Kg/m2, he used NPH and Regular insulin with a total daily dose of insulin (TDD) 1 at 1.2 IU/KG (see Table 2). Auxiliary tests showed the following results: HbA1c 8.1%, C-peptide <0.01 nmol/L, total cholesterol: 197 mg/dl, high-density lipoprotein (HDL) 56 mg/dl, low-density lipoprotein (LDL) 138 mg/dl, triglycerides: 65mg/dl, thyroid-stimulating hormone (TSH): 1.52mIU/L, creatinine 1.44mg/dl, and microalbuminuria 1.4mg/L.

Six days after the teleconsultation, a Free Style Libre 2 CGM sensor was placed. Given the high dose of daily insulin and the high frequency of hypoglycemia, the change to insulin analogs was made according to weight: glargine 18 IU/day and lispro 4/7/5 IU before breakfast, lunch, and dinner, respectively, while providing nutritional education and counseling (see Table 2). Following the manufacturer's instructions, the sensor was applied to the skin of the outer aspect of the arm. Likewise, the Libre 2 scanner was provided and he was instructed to scan the CGM sensor at least every 8 hours during the 14 days that the sensor lasts. The patient sent daily insulin dose information and photos of her food. Correction of insulin doses was coordinated with her and the accuracy of carbohydrate counting was reinforced. Additionally, during the 2 weeks of CGM use, the patient made her own minimal adjustments to the basal and preprandial insulin doses, empowering her in the education and management of her diabetes.

	At the beginning	at 4 months
BMI (weight/m2)	18.44	18.06
Weight (kg)	49.0	48.0
HbA1C (%)	8.1	7.3
Hemoglobin (g/dl)	-	13.4
Uric acid (mg/dl)	-	3.2
Total cholesterol (mg/dL)	197	162
Cholesterol HDL (mg/dL)	56	46.6
Cholesterol LDL (mg/dL)	138	104.9
Triglycerides(mg/dL)	65	63.8
Creatinine(mg/dL)	1.44	0.94
TGP or Alanine Aminotransferase	-	19
(mUI/mL)24-hour microalbuminuria(mg/L)	1.4	-
C-peptide (nmol/L)	<0.01	-
TSH (mUI/L)	1.52	-

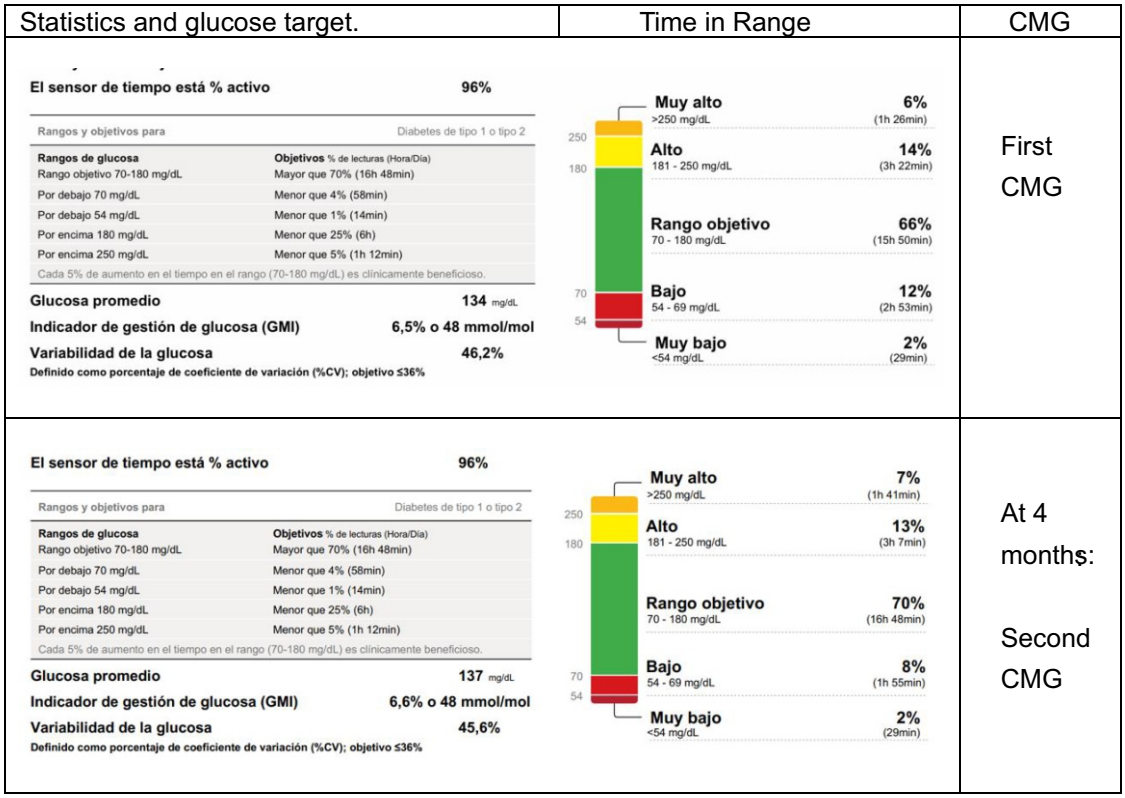
The report of the first CGM obtained a time in the range of 70 to 180 mg/dl in 66% (the hypoglycemia alarm setting was from 70 mg/dl), an average glucose of 134 mg/dl, a glucose variability 46.2% and 26 low glucose events with an average duration of 120 minutes (Figure 1). The basal insulin dose was 18 IU/day and preprandial insulin was finally divided into 2/2/2 IU on average (Table 2).

Table 2. Daily Insulin Dose and Continuous Glucose Monitor Data.

	Before the use of the CGM	First CGM	Second CGM
Daily dose of insulin (IU)	1,04 - 1.2 UI/Kg/day	0,57 UI/Kg/day	0,62 UI/Kg/day
Basal insulin(UI)	NPH 25 and 20 UI	Glargine U-100 18 UI	Glargine U-100 21 UI
Preprandial insulin (UI)	Regular -/10/- UI	Lispro 2/2-3/2 UI	Lispro ~3/3/3 UI
Average glucose (mg/dl)		134	137
Glucose variability (%Standard deviation/mean)		46,2%	45,6%
Glucose Management Indicator (GMI) or estimated HbA1c		6,5%	6,6%
Time in Range 70-180 mg/dl		66%	70%
Time between 54 and 69 mg/dl		12%	8%

Time below 54 mg/dl			2%	2%
Time above 180mg/dl			14%	13%
Time above 250mg/dl			6%	7%
Low glucose events			26	18
Mean duration of hypoglycemic episode (minutes)			120	117
Total duration of hypoglycemia in 14 days			3120 minutes 52 hours or 3.8 hours/day	2106 minutes 35.1 hours or 2.5 hours/day
Treatment changes	Before sensor	daily dose of insulin (UI)	0,69 UI/Kg/day	0,58 UI/Kg/day
		Basal Insulin UI)	Glargine U-100 18 UI	Glargine U-100 18 UI
		Preprandial insulin (UI)	Lispro 5/7/4 UI	Lispro 2-4/2-4/2 UI
	After sensor	Daily Insulin Dose(UI)	0,57 UI/Kg/day	0,62 UI/Kg/day
		Basal Insulin (UI)	Glargine U-100 18 UI	Glargine U-100 21 UI
		Preprandial insulin(UI)	Lispro 4/2-4/2 UI	Lispro ~3/3/3 UI

At the four-month outpatient follow-up, she showed better control of self-monitoring of glucose, with capillary glucose measurement four times a day, and fewer hypoglycemia episodes. It was decided to install another CGM for two weeks, with an alarm setting from 80mg/dl to prevent hypoglycemic episodes earlier. An average glucose value of 137 mg/dl, a target range at 70%, a glucose variability of 46.6% and 18 low glucose events with an average duration of 117 minutes were recorded (See Figure 1). Control laboratory tests showed the following results: HbA1C: 7.3%, total cholesterol 162 mg/dl, HDL 46.4 mg/dl, LDL 104.9 mg/dl, triglycerides 63.8 mg/dl, creatinine 0.4 mg/dl, TGP or Alanine Aminotransferase 19 mIU/mL.



* MCG: FreeStyle Free 2 Continuous Glucose Monitor.

Figure 1. Report of glucose statistics and time in range using Continuous Glucose Monitor.

The dose at four months of basal insulin with insulin glargine was 21 IU/day and insulin lispro 3/3/3 IU/day. The patient reports less hypoglycemia and better quality of life, in addition to a better understanding of the effect of the number of carbohydrates, which allows her to have more control over the disease.

DISCUSSION

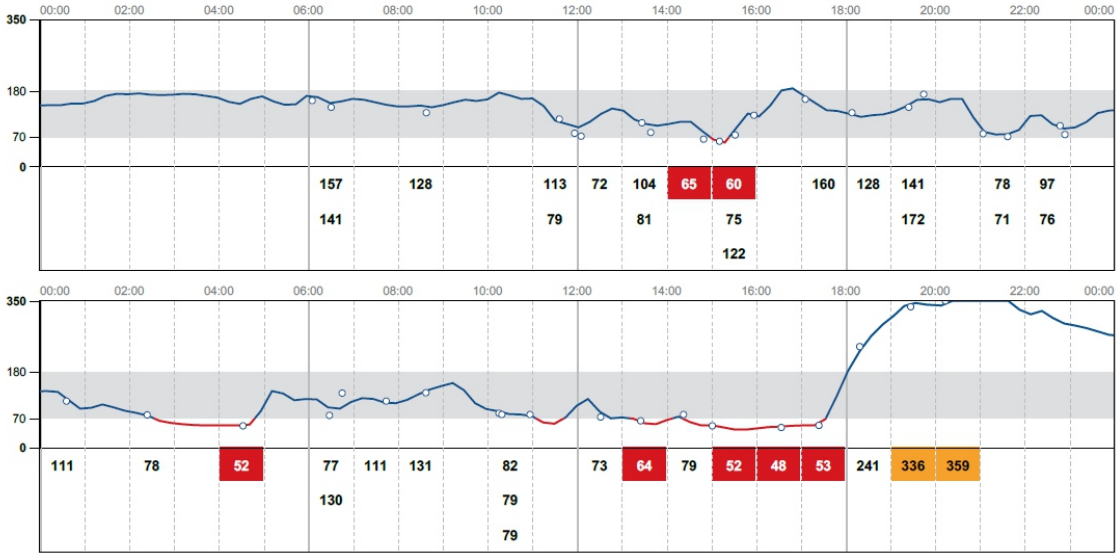
Lhypoglycemia causes cognitive impairment and is associated with mortality in 4-10% of patients with DM1, and cases have been described of patients dying during sleep after long periods of asymptomatic hypoglycemia[9,10]. In the present report, our patient decreased the number of hypoglycemic events between the first and second CGM from 24 to 18 episodes, respectively. Although the average duration was similar (120 minutes versus 117 minutes), the total time of hypoglycemia in the 14 days that each GCM lasted decreased from 3120 minutes (3.8 hours per day) in the first GCM to 2106 minutes (2.5 hours per day) in the second GCM. The higher the frequency of hypoglycemia, the higher the reactive hyperglycemia due to the fear of a hypoglycemic episode[9]. Recently, international guidelines, in addition to glycosylated hemoglobin, recommend goals based on the GCS as the longest time in range, the shortest time in hypoglycemia and the lowest glycemic variability to mitigate long-term complications[11].

In the case of our patient, she reported a decrease in hypoglycemia episodes with the switch to insulin analogs. This suggests that, with the previous regimen of NPH and regular with which she had higher daily insulin doses, the exposure to daily hypoglycemia was probably even worse. The use of real-time CGM allowed the patient to better understand the impact of carbohydrate intake and its relationship to insulin doses.

The availability of hypoglycemia alarms on the MCG is especially useful in patients with a history of asymptomatic hypoglycemia as in our patient. Many of the episodes of hypoglycemia are nocturnal and the alarm shortens the time of exposure to hypoglycemia, as was observed in a pediatric patient who did not react to hypoglycemia when using a CGM without a hypoglycemia alert, but did when she switched to a CGM with alerts that helped reduce the duration of hypoglycemia[12].

in Figure 2. The upper panel shows 20 scans (white circles), two of them with hypoglycemia around 3 PM. The previous 15 hours there was no hypoglycemia. The glucose level is seen to rise 20 minutes after hypoglycemia was detected. The next day the patient had a 2-hour episode of hypoglycemia between 2:20 and 4:40 AM. She scanned the MCG at 4:30 which yielded a value of 52 and within minutes her glucose level began to rise indicating carbohydrate intake. However, in the afternoon of the same day she had a prolonged episode of hypoglycemia between 1pm and 5:30pm. The patient performed several scans approximately 1 per hour, several of them corresponding to hypoglycemia, but the glucose level remained at about the same level suggesting no when she developed marked reactive hyperglycemia, greater than 300 mg/dL for several hours, suggesting excessive carbohydrate intake.

Hypoglycemia is known to transiently and sometimes permanently affect cognitive function [13], it is possible that the frequent episodes of hypoglycemia, especially that of the same day, may have affected the patient's decision-making ability, predisposing her to develop more hypoglycemia that same day in the afternoon.



* MCG: FreeStyle Free 2 Continuous Glucose Monitor.

Figure 2. Sample of Daily Glucose Level Recordings.

In a previous report, the case of a 29-year-old patient with long-standing DM1 who used a blinded CGM (Lizarzaburu) was described. The blinded CGM does not show the patient the glucose level in real time but at the end of the period of use (6 to 14 days later), in the mentioned case, the CGM showed a time in target range of 17% and persistent hyperglycemia, it is mentioned that there was lack of adherence to nutritional control and physical activity; subsequent controls at the third and fifth year showed gradually less hyperglycemia, better glycemic control (HbA1c) and with little evidence of hypoglycemia, however, she reached a higher BMI than at the beginning.

To our knowledge, the present report is the first Peruvian case of improvement of severe hypoglycemia and decrease in the frequency of asymptomatic hypoglycemia with the use of CGM in DM1. In addition to visualizing her glucose level, the patient had a very close medical and nutritional follow-up, which enhanced nutritional education and empowerment. This improvement continued after 4 months of follow-up when she even increased the time in target range from 66% during the first CGM to 70% in the second CGM, in addition to a clinically significant reduction of 1.3 hours of hypoglycemia per day.

In our setting, a pilot study of 28 patients in pediatric and adult populations showed that the use of the CGM, although for a short period of time, was beneficial in either type 1 diabetes (predominantly children) or type 2 diabetes (predominantly adults). In that study, those who used the Free 14-day MCG system with scanning, but without a hypoglycemia alarm, there was a correlation between the number of scans and time in the range 70-180 mg/dl, while adults who used the blinded monitor had no behavioral feedback of carbohydrate intake as the patient was "blind" to the glucose level[7]. 100 years after the discovery of insulin, patients with diabetes have empowered their diabetes treatment thanks to more stable and predictable insulins in their absorption (analogs) and the GCM technology that allows an approach to the ideal therapy of the patient with DM1. In conclusion, the CGM, especially incorporating an alarm system, is a useful tool to consider in patients with diabetes and asymptomatic hypoglycemia as it allows an optimization of the insulinization schedule therapy, empowerment of the patient with carbohydrate intake and insulin use, and a clinically significant decrease in the frequency and total duration of hypoglycemia.

Authorship contributions: SPC contributed to the conceptualization, data collection, methodology design, data analysis, writing of the initial draft, critical review of the article, writing and approval of the final version. HMH contributed to the conceptualization, methodology design, data analysis, managed the research activities, writing, and approval of the final version. JLC contributed to the conceptualization, design of the methodology, data analysis, managed the research activities and financing and provided the resources for the research (Sensors and scanners were donated by Dr. Leey), drafting and revision of the final version.

Funding sources: Self financed.

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Conflicts of interest: The authors declare that they have no conflict of interest.

Received: july 18, 2022
Approved: october 14, 2022

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