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The HbA1c, coefficient of variation of glucose levels and hypoglycaemia in a pediatric sample when using continuous glucose monitoring

Graciela Lou[a], Gemma Larramona[b], Teresa Montaner[b] and Sara Barbed[a]

[a]Pediatrician, Spanish Aragonese Health Service and [b]Bachelor of Economics and Business, Facultad de Economía y Empresa, Universidad de Zaragoza, Zaragoza, Spain

Abstract

Objectives The aim of this article is to measure the HbAc1, the coefficient of variation of glucose levels and the occurrence of hypoglycaemia, when using continuous glucose monitoring (CGM).
Study design This is a retrospective study. Data are collected from type 1 diabetes mellitus, T1DM, children diagnosed between 2003 and 2017 in the Pediatric Unit of Diabetes in Zaragoza, Spain.
Methods Descriptive and inferential statistics.
Results The use of CGM for 3–6 months decreased the HbAc1 and the incidence of severe hypoglycaemia.
Conclusions Continuous glucose monitoring device helped in the management of diabetes, although more research is needed to analyse the influence of other variables in the relations studied.
Keywords coefficient of variation; continuous glucose monitoring; haemoglobin A glycosylated; type 1 diabetes mellitus

Introduction

A standard control for type 1 diabetes mellitus is the maintenance of glucose in blood within an optimal range. The first step is to know the blood glucose concentration of the patient in continuous time, and the second is to provide the necessary dosage of insulin to maintain this level in the optimal range. The result of a good control for diabetes in the long-term is quantified through a low value of HbA1c, although new research also takes into consideration a low coefficient of variation of glucose levels.[1,2]

Continuous glucose monitoring (CGM) provides a continuous measure of the blood glucose level with a 5- to 15-min lag, as well as the predicted trend. The information provided by these devices can be useful to improve diabetes's control. CGM devices were introduced in Spain in the second decade of the 21st century, but they were not available through the public health system, so each patient had to pay for the CGM out of their own pocket. The objective of the article is to evaluate the effect of using CGM on HbA1c, the coefficient of variation and hypoglycaemia in the Pediatric Unit of Aragón.

Materials and methods

Database

Our database consisted of data collected from September to December 2017 from patient-and-family clinical data, for patients diagnosed with type 1 diabetes mellitus, between 2003 and 2017, in the Pediatric Unit of Diabetes in Zaragoza, Spain. Questionnaires were completed by doctors and patient caregivers, and the information was summarised in an anonymised database. Parents of patients were fully informed and gave their consent. The questions were completely answered by 116 individuals, from a target population of 256.

Several variables were considered: HbA1c, the coefficient of variation of the glucose levels, the number of clinically important hypoglycaemia events (glucose value of <50 mg/dl) and the

Correspondence: Gemma Larramona, Facultad de Economía y Empresa, Universidad de Zaragoza, Gran Via 2, 50005 Zaragoza, Spain.
E-mail: gemmalar@unizar.es

Table 1 Summary statistics

Sample characteristics			
Sex	$N = 116$	Female: 43.1%	Male: 56.9%
Age	$N = 116$	From 0–5: 11.2%	From 6–10: 33.6%
		More than 10: 55.2%	
Years of evolution	$N = 116$	Less than 1: 4.3%	From 1–5: 68.1%
		From 6–10: 19%	More than 10: 8.6%
Use of ISCI	$N = 116$	Yes: 29.3%	No: 70.7%
Associated pathology	$N = 116$	Yes: 14.7%	No: 85.3%
Use of CGM	$N = 116$	Yes: 50.9%	No: 49.1%
Users of CGM			
% of use by sex	$N = 59$	Female: 42%	Male: 57.6%
% of use by age	$N = 59$	From 0–5: 84.6%	From 6 to 10: 61.5%
		More than 10: 37.5%	
% of use by age of evolution	$N = 59$	Less than 1: 100%	From 1–5: 55.7%
		From 6–10: 36.4%	More than 10: 20%

	N	Dexcom	Freestyle	Medtronic
Type of CGM	59	18.6%	54.2%	27.1%
Type of sex				
Female	21	14.3%	47.6%	38.1%
Male	38	21.1%	57.9%	21.1
Type of CGM by age				
From 0–5	11	54.5%	18.2%	27.3%
From 6–10	24	12.5%	58.3%	29.2%
More than 10	24	8.3%	66.7%	25%
Type of CGM by age of evolution				
Less than 1	5	40%	60%	0%
From 1–5	44	18.2%	56.8%	25%
From 6–10	8	12.5%	37.5%	50%
More than 10	2	0%	50%	50%

Metabolic control measures

	N	Mean	Std.dev.	Min	Max
HbA1Cpre	116	7.5	1.01	5.4% (36 mmol/mol)	12.1% (109 mmol/mol)
HbA1cPOST	116	7.3	0.91	5.1% (33 mmol/mol)	10.4% (60 mmol/mol)
Coefficient of variation	71	41.5	6	25.5	58.51
Mean glycaemia	86	165.9	21.58	115	271

No. import. hypo. events	*N*	0	1or 2	3–5	6–10	More than 10
No CGM	56	45.1%	33.3%	17.6%	2%	2%
CGM	51	34.5%	34.5%	9.1%	12.7%	9.1%

Abbreviation: CGM, continuous glucose monitoring.

number of severe hypoglycaemia events (with severe cognitive impairment including coma and convulsions).[3] The variables considered were reported by doctors and glucose meter, except for hypoglycaemias information that was provided by patient caregivers.

We considered two types of patients: (1) those with CGM whose information corresponds to the moment in which each patient began to use the device (previous variables are from six to three months before that moment, and post-variables are from three to six months after the use of CGM); (2) those without CGM whose information relates to the moment the questionnaire was completed (previous variable is the previous to the last value collected, from September to December 2017).

Results

A statistical summary of the variables used in our study can be found in Table 1. More than half (52%) of the patients in the sample used CGM, and more than 94% of them used it routinely. Only three types of CGM were used in the sample: Dexcom, Medtronic, and Freestyle.

There were very few severe hypoglycaemia events in the sample. Table 2 summarises this information for the whole period of the diagnosis for all the patients. There was a clear difference, for those using CGM, between the period previous to the use of the device and the period after; the number of severe hypoglycaemia events was negligible after using the device. The comparison with patients not using CGM was also important.

Table 2 Number of patients suffering severe hypoglycaemia

Number of severe hypoglycaemia	CGM		
	Pre-CGM	Post-CGM	No CGM
1 event	5	1	6
2 events	1	0	2
3 events	2	0	0
5 events	1	0	0

Abbreviation: CGM, continuous glucose monitoring.

In relation to clinically important hypoglycaemia events (<50 mg/dl, 2.78 mmol/l) with no serious consequences reported, it shows that the use of CGM did not have a monotone effect on such events because, although it appears that the use of CGM increased the number of such events, it also increased the percentage of patients only experiencing one event in the last two months. The reason is that this device shows an awareness of hypoglycaemia.

Comparing the HbA1c available previous to the use of CGM (7.5%) and after use for the patients with device (7.2%), the results of the Wilcoxon signed-rank test leads us to determine that the scores were significantly greater before using the CGM ($Z = -2.597$, $P < 0.05$). However, in the group without CGM there are no significant differences between the initial (7.4%) and final (7.4%) measurements of the analysed period (Z: -0.339; $P = 0.734$).

When the variable considered is the coefficient of variation of glucose levels, mean values for those with CGM (mean 40.8128, SD 7.2598) were slightly lower than for those without CGM (mean 42.6880, SD 6.1807). A Mann–Whitney test indicated no significant differences between the two groups ($\text{Median}_{CGM} = 40.236$; $\text{Median}_{NO\ CGM} = 43.784$, $U = 398.5$, $P = 0.097$).

Discussion

While there are certain studies that demonstrate the efficient detection of hypoglycaemia in type 1 diabetes mellitus patients with CGM devices,[4] our work shows that severe hypoglycaemia events almost disappeared in patients in the sample considered, although the effect on clinically important hypoglycaemia of <50 mg/dl, 2.78 mmol/l, is not clear.

With respect to HbA1c improvements, some prior studies[5] find no significant differences in results, while using CGM, for patients in the age ranges of 8–24 and 4–9.[6] In our work, it is observed a lower HbA1c after using CGM.

Considering the coefficient of variation, certain studies relate the use of CGM to a decrease in the coefficient of variation.[7] However, our results did not find a significantly difference. Maybe other related factors (gender, age, pathologies, habits and so on) can have some influence. It could be convenient to use a regression model capable of removing the effect of these variables, in order to isolate the effect of using CGM.

Conclusion

This study demonstrates the positive effect of using CGM in children with T1DM, in terms of improving the HbA1c and reducing the number of severe hypoglycaemia events, supporting the addition of these devices to the services of the Regional Health System. A better control of diabetes leads to a lower probability of having costly complications (retinopathy, nephropathy, renal failure).

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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Authors' contributions

G. Lou, G. Larramona, TM and SB has the role of conception and design of the work. Data has been collected by G. Lou and SB. The analysis of data has been done by G. Larramona and TM. A revision of the work critically has been completed by G. Lou, G. Larramona, TM and SB. A final approval of the version to be published was done by G. Lou, G. Larramona, TM and SB.

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