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Short Report

Continuous glucose monitoring as a tool to identify hyperglycaemia in non-diabetic patients with acute coronary syndromes

R. P. Radermecker*†, A. Sultan‡, C. Piot§, A. S. Remy¶, A. Avignon‡ and E. Renard*

*Endocrinology Department, CHU Montpellier, Université Montpellier, Montpellier, France, †Diabetes, Nutrition and Metabolic Disorders Department, CHU Sart Tilman, Université de Liège, Liège, Belgium, ‡Metabolic Diseases Department, §Cardiology Department, CHU Montpellier, Université Montpellier, Montpellier, France and ¶Nephrology Department, CHU Sart Tilman, Université de Liège, Liège, Belgium

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Abstract

Aim To explore the occurrence and the distribution of glucose excursions > 7.8 mmol/l by continuous glucose monitoring (CGM) in non-diabetic patients admitted with acute coronary syndrome (ACS).

Methods Twenty-one non-diabetic patients without baseline hyperglycaemia admitted for ACS wore a continuous glucose monitoring system (CGMS) for a median period of 45.6 h. Occurrence and 24-h distribution of time spent with blood glucose > 7.8 mmol/l (TS > 7.8) were retrospectively investigated.

Results CGMS data disclosed time spent > 7.8 in 17 patients, whereas only seven of them showed at least one capillary blood glucose test value above the threshold for the same time period. Glucose excursions were detectable earlier from CGMS data. Hyperglycaemia was detected most frequently in the morning, more than 2 h after breakfast.

Conclusions CGM discloses early and frequent hyperglycaemia in non-diabetic patients with ACS. Intensive glucose monitoring during the morning time period is the most efficient in screening for hyperglycaemia and could be a valuable guide to initiating insulin therapy and to further investigate outcomes in ACS.

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Keywords cgms, hyperglycaemia, acute coronary syndrome, intensive care

Abbreviations ACS, acute coronary syndrome; BMI, body mass index; CBG, capillary blood glucose; CGM, continuous glucose monitoring; CGMS, continuous glucose monitoring system; CVD, cardiovascular disease; ICU, intensive care unit; TS, time spent

Introduction

Up to 57% of patients with acute coronary syndrome (ACS) have abnormal glucose metabolism [1]. In non-diabetic patients, the blood glucose level on admission, fasting levels and high levels which do not change within the first 24 h, all correlate significantly with the mortality rate in the following months [2–4]. Intensive insulin management of diabetic patients during and after ACS improves long-term survival, but hypoglycaemia with an adverse outcome in ACS is concerning [5]. To investigate the potential benefit of insulin use in patients who do not have diabetes and do not present with high blood glucose when admitted for ACS, early detection of hyperglycaemic excursions would be valuable. There is no current consensus strategy on screening for hyperglycaemia in patients with ACS. Because fasting measurements may be too restrictive and an oral glucose challenge is not easily performed in this situation, a common practice includes multiple daily capillary blood glucose (CBG) tests carried out at no specific times. Continuous glucose monitoring (CGM) devices using subcutaneous interstitial sensing provide data that correlate well with blood glucose levels in critically ill patients [6,7]. In this study, we performed CGM in a consecutive series of non-diabetic patients admitted with ACS who had normal glucose at baseline in order to detect the time periods when glucose excursions > 7.8 mmol/l are more likely to occur.

Correspondence to: R. P. Radermecker, Diabetes, Nutrition and Metabolic Disorders, CHU Sart Tilman, 4000 Liège, Belgium.
E-mail: regis.radermecker@ulg.ac.be

Patients and methods

All patients gave their informed consent to participate in the study according to our institutional ethical policy. The 21 patients (17 male/four female), aged 60 ± 13 years, with a body mass index (BMI) of 26 ± 3 kg/m^2, had been admitted to the intensive care unit (ICU) for ACS. Chest pain had started less than 24 h before admission in 15 patients and between 24 and 48 h in the remaining six patients. All patients showed ST-elevation and high troponin levels. Each patient underwent angiography with placement of at least one coated stent within the first 48 h after admission. During the study, no patient received any drug liable to cause hyperglycaemia, such as glucocorticoids, catecholamines, glucose solution or propofol. Meals were served at 07.00, 12.00 and 19.00 h with minimal deviations of less than 10 min. All patients had blood glucose levels < 6.1 mmol/l when admitted and none had been previously diagnosed as having diabetes mellitus.

A subcutaneous glucose sensor connected to a portable monitor allowing blind glucose recording [continuous glucose monitoring system (CGMS); Gold Model, MiniMed-Medtronic, Northridge, CA, USA] was implanted within the first 48 h after admission, after angiography had been performed. Sensor calibrations were performed according to the manufacturer's recommendations against four daily CBG measurements, corresponding to routine clinical CBG monitoring of these patients in our ICU. Glucose recording was stopped when the sensor signal failed to stay within acceptable limits (as warned by an alarm signal from the monitor).

After appropriate downloading to a PC, CGMS data were analysed retrospectively using MiniMed Solutions v.3.0B software. Limits of sensor accuracy during recording time were given by MiniMed Solutions v.3.0B software. Only periods when sensor measurements were considered as accurate were used for the assessment of contemporary CGM and CBG data. The distribution of glucose deviations > 7.8 mmol/l was investigated in post-meal (2-h post-breakfast, post-lunch and post-dinner) and out-of-meal (morning, except 2-h period after breakfast; afternoon, except 2-h period after lunch; evening and night-time, except 2-h after dinner) time periods. Accurate time adjustments were performed on an individual basis to prevent any error between post-meal and out-of-meal periods.

Both univariate and multivariate analysis were performed to investigate relationships between time spent above the glucose threshold of 7.8 mmol/l (TS > 7.8) and simple patient characteristics at admission such as age, sex, BMI, family history of cardiovascular disease (CVD) or diabetes mellitus.

Results

Sensor implantation was well tolerated in all patients, except five who reported a slight pain for less than 5 min after sensor insertion. Assessable median glucose recording time was 45 h 38 min (2738 min) per patient (range 445–4025 min).

Occurrence of blood glucose deviations

Seventeen (81%) of the 21 patients spent some time at levels of > 7.8 mmol/l during the CGMS recording time, whereas only seven (33%) showed at least one CBG test > 7.8 mmol/l during the same time period. The number of hyperglycaemic excursions per patient during paired recording time and the highest glucose levels recorded according to CBG tests and CGM are presented in Table 1. From a cumulated recording time of 50 410 min in the 21 patients, sensor data showed TS > 7.8 of 9565 min (19% of total time). No hypoglycaemic excursion < 4.4 mmol/l was detected by CGM or CBG.

In the 17 patients with hyperglycaemic excursions according to CGM data, 22/136 CBG values were > 7.8 mmol/l. A significant Pearson correlation was noticed between both the number of CBG values > 7.8 mmol/l and TS > 7.8 ($r = 0.935$; $P < 0.001$), and the percentage of CBG values > 7.8 mmol/l and TS > 7.8 ($r = 0.923$, $P < 0.001$).

At the individual level, 10 patients spent some time at levels of > 7.8 mmol/l for a cumulated time of 1430 min (range 5–670 min) according to CGMS data, whereas no CBG measurement disclosed any value above this threshold. In the seven patients who showed both sensor glucose above 7.8 mmol/l for some time and at least one CBG value above 7.8 mmol/l, median delay between first detected high glucose excursion on CGM and first CBG above 7.8 mmol/l was 579 min (range 60–1800). Of note, early (first 24 h) detection of blood glucose excursions above 7.8 mmol/l occurred in eight patients (38%) only by using CGM.

Distribution of blood glucose deviations

Table 2 presents the distribution of hyperglycaemic deviations according to CGM and CBG tests. The percentage of time spent above 7.8 mmol/l, according to CGM, was evenly observed in cumulated post-meal and out-of-meal time periods, as well as in the three specific post-meal periods and in the afternoon and evening/night out-of-meal periods, but was higher in the morning out-of-meal period. The percentage of CBG tests with levels > 7.8 mmol/l showed no specific distribution according to the various post-meal and out-of-meal periods.

No significant correlation between TS > 7.8 and age, sex, BMI or family history of CVD or diabetes was found. On multivariate analysis, the model shows only a trend for an association of BMI with blood glucose levels > 7.8 mmol/l ($P = 0.056$; ß coefficient = 0.42).

Discussion

This pilot study shows, as might be expected, that intensive glucose monitoring offered by CGM allows more effective screening for hyperglycaemic excursions than routine four times daily CBG measurements in non-diabetic patients with normal blood glucose levels when admitted for ACS. Moreover, glucose levels > 7.8 mmol/l are detected earlier by intensive glucose monitoring. Although this threshold might be debated, it represents a pertinent and safe glucose level which could lead to initiation of insulin therapy with a limited risk of hypoglycaemia [5]. From our data, CGM could be considered as a

Table 1 Occurrence of glucose excursions > 7.8 mmol/l and highest glucose level during recording time according to capillary blood glucose tests (CBG) vs. continuous glucose monitoring (CGM) in 21 non-diabetic patients with acute coronary syndrome

Patients (age, years/gender)	CBG excursions > 7.8 mmol/l	Number of CBG excursions > 7.8 mmol/l	Highest CBG level (mmol/l)	CGM excursions > 7.8 mmol/l	Number of CGM excursions > 7.8 mmol/l	Highest CGM level (mmol/l)
1 (81/F)	No	0	7.6	No	0	7.7
2 (65/F)	Yes	1	8.2	Yes	3	8.5
3 (65/M)	No	0	6.2	Yes	2	9.5
4 (49/M)	No	0	5.8	Yes	1	8.0
5 (57/M)	No	0	7.7	Yes	1	9.8
6 (36/M)	No	0	6.9	Yes	2	11.7
7 (76/M)	Yes	5	11.7	Yes	6	10.3
8 (64/M)	No	0	5.6	Yes	2	8.4
9 (62/F)	No	0	6.8	Yes	1	8.5
10 (56/M)	Yes	1	7.9	Yes	5	11.0
11 (64/M)	Yes	3	7.9	Yes	7	9.8
12 (58/M)	Yes	1	9.5	Yes	6	10.9
13 (45/F)	Yes	6	10.2	Yes	5	11.2
14 (49/M)	Yes	5	13.6	Yes	5	13.3
15 (62/M)	No	0	6.2	No	0	7.1
16 (61/M)	No	0	7.4	Yes	5	11.5
17 (77/M)	No	0	7.2	Yes	1	8.2
18 (31/M)	No	0	6.1	Yes	3	10.9
19 (58/M)	No	0	5.6	Yes	1	10.8
20 (77/M)	No	0	6.6	No	0	7.6
21 (57/M)	No	0	4.7	No	0	6.2

Table 2 Distribution of glucose excursions > 7.8 mmol/l according to continuous glucose monitoring (CGM) and capillary blood glucose (CBG) tests in non-diabetic patients with acute coronary syndrome showing no baseline hyperglycaemia (n = 21)

	Post-meal periods (mealtime + 2 h)				Out-of meal periods			
	Post-breakfast	Post-lunch	Post-dinner	All	Morning	Afternoon	Evening and night-time	All
CGM > 7.8 mmol/l								
Minutes	980	795	740	2575	1975	2335	13.8	7050
% time*	22.5	19.3	13.6	18.1	32.5	21.9		19.3
CBG > 7.8 mmol/l							6	
Test number	4	2	1	7	3	6	16.7	15
% tests†	15.4	14.3	9	13.7	14.3	21.4	2740	17.6

*% time refers to time spent with glucose > 7.8 mmol/l upon CGM recording time for the corresponding time period.
†% tests refers to CBG tests showing a glucose value > 7.8 mmol/l upon total number of CBG tests performed for the corresponding time period.

valuable tool to use in further trials aiming at an assessment of appropriate early insulin therapy in non-diabetic patients with ACS. Recently developed CGM devices based upon the same technology as the CGMS, but providing almost real-time data, could be used to track hyperglycaemia in these studies. Of note, setting of alarm thresholds in these systems could also be helpful for the early detection of glucose excursions.

Although well tolerated in this study and highly informative on early blood glucose excursions, sensor use to screen for hyperglycaemia in ACS represents a significant cost and would require some training for the collection of valuable data by healthcare staff with no expertise in diabetes care. Interestingly, our data identify the morning period as the most prone to high glucose exposure. Given the limitations of CGM use in common practice, more frequent capillary blood glucose monitoring at this time period would provide alternative screening for hyperglycaemia in ACS. However, whether the specific management of high glucose excursions early in an ACS event in non-diabetic patients has a significant impact on patient outcomes remains a key question.

Competing interests

Nothing to declare.

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