Performance of the Dexcom G6 continuous glucose monitoring system in persons with type 1 diabetes mellitus during moderate exercise

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Abstract

Background Real time Continuous Glucose Monitoring (rt-CGM) is used by patients with type 1 diabetes mellitus (T1DM) during various circumstances. Limited data is available concerning the performance of the widely used Dexcom G6 rt-CGM during moderate exercise.

Methods Prospective, investigator-initiated study to test the performance of the Dexcom G6 rt-CGM during moderate exercise. Seventeen participants with T1DM went hiking for 6 days, followed by 6 days of normal daily activities (NDA). Capillary glucose measurements were performed with Precision Neo Pro strips; previously verified to be closely comparable with the gold reference method.

Results Two persons dropped out of the study and 4 had incomplete data. Consequently 11 participants with a median age of 55 [interquartile range 39-62] years, 91% female and median HbA1c 55 [interquartile range 40-75] mmol/mol were analyzed. During moderate exercise the mean absolute differences and mean absolute relative differences of the Dexcom G6 rt-CGM were 20±17 mg/dl and 16±15%. Overall, the Dexcom G6 rt-CGM reported higher glucose concentrations, compared to capillary measurements, during exercise (154±64 vs. 149±70 mg/dl ($p<0.001$)). When assessing accuracy during exercise compared to the capillary measurements using Parkes error grids, 98.6% of the comparisons fell within zones A and B. According to the Integrated Continuous Glucose Monitoring Approvals (Class II–510(K)) guidelines, the Dexcom G6 rt-CGM did not reach the agreed upon cut-off levels and were more or less comparable as during NDA.

Conclusions Despite limitations, this study demonstrates that during moderate exercise the Dexcom G6 rt-CGM does not meet current benchmark criteria.

Trial registration: This study was approved by the Medical Ethical committees in The Netherlands (Isala Hospital; NL70456.075.19/190605) and in Spain (CEIm de las Áreas de Salud de León y del Bierzo; no.1981). Registered at www.trialregister.nl: NL7922.

Introduction

In the last decade, the use of real time Continuous Glucose Monitoring (rt-CGM) sensors increased substantially. This is particularly the case in persons with type 1 diabetes mellitus (T1DM) using a continuous subcutaneous insulin infusion pump (CSII) or multiple daily injections (MDI). Besides improvements in glycemic control rt-CGM also have beneficial effects on quality of life [1, 2].

Accuracy is an important aspect that should be taken into account to obtain optimal results with any device registering glucose concentrations in the interstitial space [3]. As interstitial fluid flows can vary considerably this can lead to different intensities of stimulation of the probes registering glucose content [4]. Other factors, including amongst others alterations in body temperature, metabolic rate, and body acidity may theoretically also influence accuracy of interstitial glucose sensing [4, 5].

Although we and others have assessed various glucose sensors during exercise circumstances and found limited accuracy during these circumstances, data on currently used rt-CGM devices including the Dexcom G6 rt-CGM are scarce [5, 6]. Therefore, we performed a study on the accuracy of Dexcom G6 rt-CGM in persons with T1DM during moderate exercise.

Methods

The present study has a prospective, observational design and aimed to test the accuracy of the Dexcom G6 rt-CGM during moderate exercise. Measurements were performed in 2 consecutive time periods; first 6 days with moderate exercise, followed by 6 days with only normal daily activities (NDA). This study was approved by the Medical Ethical committees in The Netherlands (Isala Hospital; NL70456.075.19/190605) and in Spain (CEIm de las Áreas de Salud de León y del Bierzo; no.1981). Registered at www.trialregister.nl: NL7922. All participants gave written informed consent prior to the start of the study. All study procedures were performed in accordance with relevant guidelines and regulations.

Measurements were performed during the Bas van de Goor Foundation (a non-profit organization aiming to stimulate exercise among persons with diabetes) 'wehike2changediabetes' challenge in September 2019. During this challenge, persons with T1DM from Spain and The Netherlands hiked from Astorga to Santiago de Compostela, over a total distance of 110.19 km and a variable amount of altitude meters spread over the days (in total 2334 meters). The inclusion criteria to participate were adult age (> 18 years), having T1DM and the ability to provide oral and written informed consent. All participants (n=17) of the challenge agreed to participate in the present study and provided (written) informed consent.

Dexcom G6 rt-CGM devices were implanted in the back of the upper arm; all device related procedures were performed according to operating instructions. Capillary self-measurements of blood glucose (SMBG) reference measurements were performed with Precision Neo Pro strips (Free Style Libre Capillary glucose measurement strip = FSLCstrip) [7]. This capillary measurement strip was previously verified to be comparable with NIST standards to the gold reference method isotope dilution mass spectrometry [7, 8]. Participants were asked to perform a total of (at least) 7 capillary SMBG per day. Participants were also instructed to perform extra SMBG if necessary, for instance when experiencing symptoms related to hypoglycemia. The SMBG results were not used to calibrate the Dexcom G6 rt-CGM.

Data from both the Dexcom G6 rt-CGM and capillary SMBG readings were extracted at the end of the study. The online software program Dexcom Clarity was used to gather the information of all glucose measurements, produced every 5 minutes by the Dexcom G6 rt-CGM of the participants. The readings of the Dexcom G6 rt-CGM that are closest in time (with a maximum window of two minutes) of the FSLC readings were used for calculations.

Primary outcome of this study was the accuracy of the Dexcom G6 rt-CGM during the 6-day exercise period. As secondary outcomes the accuracy of the Dexcom G6 rt-CGM was analyzed during the 6-day period with NDA. In addition, comparisons between the Dexcom G6 rt-CGM and the capillary reference glucose during moderate exercise and NDA were made.

Accuracy of the Dexcom G6 rt-CGM was analyzed according to the Integrated Continuous Glucose Monitoring Approvals (Class II–510(K) guidelines (ICGMA) guidelines [9] and results of both testing periods were compared using a paired t-test. Comparisons between exercise and NDA were analyzed using Parkes error grid analysis [10]. The accuracy of Dexcom G6 rt-CGM derived glucose values versus capillary reference glucose values was determined as % within the error grid zones. Values in zones A and B are deemed clinically acceptable, whereas those in zones C, D and E are considered potentially unsafe. Correlation analysis, a parameter using the intraclass correlation coefficient (ICC) was performed to assess the correlation between the sensor value and reference values [11]. For bias analysis, mean absolute differences (MAD), and mean absolute relative differences (MARD) were calculated. A significance level of 5% was considered significant. Analyses were performed using SPSS (IBM SPSS Statistics, version 25.0. Armonk, NY: IBM Corp.) and Microsoft Excel Analyse-It (2010).

Results

Of the 17 participants, 2 dropped out of the study. One person decided to withdraw consent at the start of the study. Another person had to stop the hiking period due to personal circumstances. Four participants provided insufficient data. Consequently, results are reported over 11 participants. Median age of participants was 55 [interquartile range (IQR) 39-62] years, 91% was female, BMI 25 [22-30] kg/m^2, diabetes duration 15 [IQR 4-32] years, 73% used CSII and median and HbA1c was 55 [40-75] mmol/mol. In total, 361 data sets for the exercise period and 406 data sets for de NDA period were considered adequate for analysis.

When analyzing the data according to the ICGMA guidelines, accuracy did not reach the agreed upon cut-off levels in the exercise nor the NDA period (Table 1).

Table 1
Accuracy of the Dexcom G6 according to ICGMA guideline.

	Exercise (n = 361)	Normal daily activity (n = 406)	ICGMA guideline: lower bound of one-sided 95% confidence interval
Hypoglycaemia (< 70 mg/dL)	53% (18/34)	38% (10/26)	>85% within ± 15 mg/dL
	97% (33/34)	88% (23/26)	>98% within ± 40 mg/dL
Euglycaemia (70 - 180 mg/dL)	51% (116/227)	54% (147/271)	>70% within ± 15%
	96% (218/227)	96% (261/271)	>99% within ± 40%
Hyperglycaemia (> 180 mg/dL)	72% (72/100)	72% (79/109)	>80% within ± 15%
	99% (99/100)	98% (107/109)	>99% within ± 40%
Overall	70% (253/361)	70% (283/406)	>87% within ± 20%

Table 2 shows the differences between the Dexcom G6 rt-CGM and capillary reference in glucose readings in different ranges of glucose concentrations and during the different circumstances. The Dexcom G6 rt-CGM reported overall higher outcomes as compared to the capillary reference, in particular in the glucose ranges ≤ 70 mg/dL and 71-180 mg/dL.

Table 2
Comparisons at various glucose concentrations, during moderate exercise and normal daily activities, between of Dexcom G6 and the capillary (reference) measurements.

Range (mg/dL)	Exercise			Normal daily activities		
	N	Capillary (1)	Dexcom G6 (2)	N	Capillary	Dexcom G6 (3)
≤ 70	34	55±10	70±15**	26	57±8	76±20**
71-180	227	121±30	131±33**	271	128±29	139±34**
>180	100	242±47	233±50*	109	233±48	223±43*
Overall	361	149±70	154±64**	406	152±62	158±55**
Comparisons: 2 vs. 1 and 3 vs. 1. *=p<0.05; **P<0.001						

During exercise, the MAD and MARD of the Dexcom G6 were 20±17 mg/dl and 16±15% respectively while during NDA these numbers were 21±16 mg/dl and 15±14%. There were no significant differences in MAD and MARD during moderate exercise and NDA.

When assessing the accuracy of the Dexcom G6 rt-CGM during exercise with Parkes error grid analyses, 98.6% of the comparisons with capillary reference fell within zones A and B (97.2% and 19.4% respectively, x = y line: y=0.929x +17.02) with an ICC of 0.93 (95% confidence interval 0.91 to 0.94) (Figure 1, left panel). During NDA 99.2% of the comparisons fell within zones A and B (80.5% and 18.7% respectively, x = y line: y=0.917x +19.5) with an ICC of 0.91 (95% confidence interval 0.89 to 0.92) (Figure 1, right panel)

Discussion

This study demonstrates that during moderate intensive exercise the Dexcom G6 rt-CGM does not meet ICGMA criteria. In addition, MARD during exercise (16%) was considerably higher than the MARD found in other studies (approximately 9% [12, 13]). According to Parkes error grid analyses the vast majority of readings still fall in clinically safe zones.

To date most studies towards performance of rt-CGM devices are performed under well-controlled (clinical) circumstances. This may also explain the higher MARD – as compared to previous literature – in the current study. Glucose sensor measure glucose in the interstitial fluid: changes in the interstitial fluid (amongst others composition and fluid flow) will influence the eventual readings. Since the sensor algorithms used are calibrated in a standardized situation the large changes in composition and flow e.g. during exercise will result in changes in glucose readings, thus possibly leading to less accurate glucose results. When ambient temperature is low and the skin and the interstitial measurement device are exposed to that temperature, the interstitial fluid flow will decrease, and the sensor device might be less reactive. In contrast, with a high ambient temperature, interstitial fluid flow will increase. This is also the case with extreme sports and intensive exercise, and in earlier studies we have shown, that interstitial measurement devices become less accurate with regards to glucose readings when mountain biking [6, 14]. Attempts are made to improve performance of glucose sensors by integrating physical activity information [15].

Of course, limitations of the present study might have influenced the results and should be taken into account in interpreting our findings. The small number of participants, of which most are female and the inability to strictly control test- and measurement circumstances and the limited amount of data sets, especially with hypoglycemic ranges might well influence our findings. Nevertheless, as most persons with diabetes will use rt-CGM devices during real-life circumstances and also during exercise, our findings are of direct relevance for patients and healthcare providers. An accuracy that is less than desired might be considered a poor outcome to base proper decisions with regards to diabetes management upon. Still, many users glucose sensors, although aware of this potential shortcoming, still value the use of such a device [14]. Some consider seeing glucose trends as being more important than absolute accuracy, others value the early warning signs of their rt-CGM when glucose levels are dropping quickly, thus preventing the occurrence of severe hypoglycemia by being able to react before clinical signs of hypoglycemia occur. Therefore, despite the current findings, we argue that the use of glucose sensors such as the Dexcom G6 rt-CGM are of added value for persons with DM during exercise. Nevertheless, shortcomings should be

acknowledged; based on the present data it seems expedient to advise Dexcom G6 rt-CGM users to confirm rt-CGM derived glucose outcomes – in particular in the hypo and hyperglycemic range – with a capillary measurement during exercise.

Conclusions

Although the accuracy was high the Dexcom G6 rt-CGM did not reach the current guidelines for CGM performance. While this small study has limitations, confirmatory self-monitored capillary glucose testing should be considered during moderate exercise.

Abbreviations

ICC Intraclass correlation coefficient

ICGMA Integrated Continuous Glucose Monitoring Approvals (Class II–510(K) guidelines

MAD Mean absolute differences

MARD Mean absolute relative differences

Rt-CGM Real time Continuous Glucose Monitoring

T1DM Type 1 diabetes mellitus

Declarations

Ethics approval and consent to participate:

This study was approved by the Medical Ethical committees in The Netherlands (Isala Hospital; NL70456.075.19/190605) and in Spain (CEIm de las Áreas de Salud de León y del Bierzo; no.1981). Registered at www.trialregister.nl: NL7922. All participants gave written informed consent prior to the start of the study.

Consent for publication:

Not applicable.

Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable requesCompeting interests: None.

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Authors' contributions:

Nicole Lommerde did the practical examination, researched data, wrote manuscript, contributed to discussion. Marion Fokkert wrote protocol, did the practical examination, researched data, contributed to discussion, reviewed/edited manuscript. Peter van Dijk researched data, contributed to discussion, wrote the manuscript, reviewed/edited manuscript. Mireille Edens and Robbert Slingerland contributed to discussion, reviewed/edited the manuscript. Alberto Diéz Hernández and Elias Delgado Álvarez did the practical examination, contributed to discussion, reviewed/edited manuscript. Henk Bilo co-wrote protocol, contributed to discussion, reviewed/edited manuscript.

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Figures

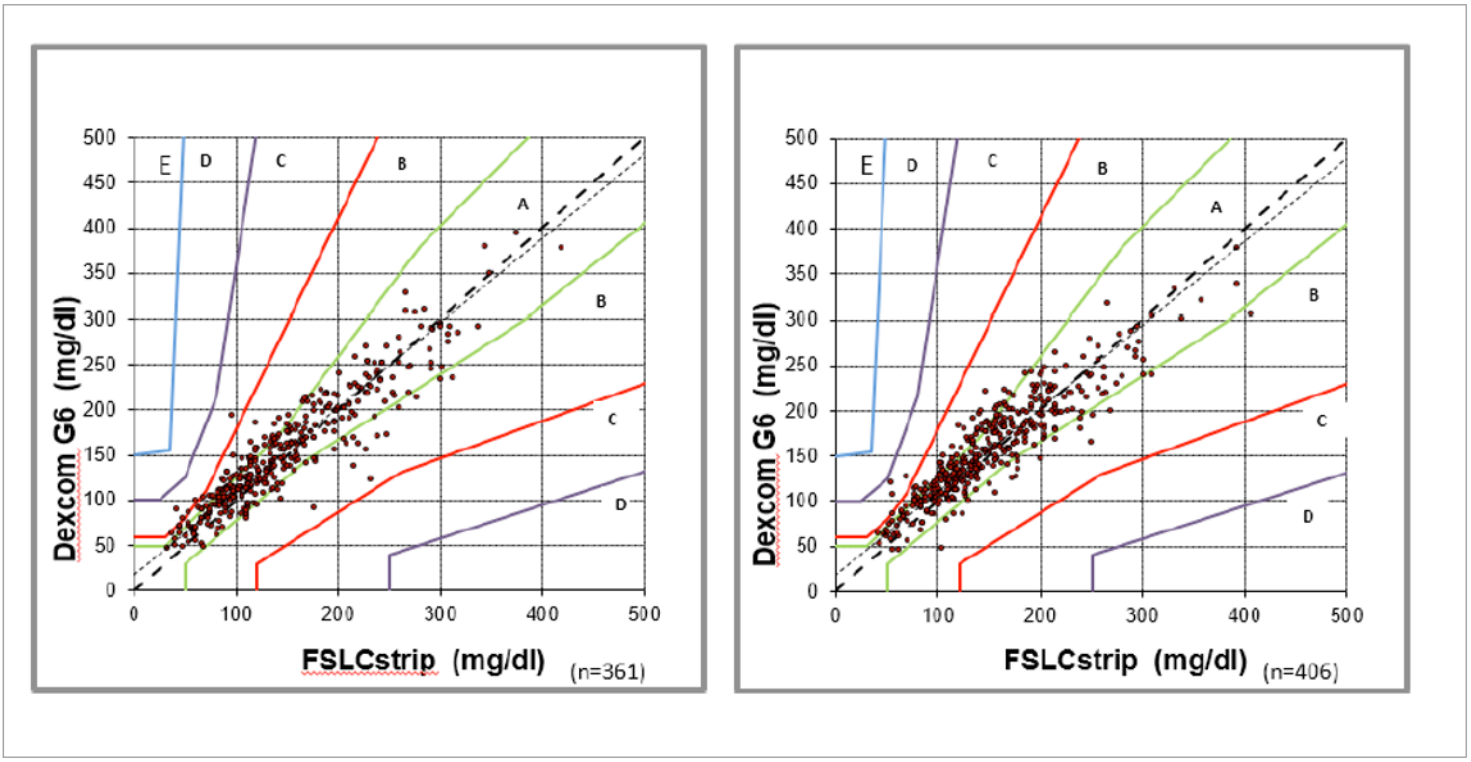

Figure 1

Parkes error grid for the Dexcom G6 during moderate exercise (left panel) and normal daily activities (right panel)