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Article

Accuracy Assessment of the GlucoMen® Day CGM System in Individuals with Type 1 Diabetes: a Pilot Study

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Abstract: Aim of this study was to evaluate the accuracy and usability of a novel continuous glucose monitoring (CGM) system designed for needle-free insertion and reduced environmental impact. We assessed sensor performance of two GlucoMen® Day CGM systems worn simultaneously in eight participants with type 1 diabetes. Self-monitoring of blood glucose (SMBG) was performed regularly over 14 days at home. Participants underwent two standardized 5-hour meal challenges with frequent plasma glucose (PG) measurements using a laboratory reference instrument at the research center. When comparing CGM to PG the overall mean absolute relative difference (MARD) was 9.7 [2.6-14.6]%. The overall MARD of CGM vs SMBG was 13.1 [3.5-18.6]%. In the consensus error grid (CEG) analysis, 98% of both CGM/PG and CGM/SMBG pairs were in the clinically acceptable zones A and B. The analysis confirms that GlucoMen® Day CGM meets the clinical requirements for state-of-the-art CGM. The needle-free insertion technology is well tolerated by users and reduces medical waste compared to conventional CGM systems.

Keywords: Diabetes Technology; CGM; Accuracy; Type 1 Diabetes; Sustainability

1. Introduction

The introduction of continuous glucose monitoring (CGM) was one of the most important advances within diabetes treatment and self-management over the last decades. The easy access to current glucose levels, trends and retrospective analysis of glucose excursions facilitates diabetes management for people living with diabetes (PLWD) and health care professionals. As a result, PLWD using CGM technology show improvement in HbA1c, glucose variability, hypoglycemic events, well-being, treatment satisfaction and less fear of hypoglycemia compared to SMBG [1-3].

One critical aspect of this technology still is accuracy of glucose measurements, even though vast improvements over the last years are evident [4-7]. Current CGM have reached accuracy levels of SMBG and are labelled for nonadjunctive use by regulators, meaning that CGM can be utilized for treatment decisions without confirmation by SMBG [10-13]. Nevertheless, further enhancement in CGM accuracy is crucial for developing reliable diabetes technology, such as closed loop insulin delivery systems, and thus to reducing the burden of diabetes management for PLWD.

Another key aspect of CGM technology is comfort in both wearing and inserting sensors as this is crucial to CGM adherence. Registry data show that discomfort when wearing is the prevailing factor for CGM discontinuation [14]. New developments in diabetes technology aim for reducing discomfort in diabetes management and thereby facilitating life with diabetes.

As CGM technology is made available to more and more PLWD the negative impact on environment and natural resources increases due to use of disposable products and accumulating plastic and hazardous medical waste, including hazardous parts like inser-

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tion needles. Therefore, the Diabetes Technology Society started its Green Diabetes Initiative to positively influence the development of medical devices in terms of sustainability and to reduce the environmental burden of advancement in diabetes technology [15].

In the present analysis, we aimed to assess the accuracy and usability of a novel CGM system consisting of predominately reusable components featuring needle-free insertion.

2. Materials and Methods

In this monocentric, open-label, non-randomized, single-arm clinical study 8 individuals with type 1 diabetes were equipped with 2 GlucoMen® Day CGM (Waveform Cascade, A. Menarini Diagnostics, Florence, Italy) sensors worn in parallel. Sensors were placed in the subcutaneous adipose tissue of the lower abdomen and worn for 14-days. Additionally, participants were requested to calibrate the CGM device once daily and perform 8-9 finger-prick glucose tests per day (GlucoMen Day METER, A. Menarini Diagnostics, Florence, Italy).

Primary objective was to assess the device accuracy by comparison to a laboratory reference instrument (YSI 2300, Yellow Springs, Ohio, USA). Secondary objectives included comparison of CGM to SMBG and precision assessment by evaluating the agreement between two sensors worn in parallel.

Meal/insulin challenge

On days four and ten of the study, a 5-hour meal and insulin challenge was performed. Standardized meals containing 100g of carbohydrates were consumed and an increased insulin bolus (20% of regular bolus insulin dose) was administered subcutaneously. Venous plasma and capillary blood samples were collected in parallel every 20 minutes. Plasma glucose was measured at site with YSI. SMBG was measured using the study-specific BG meter.

Data analysis

CGM accuracy was assessed by calculation of MARD, mean absolute difference (MAD) and CEG for both CGM/YSI and CGM/SMBG matched pairs. MARD was calculated for glucose values in the range between 100 and 400 mg/dl. MAD was used for glucose values ranging from 40-99 mg/dl. Delay for each single sensor was calculated as the shift in time (between CGM and blood glucose data) which provided the best correlation, using the Poincarè method (time shift giving the best R 2 vs. references) and was adjusted individually for SMBG and YSI data, and, for YSI data, individually for each sensor. This delay was noted for each sensor, and applied prior of the MARD and MAD calculation. The average delay was calculated as the weighted average (based on the respective N of data) of the delay of all the sensors. All statistical analyses were performed following the Intention-to-treat Principle.

3. Results

Eight participants (age 41.6 ± 13.3 years, 3 female (37.5%), BMI 28.0 ± 6.1 kg/m², HbA1c 55.6 ± 12.2 mmol/mol and diabetes duration 13.9 ± 6.5 years) completed the study.

During the study period on average 94.4% of the theoretically possible data were collected. 94.5% of the collected data was used for analysis after applying pre-specified exclusion criteria for data recording (estimated CGM signal).

3.1. Accuracy CGM vs. YSI

Overall 450 CGM/YSI matched pairs were collected within the range of 40-400mg/dl. This resulted in a MARD of 9.7 (2.6-14.6)% and a MAD of 20.5 (9.5-24.0) mg/dl. Sensor performance assessed by MARD was better in the range of 201-400 mg/dl, compared to the range of 100-200 mg/dl (6.1 vs. 10.7 %). MAD was lower in the range of 40-70mg/dl compared to the range of 71-99 mg/dl (19.5 vs. 20.9 mg/dl). MARD and MAD were lower on day 4 compared to day 10 (7.4 vs 11.4% and 17.7 vs 27.3 mg/dl). In the CEG analysis

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84.9% of CGM/YSI data pairs were in the most clinically acceptable zone A, while the combined percentage in zone A and B was 97.8%. CEG is displayed in figure 1a.

3.2. Accuracy CGM vs. SMBG

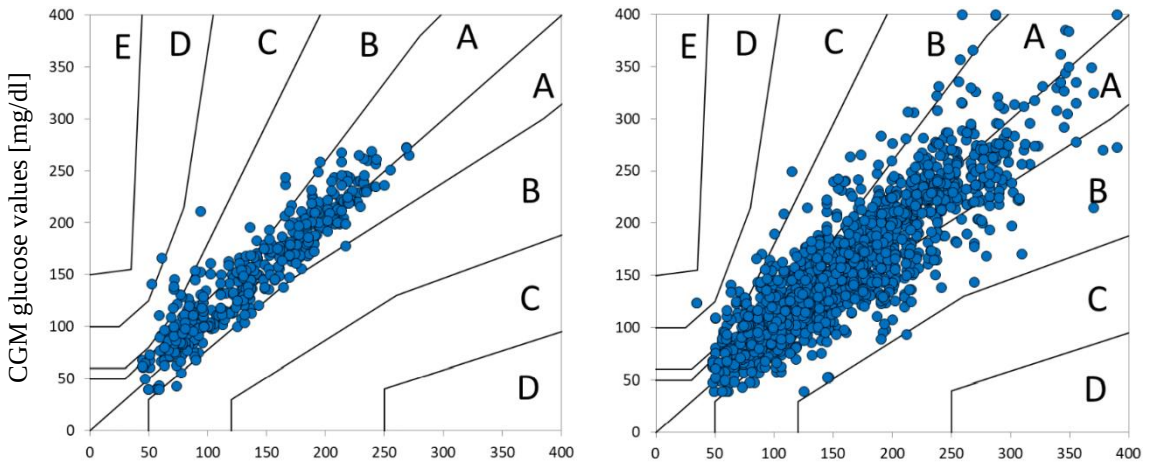
During sensor use at the research center and at home, a total of 1957 CGM/SMBG matched data pairs were collected in the range of 40-400 mg/dl. The overall MARD was 13.1 (3.5-18.6)% for values between 100-400 mg/dl. The MAD for glucose values from 40-99 mg/dl was 16.6 (3.0-23.0) mg/dl. Similar to what observed for YSI, lower MARD and MAD was found when glucose levels were higher: (13.4% for 100-200mg/dl vs. 12.2% for 201-400 mg/dl and 20.2mg/dl for 40-70 mg/dl vs. vs. 15.2mg/dl for 71-99mg/dl). CEG analysis showed a combined percentage in zone A and B of 98.2% (Figure 1b).

3.3. Sensor precision

For each participant glucose values of the two sensors worn in parallel were evaluated by using mean of the SD and coefficient of variation (CV). An average SD of 11.1 mg/dl and an average CV% of 9.7% were observed, demonstrating acceptable agreement between two sensors.

3.4. Usability

The participants were requested to complete a questionnaire containing ten questions with a ordinal 5 scale answer rating. When asked about pain perception at insertion 50% stated that the procedure was painless and 25% claimed it to be less painful than finger prick measurements. There was also predominant satisfaction with the used adhesive, wearability, calibration procedure and user friendliness of the dedicated mobile application. The results of the usability assessment can be found in the supplementary appendix (Figure S1).



(**a**) (**b**)

Figure 1 a-b. CEG during study phases. (**a**) CGM compared to venous reference glucose values during in center meal challenge; (**b**) CGM compared to capillary glucose values at home.

4. Discussion

Accuracy of CGM is essential for diabetes management, especially when readings are used for calculation of time in range (TIR), which has become increasingly popular for treatment decisions and assessing glycemic control. MARD is a widely used parameter to assess CGM accuracy. Good CGM performance is generally assumed in systems with an overall MARD <10% [8]. In the present analysis the GlucoMen® Day CGM, using one

calibration daily, achieved an MARD of 9.7% in comparison to YSI during meal/insulin challenges. In comparison to SMBG an MARD of 13.1% was obtained over the 14-day wear-period. The higher MARD when compared to SMBG might be caused by the lower accuracy of glucose meters compared to laboratory reference. This finding is often seen during home phase assessment of CGM devices [16-18]. Besides MARD/MAD as measures of numerical accuracy, clinical accuracy should be evaluated to support performance data. CEG analysis provides assessment of clinical accuracy; in our analysis for both reference methods, 98% of data pairs were in the most clinically useful zones A and B, verifying the clinical accuracy of GlucoMen® Day.

Advances in diabetes technology drastically decreased the burden for people with diabetes. Especially reduction of painful procedures for diabetes management improved quality of life and facilitated achievement of glycemic control [19-21]. In the present analysis the needle-free insertion resulted in high user satisfaction with a majority of users claiming the insertion procedure to be painless or less painful than finger-prick measurements.

An important aspect of this new device which is also often addressed by users is the ecological footprint of diabetes equipment. In clinical routine more and more people using CGM technology are demanding reusable products. GlucoMen® Day includes a rechargeable transmitter, and a reusable needle free sensor insertion tool, both can be used up to five years. Usually those parts are disposable and attribute to a substantial increase in plastic waste and potentially hazardous medical waste containing sharps, which is an increasing problem worldwide and is fuelled by the, per se favourable, rising availability of CGM. This problem is already acknowledged by the scientific community and is subject to ongoing discussion [15,22]. Therefore, needle-free systems with reusable components can help furthering sustainable diabetes technology and may be a stimulus for other positive developments in this sector including biodegradable solutions or else.

5. Conclusions

The present analysis suggests that the GlucoMen® Day CGM is a user- and environmental-friendly system meeting the current clinical requirements for state-of-the-art CGM.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Figure S1: Usability Questionnaire Results (N = 8)

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on reasonable request from the corresponding author. The data are not publicly available due to company policy of data privacy so that competitors cannot directly assess the full data set.

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Conflicts of Interest: JM is a member in the advisory board of Abbott Diabetes Care, Becton-Dickinson, Boehringer Ingelheim, Eli Lilly, Medtronic, Prediktor A/S, Roche Diabetes Care, Sanofi-

Aventis and received speaker honoraria from Abbott Diabetes Care, AstraZeneca, Becton-Dickinson, Boehringer Ingelheim, Dexcom, Eli Lilly, MSD, NovoNordisk A/S, Roche Diabetes Care, Sanofi, and Servier. JM is shareholder of decide Clinical Software GmbH. The other authors do not have a conflict of interest to report.

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