



Feasibility of FreeStyle Libre Flash Glucose Monitoring System in pregnant woman affected by type 1 diabetes

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Introduction

Pregnant patients affected by type 1 diabetes (T1DM) are at increased risk for maternal and fetal risk, including congenital malformations, preeclampsia, macrosomia, spontaneous abortion, and perinatal mortality [1]. Tight glycemic control is required to reduce the occurrence of diabetes related pregnancy complications. The more stringent glucose targets and the wide variability in insulin requirement during pregnancy may predispose to hypoglycemic events, and severe hypoglycemia occurs in up to 50% of pregnancies women with T1DM [1, 2]. The National Institute for Health and Care Excellence recommends that blood glucose levels are tested up to eight times daily to achieve glycemic targets [2]. However, many patients experience barriers to frequent testing, including pain and discomfort associated with the multiple finger-stick blood samples. Continuous glucose monitoring (CGM) may improve quality of life in T1DM patients, providing a good accuracy without the pain and the inconvenience of regular finger pricking. Nevertheless, the evidence to support the CGM use in T1DM pregnant women is limited and conflicting [3]. The FreeStyle Libre Flash Glucose Monitoring System (Abbott Diabetes Care, Witney, UK) provides comprehensive glucose data by measuring the glucose concentration in the interstitial fluid, without the need for calibration. Sensor measurements may replace

the self-monitoring blood glucose (SMBG) testing, and each device may be worn for up to 14 days. The FreeStyle Libre System improves outcome and quality of life in T1DM patients [4], however it is approved with a restriction of the use during pregnancy. Only a study assessed accuracy and safety of FreeStyle Libre System in pregnant women with T1DM [5]. We report a case of pregnant woman affected by T1DM in which feasibility of FreeStyle Libre System is tested.

Methods

A 30-years-old woman with a T1DM duration of 9 years and at 26 weeks gestation (25 + 5) was evaluated. HbA1c was 6.2% before the pregnancy, 5.8% at 7 weeks gestation and 4.3% at 26 weeks. The patient followed a basal-bolus insulin regimen, consisting of an average of 26 insulin aspart units/day at meals, and of a mean of 11 insulin glargine units/day at 8:00 p.m. The patients performed for 14 days 12 SMBG test daily using the blood glucose OneTouch Verio test strips (Lifescan, Johnson & Johnson, Italy). Three measurements were acquired premeal, three at 1 and 2 h after each meal, once in the afternoon, once at bedtime and once in the middle of the night. Additional tests were performed if symptoms of hypoglycemia or hyperglycemia were reported or suspected. Each SMBG test was immediately followed by FreeStyle Libre System measurement with the aim to compare values achieved from the two methods. Upon completion of the 14 days, values were downloaded by the two systems. Bland–Altman plot was created correlating the mean of each pair of measurements with the absolute difference between the two values. The Pearson correlation coefficient between the two continuous variables (FreeStyle Libre and SMBG measurements) was also calculated. The

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accuracy was assessed by Consensus Error Grid analysis. Finally, the mean absolute relative difference (MARD) between interstitial glucose values of FreeStyle Libre and SMBG measurements [$ARD = (|capillary\ glucose - interstitial\ glucose|) / capillary\ glucose \times 100$] was calculated. The proportion of results within 20% of ARD for glucose levels < 70 mg/dL, 70–180 mg/dL and > 180 mg/dL was also analyzed.

Results

A total of 178 paired capillary blood glucose to sensor glucose measurements were performed in 14 days, with a mean of 12.7 tests/day. Bland–Altman plot showed a mean absolute difference between interstitial and capillary glucose values of 2.61 ± 13.71 (Fig. 1a). 75.8% of absolute differences between capillary and interstitial glucose values fell within the mean \pm standard deviation. The Pearson correlation coefficient between glucose values measured by FreeStyle Libre

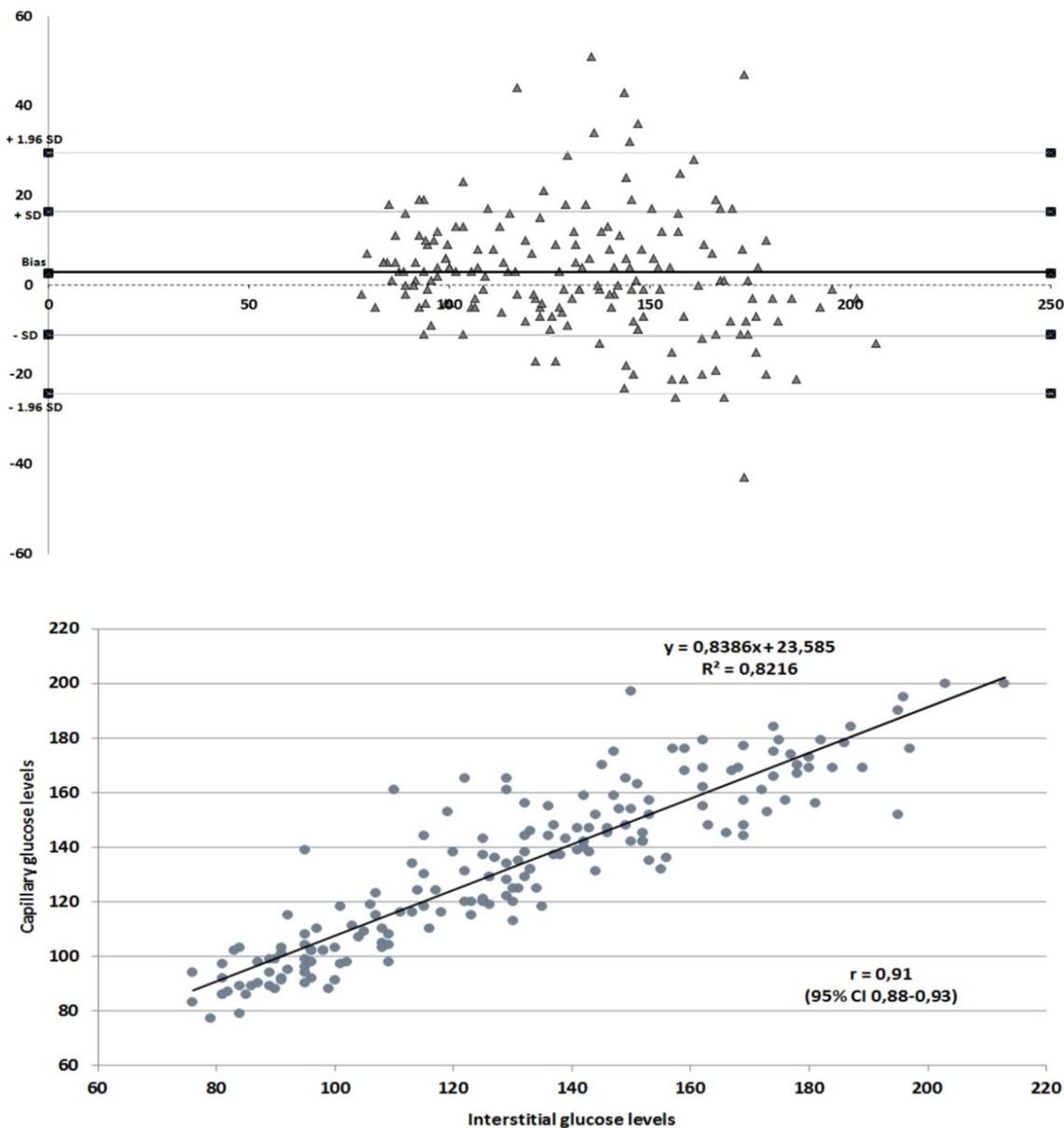


Fig. 1 a Bland–Altman plot. Black line represents the mean of the absolute differences between FreeStyle Libre sensor values and SMBG values (bias); gray lines represent ± 1 standard deviation and

± 1.96 standard deviations. **b** Scatter plot of measurements of glucose levels by FreeStyle Libre sensor versus SMBG. A strong positive correlation is found ($r=0.91$)

Table 1 Consensus Error Grid analyses comparing FreeStyle Libre sensor results to capillary SMBG results

Zone	N	%
A	170	95.5
B	8	4.5
C	0	0.0
D	0	0.0
E	0	0.0
Total	178	100

and SMBG was 0.91 (95% CI 0.88–0.93; Fig. 1b), resulting in a correlation equation of $y = 0.84x + 23.59$. Consensus Error Grid analysis demonstrated 95.5% of results in zone A and 100% in zones A and B (Table 1). The mean ARD was $7.46\% \pm 6.33\%$. 172 out of 178 paired results ranged from 70 to 180 mg/dL, 6 were > 180 mg/dL while none was < 70 mg/dL. ARD was < 20% in 95.9% of values range between 70 and 180 mg/dL and 83.3% of values > 180 mg/dL.

Discussion

Our case report provides a strong positive correlation between interstitial glucose levels measured by FreeStyle Libre sensor and capillary SMBG in a pregnant woman affected by T1DM. To our knowledge, only one study [5] evaluated the accuracy of FreeStyle Libre System in 24 pregnant women with T1DM, reporting a good agreement between interstitial and blood glucose levels (88.1% in zone A of Consensus Error Grid). In our case Consensus Error Grid analysis showed 95.5% of values in zone A and 100% in zones A and B. Furthermore, the accuracy of FreeStyle System is underlined by Bland–Altman plot and Pearson correlation coefficient. Pregnant women require tight glycemic control to reduce the occurrence of diabetes related complications [1, 2]. SMBG represents the standard-of-care to achieve the best glycemic control in pregnant women affected T1DM, requesting regular and frequent tests. However, SMBG provides only single and intermittent glucose values which may not represent the real-life glucose excursions experienced daily during pregnancy. In comparison, FreeStyle Libre sensor provides important glucose trend information at each scan, helping to guide challenging treatment decisions in pregnant women affected by T1DM. Consequently, FreeStyle Libre System may improve glycemic control in this population. In our case, FreeStyle Libre System helped to achieve an optimal clinical target in term of HbA1c (4.3% at 26 week gestation vs 6.2% before the pregnancy). Finally, the use up to 14 days and the avoidance of discomfort caused by several finger-stick tests may improve quality of life in comparison to SMBG. Limitations have to be addressed. We report only a single case of a pregnant woman using FreeStyle Libre sensor for diabetes control, so conclusions may not be applicable to all pregnant women affected by T1DM. However, studies evaluating the use of FreeStyle Libre System in pregnancy are infrequent,

with only 24 cases of T1DM pregnant women reported [5]. In our case only a single sensor was evaluated, so applicable and comprehensive results for accuracy may not be obtained. Interstitial values were not blinded to the patient, aiming to achieve the best glycemic control during pregnancy. Consequently, none of the 178 interstitial measurements reported a glucose value < 70 mg/dL, and only 6 were > 180 mg/dL, so the accuracy of FreeStyle Libre System in case of hypoglycemia or hyperglycemia cannot be discussed. However, the absence of hypoglycemic events and the limitation in the occurrence of hyperglycemia may be related to the interpretation of glucose trend, helping to obtain an optimal clinical outcome in term of HbA1c. In conclusion FreeStyle Libre System may play an important role in improving glycemic control and quality of life of pregnant women affected by T1DM. Further randomized controlled studies are required to assess the accuracy of FreeStyle Libre System in pregnancy.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest. Case report was performed as part of routine work and fully independently of the FreeStyle Libre manufacturer.

Ethical standard statement The study was performed in accordance with the ethical standards (institutional and national) laid down in Declaration of Helsinki.

Informed consent The patient gave her informed consent for being included in the study.

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