ORIGINAL ARTICLE

Use of Freestyle Libre Pro™ Flash Glucose Monitoring System in Different Clinical Situations at a Diabetes Centre

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Abstract

Flash Glucose Monitoring (FGM) is a newly introduced Glucose Monitoring system. FGM provides both graphical representation of qualitative and quantitative changes in glucose levels occurring over 14-day period collapsed into single modal day graph as well as day by day graphs. In this report, we present our experience with FGM in different clinical situations. In our experience FGM is an extremely useful clinical tool for detection of glucose variability, hyperglycemia and hypoglycemia. It can also be used as an effective educational tool when the data from FGM is shared with the patient. This helps in motivating the patient in achieving better glycemic control.

Editorial Viewpoint

- Ambulatory glucose monitoring is a novel method for monitoring.
- It can be used to adjust drug dose.
- It can be useful to motivate the patient to achieve good glycemic control.

Introduction

Adequate control of blood glucose levels largely depends upon frequent monitoring of control both at the clinic as well as at home by the patient. Self monitoring of blood glucose (SMBG), introduced in the 1980s, is the most widely used method of all the glucose monitoring techniques. It is most useful in patients on multiple insulin doses or on continuous subcutaneous insulin pump. It may also be helpful for treatment or self management for patients using less frequent insulin injections or on non-insulin therapies.[1] SMBG however only gives point of test blood glucose measurements without predicting the direction or rate of change of blood glucose or a continuous monitoring. Moreover, the need for frequent painful finger pricks, issues with calibration and accuracy of the glucose meter as well as the cost of strips contribute to poor patient compliance. As the concept of glycemic variability and its importance evolved, techniques to measure glycemic variability have simultaneously been developed.[2,3] An example is the Continuous Glucose Monitoring System (CGMS) that has been in use for several years.[4] We have earlier reported on our initial experience with CGMS at our centre.[5] The limitations of the currently available CGMS devices include the need for multiple finger stick calibrations, pain at sensor insertion site, expense and the relatively short life of the sensor (up to 7 days only).[6]

Flash Glucose Monitoring (FGM) is a newly introduced method of flash glucose monitoring. It combines inputs from multiple days of glucose data and collapses them into a 24-hour modal day period. It allows quick analysis of poor glycemic control and glycemic variability and can be used as a patient education tool. It consists of three parts: a disposable sensor, a hand-held reader and a proprietary software. The sensor is placed on the back of upper arm with the help of an applicator (Figure 1). The sensor has a small, flexible 4mm-long tip inserted just under the skin; it can be worn up to 14 days. Its amperometric electrochemical sensor measures glucose readings in the 40 to 500 mg/dl range every 15 minutes during the entire wear period and stores them. Using near field communication technology, the sensor data is downloaded into the reader. While the sensor is

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single-use only, the reader can be used to collect data from multiple sensors. The report is generated by connecting the reader to a computer in which the software has been installed. The graphical data provided by FGM includes mean of glucose values at different point of day, a median curve representing the 50th percentile and also the 75th percentile and 25th percentile curves defining the Inter Quartile Range (IQR). The width of the band between the 10th and 90th percentile curve is an index of the glucose excursion (variability). The glycemic trends for individual days can also be obtained in a graphical way. For the purpose of this paper, we have also manually calculated the Mean Amplitude of Glycemic Expression (MAGE) as the arithmetic mean of differences between consecutive peaks and nadirs of the glucose readings. The MAGE was calculated by taking 24-hour glucose values of Day 2 and we compared this with 24-hour glucose readings of Day 13, Days 1 and 14 were not considered, as they usually have only incomplete readings depending on time of application and removal.

The aim of this paper is to show the use of FGM in a few clinical situations. Specifically, we report on cases illustrating the use of FGM in different types of diabetes.

Fig. 1 : FGM showing sensor and reader

Case 1 (FGM in a Normal Person)

This was a 61 year old person with normal glucose tolerance in whom FGM was applied for a few days to see the normal glycemic variability. His fasting plasma glucose (FPG) was 96 mg/dl, post prandial plasma glucose (PPPG) 128 mg/dl and HbA1c, 5.6%. The MAGE on Day 2 was 37mg/dl with the lowest recorded glucose reading of 74 mg/dl and highest of 151 mg/dl during the days when he wore the FGM (Figures 2A and 2B).

Case 2 (Type 2 diabetes of short duration)

This was a 44 year old male patient with type 2 diabetes of 3 years duration, on Tab. Glimepiride 2 mg two times a day. His FPG was 162 mg/dl, PPPG 296 mg/dl and

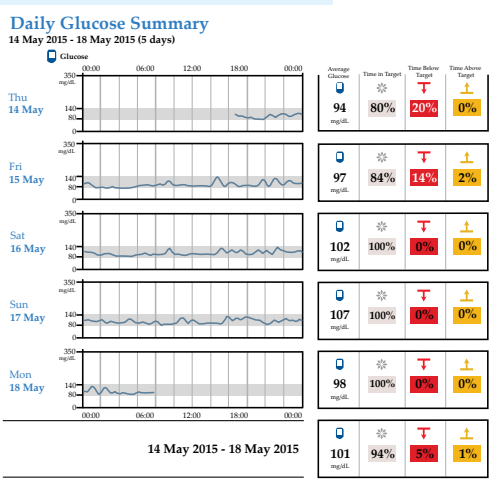

Fig. 2A: FGM in a normal person

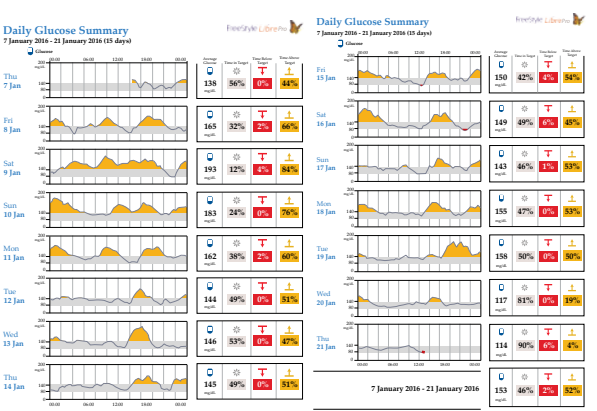

Fig. 3A: Type 2 diabetes of short duration

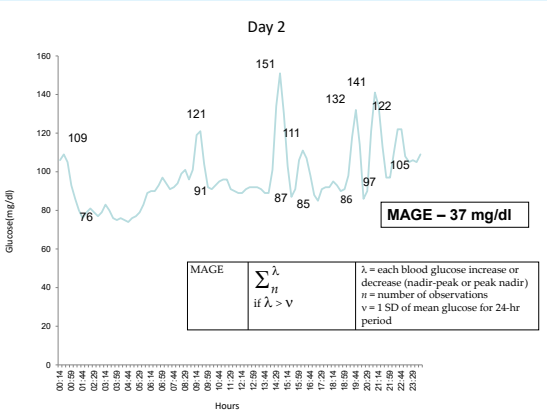

Fig. 2B: MAGE on day 2 (Case 1)

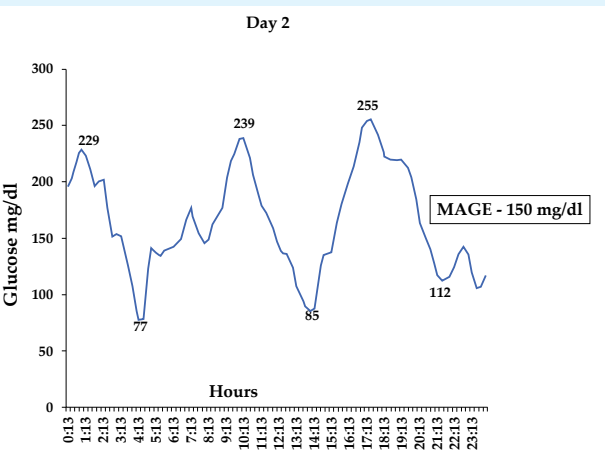

Fig. 3B: MAGE on day 2 (Case 2)

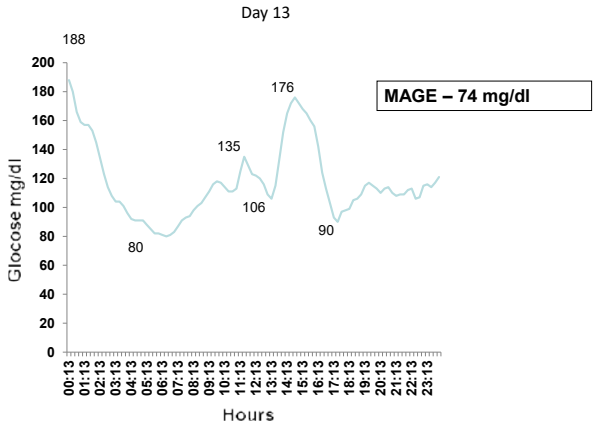

Fig. 3C: MAGE on day 13 (Case 2)

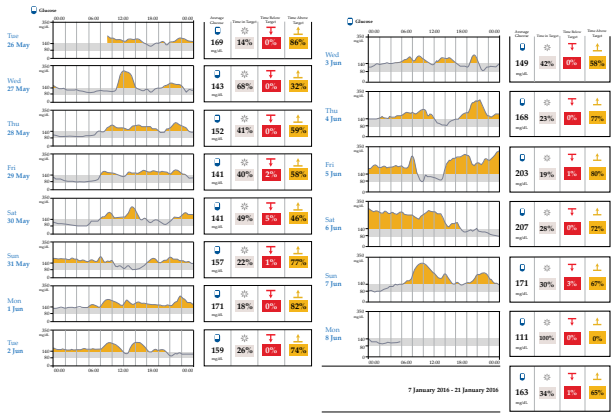

Fig. 4A: Long duration of type 2 diabetes

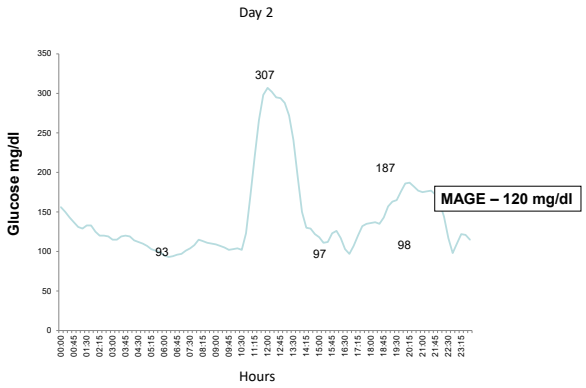

Fig. 4B: MAGE on day 2 (Case 3)

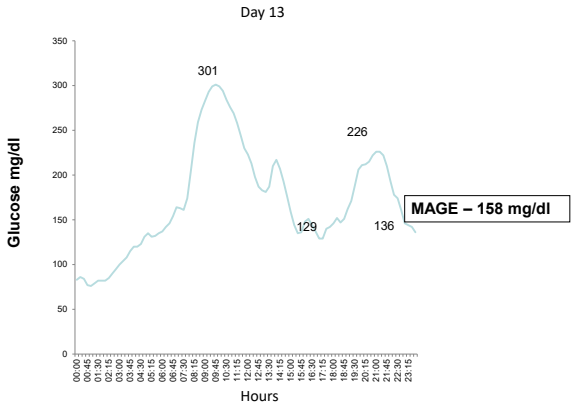

Fig. 4C: MAGE on day 13 (Case 3)

HbA1c, 8.2%. He was started on Inj. Glargine 10 units at bedtime along with tab Glimepiride 2 mg + Metformin 500 mg two times a day in view of high blood glucose levels. His AGP (Figure 3A) shows high blood glucose levels during the first week, which improved during second week with no hypoglycemic episodes. The MAGE was 150 mg/dl on Day 2 which improved to 74 mg/dl on Day 13 (Figure 3B and 3C). The dose of glargine was later reduced and eventually withdrawn. In this case AGP helped us to analyse the glycemic control after initiation of insulin and also helped to document improvement in glycemic variability.

Case 3 (Type 2 diabetes of long duration)

This was a 55 year old male patient with type 2 diabetes of 20 years' duration with diabetic retinopathy, diabetic nephropathy, systemic hypertension, ischaemic heart disease, dyslipidemia and hypothyroidism. His FPG was 227 mg/ dl, PPPG 236 mg/dl and HbA1c, 8.6%. He was on Inj Aspart 16U-8U-4U plus inj Glargine 28U at bedtime, along with Tab Gliclazide 30mg once a day and Tab Linagliptin 5 mg once a day. FGM was initiated for achieving a better glycemic control in view of the comorbidities especially organ related complications. FGM (Figure 4A) showed uncontrolled diabetes at several points of the day during the two week period. On Day 2 (Figure 4B) MAGE was 120 mg/dl. On Day 13 (Figure 4C) MAGE was still 158 mg/dl. Further adjustments were made in insulin doses based on sensor readings. The lab reports post treatment change were FPG 122 mg/dl, PPPG 150mg/dl and HbA1c of 7.7%. A second FGM sensor was initiated to know if the improved blood sugars were stable and within the expected range. The second FGM report (Figure 4D) shows much better control with less glycemic variability shown by reduction in MAGE to 83 mg/dl on Day 2 (Figure 4E) to 86 mg/dl on Day 13 (Figure 4F). In this patient, AGP, along with adjustment of dosage of drugs enabled us to achieve better glycemic control with a reduction in HbA1c level by 0.9%.

Case 4 (Gestational Diabetes Mellitus)

This was a 26 year primigravida diagnosed with gestational diabetes mellitus (GDM) in the second trimester of pregnancy. Her FPG was 125 mg/dl, PPPG-229 mg/dl and HbA1c, 5.8 mg/dl. She was started on Inj Biphasic insulin Aspart 8U-0-6U. FGM was initiated to monitor glycemic control during pregnancy. FGM showed (Figure 5A) high postprandial blood glucose during the day time, with few low blood glucose levels early morning during initial first week

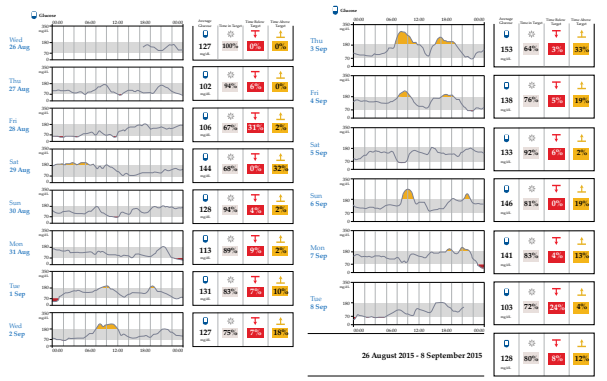

Fig. 4D: Long duration of type 2 diabetes: A second FGM sensor

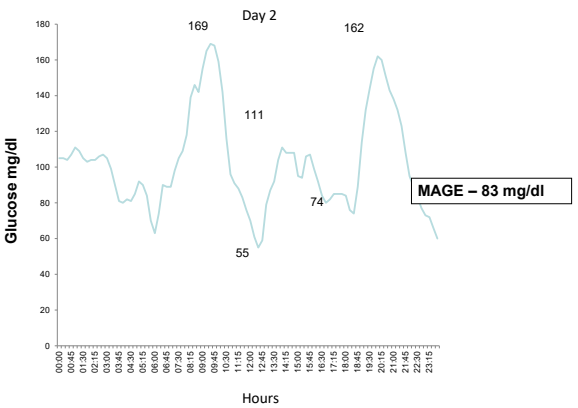

Fig. 4E: MAGE on day 2 while wearing second sensor (Case 3)

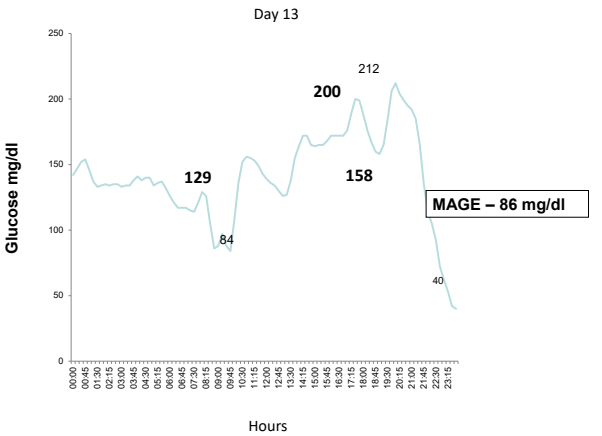

Fig. 4F: MAGE on day 13 while wearing second sensor (Case 3)

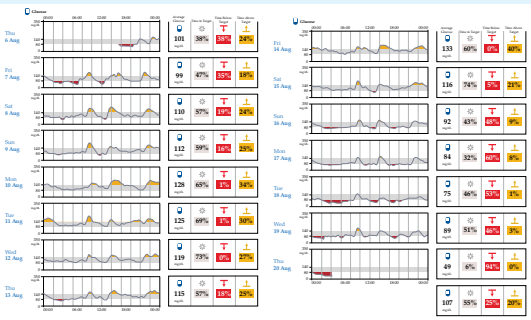

Fig. 5A: Gestational diabetes mellitus

period. During the second week of sensor use, there was significant improvement in the post prandial blood glucose levels with a few hypoglycaemic episodes persisting during early morning hours. The MAGE of 108 mg/dl on Day 2 (Figure 5B), decreased to 59 mg/dl on Day 13 (Figure 5C). The morning dose of insulin was increased to 10 U for further control of postprandial spikes, with reduction in the night dose in view of early morning hypoglycemia. Thus FGM enabled us to achieve strict glycemic control in pregnancy and detect the asymptomatic hypoglycemia which helped in insulin dose adjustment.

Case 5 (Type 1 Diabetes)

This was a 10 year old boy with Type 1 DM of 5 months duration. His blood glucose values were FPG 162 mg/dl, PPPG 174 mg/dl and HbA1c of 9.7%. He was on Inj Aspart 3U-3U-3U along with Inj Glargine 8U at bedtime. FGM was initiated to see why his HbA1c was so high, in spite of relatively acceptable fasting and postprandial glucose levels. His FGM (Figure 6A) showed high blood sugar levels at several points during the day with occasional hypoglycemic episodes. The MAGE on Day 2 was 88 mg/dl (Figure 6B) and 284 mg/dl on Day 13 (Figure 6C). This type of profile is characteristic of type 1 diabetes. The dose of insulin was adjusted to Inj Aspart 3U-2U-2U and Inj. Glargine 10 U. In this case, the FGM enabled us to detect wide fluctuations in the blood glucose levels and to improve the diabetes control by adjusting the insulin doses.

Case 6 (Fibrocalculous Pancreatic Diabetes)

This was a 55 year patient with fibrocalculous pancreatic diabetes of 18 years' duration. His current medications were Inj Biphasic Isophane insulin 22U-0-8U. His FPG was 99 mg/dl, PPPG 252 mg/dl and HbA1c, 7%. FGM was initiated to study the blood sugar fluctuations. FGM showed high blood glucose levels during postprandial periods, with a few hypoglycemic episodes during early morning hours (Figure 7A). Even though HbA1c was 7%, AGP showed high glycemic variability with MAGE of 120 mg/dl on Day 2 (Figure 7B) and 93 mg/dl on Day 13 (Figure 7C). In this case, the FGM enabled us to visualize the day to day variability of blood glucose even when the patient's HbA1c was apparently under control and helped us to make adjustments in the dosage of insulin.

Discussion

In this paper we have presented 5 different clinical types of diabetes in which FGM was initiated and also 1 normal individual. The first case shows a normal glucose tolerant subject where there is

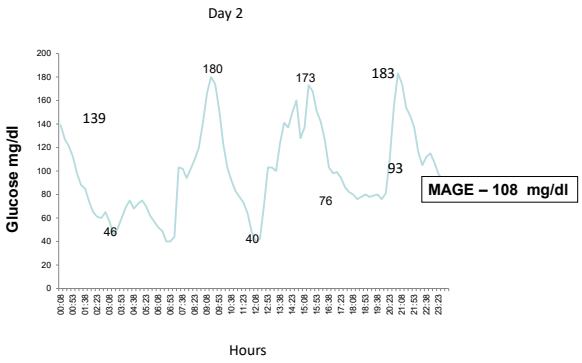

Fig. 5B: MAGE on day 2 (Case 4)

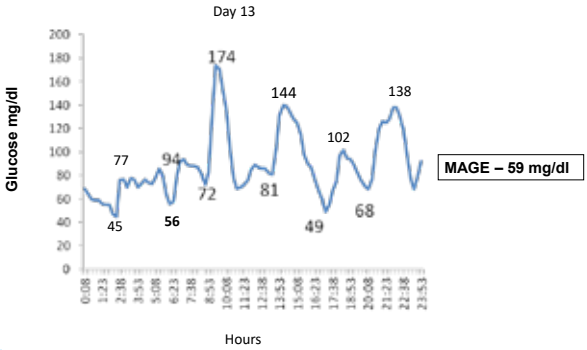

Fig. 5C: MAGE on day 13 (Case 4)

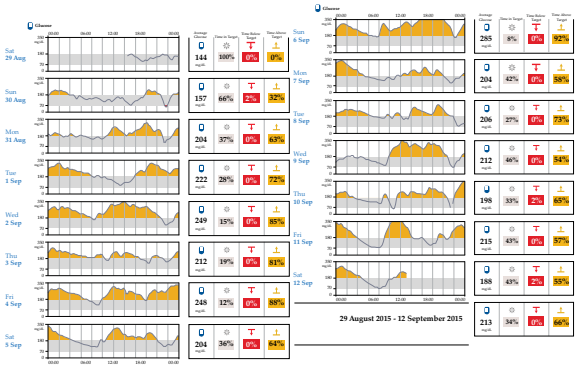

Fig. 6A: Type 1 diabetes

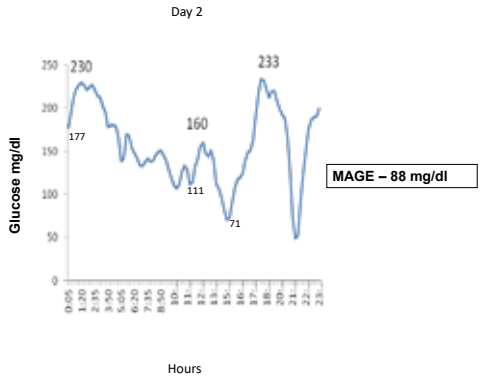

Fig. 6B: MAGE on day 2 (Case 5)

practically very little fluctuation of glucose levels. The second case shows how, in a recent onset T2DM patient, after starting treatment, the MAGE dramatically decreased and the control of diabetes improved. Till such technology became available, physicians would only get a snapshot of the improvement based on occasional SMBG's that are done. Case 3 illustrates greater fluctuations in a T2DM patient with longer duration of diabetes. Case 5 shows the marked fluctuations in a case of type 1 diabetes illustrating the 'brittle diabetes' in this patient. In contrast, Case 4, a patient with GDM shows how mild the diabetes is, and how quickly GDM responds to treatment. The case with FCPD demonstrates more fluctuations in glucose levels like the type 1 patient.

The FGM is a very useful tool to learn about the glycemic status of the patient over a 14 day period after initiating or altering a patient's antidiabetic drug regimen. As it provides day to day information about blood glucose levels for 2 weeks after a clinic visit, this is most useful to adjust dosage of drugs. It also helps us to educate and motivate the patients to achieve good glycemic control.

Mazze et al[7] first introduced Universal Software report (Ambulatory Glucose Profile for systematic presentation of SMBG data) and this was further developed by the same group.[8] An expert panel of diabetes specialists has given recommendations for standardizing glucose reporting and analysis of FGM to optimize clinical decision making.[9] A study by European diabetologists supports the use of FGM for glucose data analysis and to take treatment decisions.[10] FGM is considered as a valuable tool in the case of patients with type 1 diabetes and type 2 diabetes who are on insulin to identify poor glycemic control, to detect hypoglycemia and to study glycemic variability.[11]

It is now believed that the risk of complications of diabetes is not solely determined by exposure to sustained chronic hyperglycemia but also by the oxidative stress generated by glycemic variability.[12] The FGM provides an easy visual analysis of presence of glycemic variability. Glycemic variability is said to present when glucose values are widely spread, for example, when the IQR and 10th and 90th percentile curves cover a wider area. Asymptomatic hypoglycemia can be also detected.

In this report, we calculated the intraday glycemic variability by manually calculating the MAGE.[13] By comparing MAGE on Day 2 with that on Day 13 we could analyse the effect of the treatment prescribed over the 2 week duration and make adjustments to the prescription given at the clinic 2 weeks earlier.

In our experience, FGM helps us to easily visualize whether patient blood glucose level is within the target range. When FGM report is communicated to the patient, they can understand the glucose levels better and become more involved in diabetes management. This ultimately helps to reduce the

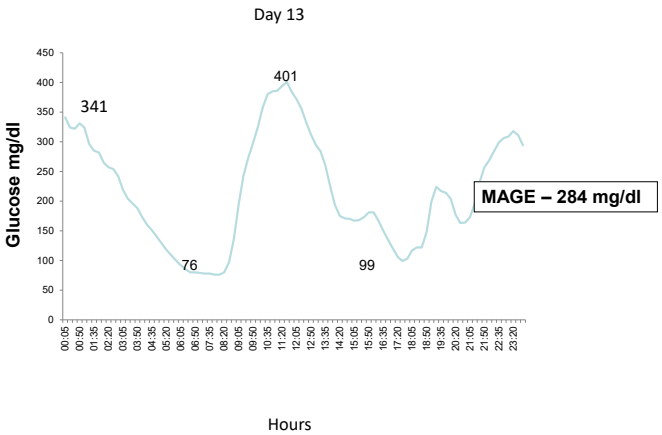

Fig. 6C: MAGE on day 13 (Case 5)

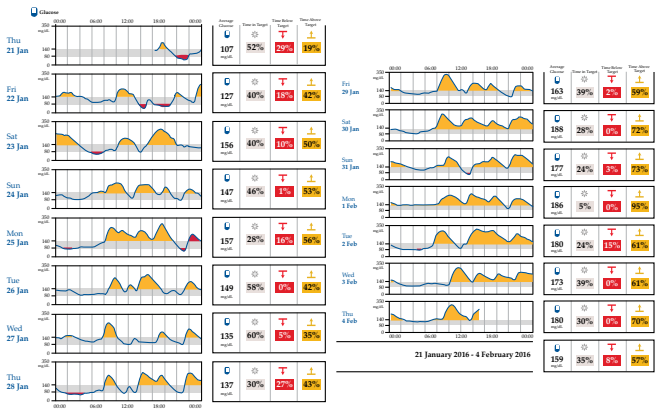

Fig. 7A: Fibrocalculous pancreatic diabetes

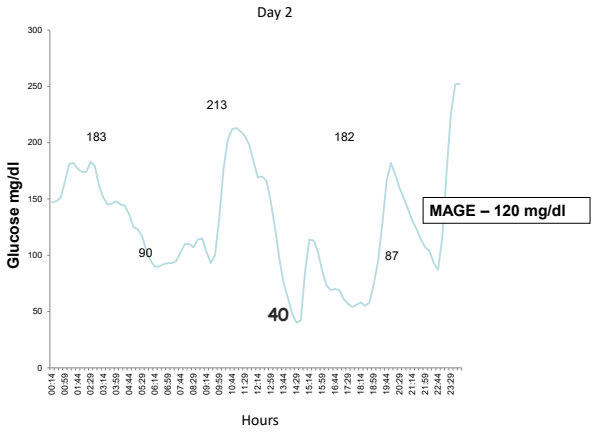

Fig. 7B: MAGE on day 2 (Case 6)

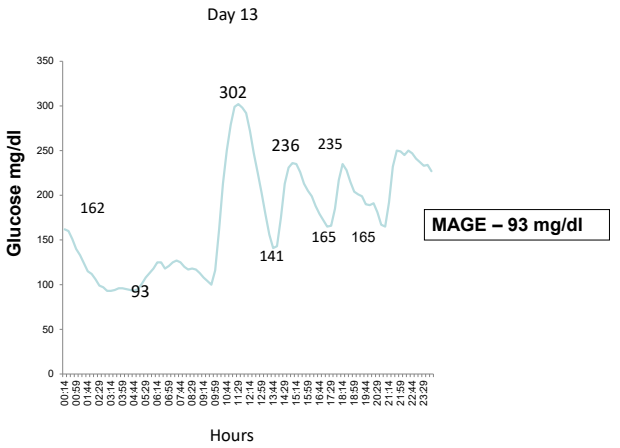

Fig. 7C: MAGE on day 13 (Case 6)

fluctuations of glucose readings and to improve HbA1c values. We therefore feel that the FGM is an excellent new tool in the physician's armamentarium to assess response to therapy. This paper is an illustration of different scenarios where the Freestyle Libre Pro™ FGM system can be used in clinical practice.

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