Chapter 43
Continuous Glucose Monitoring System

Johny Jose Kannampilly

INTRODUCTION

The blood sugar of a person with diabetes is continuously changing every minute of the day throughout the person’s life. Patients may use glucometers to check blood sugar, but this gives the value of blood sugar only at the particular time when the test is done. However, since blood sugar levels of a patient are changing from minute to minute, checking simply with blood glucose meters may not be sufficient. Additionally, 60% of glucose lows may not be revealed with self-monitoring of blood glucose (SMBG) alone.

Another standard way to monitor blood glucose is through the measurement of glycosylated hemoglobin, more commonly known as hemoglobin A\(_1c\) (HbA\(_1c\)). But again, HbA\(_1c\) does not tell the whole story as while it provides information about glucose exposure it is not able to track glycemic variability; HbA\(_1c\) is a very useful test to detect how well blood sugar is controlled over the previous 3 months. However, since HbA\(_1c\) indicates the average blood sugar, it does not give a correct picture of how much fluctuations occur. In fact, if a patient has frequent low blood sugar, it could result in low HbA\(_1c\) (because HbA\(_1c\) denotes an average value) and a false sense of security to the patient and doctor, even when the blood sugar is often high and is actually poorly controlled (Figures 1 and 2).

Thus, while SMBG and HbA\(_1c\) are important—they do not tell us the complete picture—especially information on glycemic variability of the patient.

Continuous glucose monitoring (CGM) can help complete the picture for a patient’s glucose control. An effective way to monitor sugar levels to understand how the blood sugar is changing throughout the day and to understand the state of glycemic excursions in a patient is with the help of a technology called continuous glucose monitoring system (CGMS). It reads the sugar levels of the person every 10 seconds and keeps a record every 5 minutes so that we can get 288 readings per day during the CGMS study period. A tiny, sterile, flexible electrode is inserted just under the skin that measures glucose in the interstitial fluid (ISF). This data is then uploaded onto a computer and clearly visible in the form of a graph which any one can understand.

There are plenty of patients who have high blood sugar at odd times of the day which is not detected by the routine tests like fasting blood sugar (FBS) and postprandial blood sugar (PPBS) (blood sugar after food) or who are unaware that they may be experiencing low blood sugars at night. The use of a CGMS can provide essential information to the doctor to allow him/her to appropriately modify the treatment of their patients to get better control of blood sugar throughout the day.

WHAT IS CONTINUOUS GLUCOSE MONITORING?

In the 1970s, blood glucose meters became available and transformed the nature of diabetes self-monitoring. However, periodic blood glucose measurements via blood glucose meters only show a snapshot of blood glucose at any given test time. As the illustration depicts, blood glucose meter tests (reflected by blue rectangles) provide only instantaneous snapshots of glucose activity; periodic blood glucose measurements may not truly depict the profile of a patient’s glucose control.

Continuous glucose monitoring tells the whole story like a “movie”, not just snapshots of the glucose levels. It provides insight into glucose trends between blood glucose tests, leading to improved knowledge and improved glucose control.

BASICS OF CONTINUOUS GLUCOSE MONITORING

The sensor is placed subcutaneously and measures glucose in the fluid between the blood vessels and the cells, called the ISF. Blood glucose meters measure glucose in the blood capillary. Glucose (primarily from carbohydrates) passes from blood vessels, through the ISF, to cells. So, the glucose level recorded in the ISF briefly lags
the glucose level recorded in the blood. CGM technology uses a glucose sensor inserted into the ISF. Glucose in the ISF penetrates the semipermeable membrane of the sensor and reacts with the glucose oxidase found within the sensor. This reaction produces electrons, which are measured as what we call the input signal (ISIG) (it indicates the input signal value that is captured by the sensor in the form of electron values in nanoamperes). This ISIG is then converted into the sensor glucose value by using calibration blood glucose values. Illustrated below is a model of plasma (G1) and ISF (G2) glucose kinetics (Figures 3A and B). Subcutaneous ISF glucose sensing accurately reflects plasma glucose values across a wide range of glucose profiles, regardless of changes in plasma insulin.

Note: Since blood glucose meter tests are used to calibrate the iPro2 System, it is critical to verify that blood glucose meter tests are performed properly and that the meter is functioning properly. See blood glucose meter user guide for test instructions.

What Types of Continuous Glucose Monitoring Systems are there?
There are two types of CGMs: (1) Professional CGM (Figure 4) and (2) Personal (REAL-Time) CGM (Figures 5A and B).

Professional Continuous Glucose Monitoring (for Health Care Providers)
- Ideal for short-term blinded CGM evaluation and retrospective analysis
- Quick and easy to set-up
  - minimal patient training
  - no alarm
- Can be used on all patients with diabetes to reveal excursions and patterns.

Personal (REAL-Time) Continuous Glucose Monitoring (for Patients)
- Glucose sensor readings are updated every 5 minutes on the monitor
- Trend graphs, arrows and alerts help the patient avoiding lows and highs
- Patient’s motivation and training are key to success.

Who is a Good Candidate for Continuous Glucose Monitoring?
The information provided by the iPro2 System can assist you in designing individualized diabetes treatment programs. The data is also useful as an educational tool to improve motivation and collaboration with patients. While the system may be used effectively with patients with diabetes, it may be of particular use in evaluating the following conditions and situations:
- Elevated A1c levels
- Nocturnal hypoglycemia (low blood glucose) and hypoglycemic unawareness
- Postprandial hyperglycemia (high blood glucose)
- Fluctuating glucose levels
- Poor glycemic control (patients who desire better control)
- Logbooks not reflecting A1c
- Pregnant women with diabetes
- Children with diabetes
- Patients who test infrequently.

Benefits of Continuous Glucose Monitoring
Continuous glucose monitoring shows the complete picture of glucose activity, not just snapshots of glucose levels. It allows users and clinicians to gain more insight by providing real-time information about glucose levels and showing glucose trends between fingersticks, leading to improved glucose control. CGM also provides additional information beyond the “average” of overall glucose levels that is represented by HbA1c. A recent study has shown that patients who use CGM at least 6 days a week substantially lower their A1c levels without an increase in hypoglycemia, compared with
patients who use it less frequently.\textsuperscript{1,2} Continuous glucose readings allow patients to better manage their diabetes by intervening on a real-time basis to reduce the frequency and severity of hypoglycemic or hyperglycemic episodes. Patients can learn how diet, exercise, medication, lifestyle and episodes of illness affect their glucose levels. Furthermore, historical analysis provides insights for both patients and health care professionals (HCPs) that can be translated into treatment adjustments and optimization. Several studies have demonstrated a significant difference in A1c outcomes on the basis of adjustments in insulin regimens in response to CGM.\textsuperscript{3-5} Hirsch (2002) has also demonstrated that use of CGM in clinical practice would provide the required monitoring tool to minimize glycemic variability and superoxide overproduction and may potentially reduce diabetic complications.\textsuperscript{6}

CONCLUSION
Understanding glucose variability in a patient is extremely important and some research suggests that variable blood sugars may be more damaging than consistently high blood sugars. Fluctuations of glucose values can lead to oxidative stress\textsuperscript{7} and potentially to cell damage and increased risk for microvascular and macrovascular complications. The use of CGM in clinical practice would provide the required monitoring tool to minimize glycemic variability and superoxide overproduction and may potentially reduce diabetic complications.\textsuperscript{2} According to the American Association of Clinical Endocrinologists (AACE), CGM technology is not only novel, but it can improve the lives of patients who incorporate it into a comprehensive diabetes management plan.

REFERENCES