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MEETING PROCEEDINGS

Establishing a Continuous Glucose Monitoring Program

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Abstract

Real-time continuous glucose monitoring (RT-CGM) devices provide detailed information on glucose patterns and trends, and alarms that alert the patient to both hyper- and hypoglycemia. This technology can dramatically improve the day-to-day management of patients with diabetes and promises to be a major advance in diabetes care. The safe and effective use of RT-CGM in diabetes management rests on an understanding of several physiological as well as technological issues. This article outlines the key issues that should be addressed in the training curriculum for patients starting on RT-CGM: (1) physiologic lag between interstitial and blood glucose levels and the implications for device calibration, and interpretation and use of data in diabetes management; (2) practical considerations with the use of sensor alarms and caveats in the setting of alarm thresholds; and (3) potential risk for hypoglycemia related to excessive postprandial bolusing by RT-CGM users, and the practical implications for patient training.

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Real-time continuous glucose monitoring (RT-CGM) devices provide detailed information on glucose patterns and trends and on alarms that alert the patient to both hyper- and hypoglycemia. This technology can dramatically improve the day-to-day management of patients with diabetes and promises to be a major advance in diabetes care.[1,2] To derive the full potential benefit from RT-CGM the patient needs to have good diabetes self-management skills. This article covers some of the key issues and concepts related to interstitial glucose measurements and continuous sensing that need to be covered in the training curriculum for patients starting on RT-CGM.

Patients' Education around RT-CGM, the Main Issues

The safe and effective use of CGM in diabetes management rests on an understanding of several physiological as well as technological issues. The key issues that need to be addressed in the training curriculum for patients starting on RT-CGM include (1) implication of physiologic lag in the calibration of devices, and interpreting and using data in diabetes management; (2) considerations in the use of alarms and caveats in the setting of alarm thresholds; and (3) potential risk for hypoglycemia related to excessive postprandial blousing in RT-CGM users and some of the practical implications for patient training.

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Abbreviations: (CGM) continuous glucose monitoring, (RT-CGM) real-time CGM

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Interstitial Glucose Measurement and Lag Time Importance

Currently available CGM devices measure interstitial glucose, whereas finger stick devices measure capillary glucose. Usually because of a physiologic lag in equilibration between these two compartments, an increase or decrease in glucose levels will first be apparent in the blood, followed by the interstitial fluid. Because the CGM device is calibrated using finger stick capillary blood glucose measurements, the lag has important implications for the calibration of sensors. One of the important issues that needs to be strongly emphasized in patient education is the fact that the sensor should only be calibrated when the glucose level is relatively stable and there is steady-state equilibration between glucose concentrations in the blood and interstitial fluid compartment. In practice, this means that calibration measurements should be performed preprandially or at least 3 hours after a bolus. For optimal accuracy, CGM devices should be calibrated three to four times per day. After meals the glucose level will often increase by over 3 mg/dl/min and this, in conjunction with the physiologic lag in equilibration of the blood and interstitial glucose, which is often 10–15 minutes in duration, can lead to differences between glucose levels in the blood and interstitium of as much as 30–45 mg/dl.[3] If the CGM is calibrated with a blood glucose measurement postprandially, this will result in an upward bias of the sensor readings and compromise the accuracy of the device in detecting hypoglycemia. Patients should also be reminded that blood glucose measurements taken around exercise should *not* be used for calibration. In addition, it is critically important that the patient follow proper procedures in performing glucose measurements when calibrating the continuous monitor. Alternate site measurements *must* not be used, and attention must be given to ensuring that fingertips are clean and that the blood glucose monitor is coded correctly according to the manufacturer's instructions.

The physiologic lag can have important implications with regard to the detection and treatment of hypoglycemia. When the glucose is declining the interstitial glucose generally lags behind blood, and in this situation the actual blood glucose level could be quite low even when the interstitial/sensor glucose level is normal.[4] The practical implication is that in situations when the glucose is declining (such as after exercise in the gym or even mild activity such as walking in the mall), even if the sensor glucose is normal, the patient needs to perform finger stick glucose measurements before driving. Usually in this situation the trend graph on the sensor display or the rate of change arrows would indicate that the glucose is falling, which would serve as a prompt for the patient to check the finger stick blood glucose. However, patients need to remember that there are circumstances, as demonstrated in the study by Wilson and colleagues,[5] where physiologic lag can also lead to underestimation by the rate of change indicator of the CGM device. The practical implication is that if the sensor indicates that the glucose is normal and also stable but the patient feels hypoglycemic or has reason to suspect that glucose is declining, he/she should disregard sensor data and do a finger stick measurement.

Another area where these lag phenomena can be of clinical importance relates to the treatment of hypoglycemia. If patients use the sensor to assess whether they are responding to treatment of hypoglycemia, they can end up overtreating the low. During the recovery from hypoglycemia, the increase in the interstitial glucose will often lag behind the blood glucose,[6] and at a time when blood glucose has already normalized the sensor/interstitial glucose may still be in the low range. Patients who rely on a sensor to assess whether their glucose level is improving following the ingestion of carbohydrates will mistakenly assume that they need to consume more. The practical implication is that the patient should be instructed of the need to perform finger stick glucose measurements to assess recovery from hypoglycemia.

Patients need to be aware that if the sensor tracing or the rate of change arrow indicates that the glucose level is either rising or falling, they must perform a finger stick blood glucose measurement before taking insulin. In these situations, blind bolusing without confirmatory finger stick measurements can be dangerous. In addition, the patient who understands the physiologic basis for differences between sensor readings and finger stick measurements and that these discrepancies do *not* necessarily indicate sensor inaccuracy may be less prone to lose confidence in the technology.

Adjusting Alarm Thresholds

The alarms for hypo- and hyperglycemia are a very important feature of RT-CGM devices. **Table 1** outlines some of the considerations in setting alarm thresholds. The trade-off between sensitivity and specificity is an important consideration in deciding about these settings.

Individuals with hypoglycemia unawareness and a history of severe hypoglycemic reactions typically want the reassurance of being alerted whenever they are heading into the hypoglycemic range; for these

Table 1.
Setting Alarm Thresholds: The Trade-Offs

Set alarms at the "ideal" level	Set the alarm limits more widely
For example: 80 for low, 180 for high	For example: 55 for low, 250 for high
Advantage: Patient will be warned of most lows and highs.	Advantage: Patient will have fewer false alarms. Alarm will generally only go off when the glucose is, in fact, low or high so there are less irritating and intrusive alarms and less risk for alarm burnout.
Disadvantages: Patient will experience frequent false alarms when the glucose is not, in fact, low or high. These alarms can disrupt sleep and become a source of irritation and frustration to the patient and his/her partner/family, leading to alarm burnout and reduced sensor use.	Disadvantage: Patient will not always be warned when the glucose level is low or high.

individuals, the low threshold should be set at 80 mg/dl or higher. Because of a physiologic lag, when the alarm goes off the blood glucose levels will generally be lower than the sensor measurement, and this needs to be taken into consideration in deciding about alarm thresholds. The downside of setting the low alarm at a relatively high threshold is that there may be frequent false alarms. For some, this can lead to alarm burnout and an associated tendency to ignore sensor alarms or even discontinue use of the RT-CGM device.

Preventing alarm burnout is an important clinical priority. For individuals starting on RT-CGM who do not have a history of problematic hypoglycemia, it is reasonable to set alarms with a low threshold at 55–60 mg/dl and a high threshold at 250 mg/dl or even greater. This ensures that there will not be too many intrusive and often irritating alarms while the patient is initially learning to use the sensor and smoothing out their glucose patterns. As patient mastery advances, threshold settings can be brought closer to target glucose levels, which can assist with further tightening of glucose control.

Minimizing the Risk for Hypoglycemia from Excessive Postprandial Bolusing

Continuous glucose monitoring provides the patient with added information about postprandial glucose patterns, which can be extremely helpful in guiding the patient about when additional insulin coverage is required to reach the target glucose range. The downside is that patients will sometimes overreact to this added glucose data by taking excessive amounts of insulin, leading to an increased risk of hypoglycemia.[7] This tendency for excessive postprandial bolusing is a common problem with RT-CGM, and a major focus of education and follow-up care of the patient using RT-CGM will often need to be addressed at reducing this risk.

Before taking extra insulin to treat postprandial hyperglycemia the patient should consider the following.

- The amount of residual insulin "on board" from a premeal bolus. In this context it is important that the patient understand that the pharmacodynamics (biologic action) of a bolus of monomeric insulin lasts considerably longer (4–6 hours) than is suggested from pharmacokinetic (insulin level) data.[8] Pumps with bolus calculators can assist in making appropriate dose reductions.
- The direction of the "trend" arrow on the glucose sensor. **Table 2** shows algorithms for adjusting insulin boluses based on the rate of change of the glucose level as outlined in the training materials for the STAR 1 trial[7] and Juvenile Diabetes Research Foundation-sponsored randomized control trials.
- The type of carbohydrate eaten.

Table 2.
Adjusting Bolus Dose Based on Rate of Change of Glucose

If glucose is increasing 1–2 mg/dl/min	add 10% to calculated food/correction bolus
If glucose is increasing >2 mg/dl/min	add 20% to calculated food/correction bolus
If glucose is decreasing 1–2 mg/dl/min	subtract 10% from calculated food/correction bolus
If glucose is decreasing >2 mg/dl/min	subtract 20% from calculated food/correction bolus

Following a *high* glycemic index of carbohydrate foods there is a rapid spike in the glucose level, and at the time when glucose is peaking there may be a substantial amount of residual insulin "on board" from the premeal bolus. If the patient were to take a correction bolus within 2–3 hours after the initial premeal bolus there can be a considerable risk for hypoglycemia from dose stacking. The converse situation is a *low* glycemic index meal, such as pasta, which is digested slowly. At a time point 2–3 hours after the meal a significant proportion of the carbohydrate load still has not entered the circulation and usually the glucose level will continue rising as the remaining glucose is absorbed; if the glucose level is increased at this time, an additional bolus may be

advisable. Knowledge about the glycemic index[9] can be helpful in deciding whether it is safe/advisable to take additional postprandial boluses; this subject should be incorporated into the training curriculum for the RT-CGM user.

Conclusion

It is clear that RT-CGM has immense potential for transforming the lives of people with diabetes. Patients need to be very skilled in their diabetes self-management to be able to use this technology safely and effectively. This article outlined some of the key issues that need to be addressed in the educational curriculum for CGM programs.

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