Realtime Continuous Glucose Monitoring in Children and Adolescents—An Overview of the Current Technology and its Impact on Patient Outcomes

Jeniece Trast, RN, MA, CDE[1] and Neesha Ramchandani, PNP, CDE[2]

1. Clinical Research Nurse and Certified Diabetes Educator; 2. Pediatric Nurse Practitioner and Certified Diabetes Educator, Division of Pediatric Endocrinology and Diabetes, The Children's Hospital at Montefiore, New York, US

Abstract

Continuous glucose monitoring (CGM) systems, available for patient use since 1999, and realtime continuous glucose monitoring (RT-CGM) systems, available since 2006, have helped optimize diabetes management. Previously, RT-CGM studies found benefits mainly in patients with type 1 diabetes over the age of 25. Children and adolescents often present a challenge when managing type 1 diabetes. However, it is now apparent that RT-CGM has clear benefits in these age groups as well as in adults. Not only have studies shown improvements in glycemic control in this population, they have also demonstrated parental satisfaction with the technology. Challenges with RT-CGM use still exist and must be addressed. Nevertheless, RT-CGM is a beneficial tool to assist in diabetes management, and its use should be encouraged in the majority of pediatric patients with type 1 diabetes.

Keywords

Type 1 diabetes, continuous glucose monitoring system, pediatric patients, children, adolescents, glucose sensor, diabetes technology

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Correspondence: Neesha Ramchandani, PNP, CDE, Division of Pediatric Endocrinology and Diabetes, The Children's Hospital at Montefiore, 3415 Bainbridge Ave., Bronx, NY 10467, US. E: neesha.ramchandani@gmail.com

Continuous glucose monitoring (CGM) systems have been available for patient use since 1999 and realtime continuous glucose monitoring (RT-CGM) systems have been available since 2006.[1] The early systems were blinded and used as a tool by diabetes clinicians for diagnostic purposes (diagnosis of hypo- and hyperglycemia) and to get a more complete picture of a patient's blood sugar trends over several consecutive days. Data on glucose values, measured every five minutes in the interstitial fluid, could be reviewed only after they had been downloaded from the CGM device onto a computer. Since then, newer systems have been developed and improved upon, and are becoming increasingly accepted by patients with type 1 diabetes. Blinded CGM systems still exist in updated versions (e.g., Medtronic's iPro®) and are used for diagnostic and research purposes. However, the advent of RT-CGM allows patients to see their own glucose values and trends in realtime and intervene as necessary.

Currently, people with type 1 diabetes of all ages use RT-CGM, which helps them optimize their glycemic control. By having RT-CGM information on glucose levels every one to five minutes, patients and parents/care-givers are able to make more educated decisions when adjusting insulin, activity, and food intake. It enables them to have more control over their own or their child's diabetes. Many studies have been done to evaluate the efficacy and benefits of RT-CGM, although few have specific information regarding RT-CGM use and benefits in children and adolescents.[2]

It can be challenging to maintain euglycemia in children and adolescents with type 1 diabetes due to their eating habits, growing and changing bodies, erratic schedules, still developing cognitive systems, inability to manage their diabetes on their own, and presence of multiple care-givers. RT-CGM systems can be used in this group of patients to more closely monitor their varying glucose levels and help them achieve good glycemic control. Previously, studies of patients with type 1 diabetes using CGM did not show the same benefits in the younger population as in adults.[3–5] However, recent reports have found benefits of using RT-CGM in youth.[6–10] RT-CGM use in children and adolescents has increased, but it is still not as wide as in adults.

Initial Research Studies

Early studies of RT-CGM found that only patients with type 1 diabetes who were at least 25 years of age and who wore glucose sensors at least 60 % of the time significantly benefited from this technology.[3,5,11,12] This was the case, for example, of the Juvenile Diabetes Research Foundation (JDRF) study, which found that RT-CGM effectively lowered glycated hemoglobin (HbA_{1c}) in such patients and decreased the time they spent in hyperglycemia.[3] A more recent study found glycemic benefits in those who wore glucose sensors at least 41–60 % of the time,[13] showing that RT-CGM can be beneficial even when used less frequently.

Although RT-CGM has been shown to benefit patients,[2,5,6,11,13] some studies still fail to specifically show improvements in glycemic control

in youth.[14,15] It should be noted that these same studies do not show any negative effect and usually report a high degree of parental satisfaction with having realtime glucose values available.[14,15] Still, the greatest effects on glycemic control are generally seen in patients who use RT-CGM consistently.[3,6,8,16] For example, a recent study conducted in children aged 4–9 years did not demonstrate improvements in glycemic control with RT-CGM use, even though there was a high degree of parental satisfaction, and this lack of glycemic benefit was attributed to limited RT-CGM use.[15]

Newer studies have found significant benefits in children with type 1 diabetes who use RT-CGM compared with those who do not.[10,13,16,17] Nevertheless, there are still some barriers to the adoption of RT-CGM in this patient group. One study that examined reasons why pediatric patients with type 1 diabetes do not use sensors continuously found that the most disliked aspects of RT-CGM were pain and discomfort. Other study subjects reported RT-CGM to be annoying, to be a hassle, and to interfere with their lives. There were also issues with the device itself and with insurance coverage.[18] Barriers to consistent RT-CGM use must be overcome in order for children and adolescents to maximize both the glycemic and quality-of-life benefits of this technology.

Existing Devices

Existing RT-CGM devices consist of three pieces: a sensor electrode that must be inserted subcutaneously; a transmitter that is connected to the sensor electrode and relays the information to the receiver via radiofrequency; and a receiver that receives the electrochemical signal from the transmitter, converts it into a glucose value, and displays that value on the transmitter. Devices display new glucose values every few minutes, providing a more complete picture of glucose variability throughout the day. RT-CGM can also alert the user of a potential or actual out-of-range blood sugar level. Sensor electrodes can be worn for three to seven days depending on the brand and patient.

There are currently three RT-CGM devices available for personal use. These are the DexCom SEVEN® PLUS, the Medtronic Paradigm® REAL–Time System, and the Medtronic Guardian® REAL-Time.[19] Their characteristics are summarized in *Table 1*. The Abbott Freestyle Navigator® System has been discontinued.[20]

Warm-up Period and Calibration

Sensor electrodes need to be sufficiently wet from the interstitial fluid before any readings can be recorded. As a result, currently available sensors have a warm-up period of two hours before they can start reading. The device must be calibrated with a finger-stick blood sugar value before it can display its own output values. After the first calibration is done, sensors must be recalibrated throughout the day to keep them functioning correctly. Calibration is important to ensure the device continues to read within an acceptable range of the actual blood sugar.

Lag Time

There is a noted lag time between sensor blood glucose values and actual blood glucose values because the sensor is detecting glucose in the interstitial fluid and not in the blood, which gets the glucose level more rapidly. This is why CGM systems have been approved only as an adjunct to self-monitoring of blood glucose (SMBG). The lag time between blood glucose and interstitial fluid glucose is approximately 5–10 minutes, but can be exaggerated if there is a rapid change in glucose level.[21] Because of this, a patient should not rely solely on RT-CGM glucose levels but should use them only as a guide.

Accuracy

Sensor accuracy has improved markedly over the years, but it is not perfect. The DexCom SEVEN PLUS has an overall accuracy of 13.0 % (median absolute relative difference [ARD]) and a hypoglycemia (blood glucose <70 mg/dl) accuracy of 27 % (mean ARD). The two Medtronic systems both have an overall accuracy of 10.5 % (median ARD) and 15.2 % (mean ARD) and a hypoglycemia accuracy of 16.9 % (mean ARD).[19] A lower ARD signifies greater accuracy. If a sensor is reading inaccurately, it may be that the sensor is faulty, has been placed incorrectly, or has been calibrated improperly. Additionally, acetaminophen and vitamin C can interfere with the readings on some devices.[22] Ramchandani et al. found that the major reasons why a person wearing the sensor would stop using it were problematic equipment and inaccuracy.[18]

Recommendations for Use of Continuous Glucose Monitoring in Youth

The American Association of Clinical Endocrinologist's consensus panel on CGM published a statement in 2010 regarding the use and practice of CGM technology, including in youth.[23] The panel recommended use in children and adolescents with type 1 diabetes who have achieved HbA_{1c} levels <7 % (these patients and their families are typically highly motivated, which is crucial for device effectiveness)[2] as well as youth with type 1 diabetes who have HbA_{1c} levels of 7 % or higher and are able to use the device on a near daily basis. The panel also recommended a trial period of 2–4 weeks for youth who frequently monitor their blood glucose levels and committed families of young children under the age of eight, especially if the patient is having problems with hypoglycemia. Intermittent use of a professional CGM device is recommended for youth who have nocturnal hypoglycemia/dawn phenomenon, hypoglycemia unawareness, and post-prandial hyperglycemia.[23]

Benefits of Using Continuous Glucose Monitoring in Children and Adolescents

Maintaining near normal glucose levels in children and adolescents with type 1 diabetes can be challenging. Additionally, fear of hypoglycemia—especially in parents of children who have experienced an episode of severe hypoglycemia—is a major barrier to keeping blood sugars in the target range.[15,24] Using RT-CGM in pediatric patients with type 1 diabetes has the potential to greatly improve their diabetes control while at the same time minimizing many of the fears associated with diabetes management.[23,25] RT-CGM provides additional assistance in patients who may be too young to communicate low blood sugar, who refuse finger-stick tests, or who are dependent on their parents/care-givers for care. It can also help to address parents' fear of overnight hypoglycemia, demonstrate to teenagers and parents the glycemic effects of taking a bolus dose after meals, and serve as an eye-opener for adolescents with high HbA_{1c} levels or children who refuse to perform any diabetes self-care tasks during school hours.

Table 1: Characteristics of Currently Available Realtime Continuous Glucose Monitoring Devices

Device	SEVEN® PLUS	Paradigm® REAL–Time System	Guardian® REAL-Time
Manufacturer	DexCom	Medtronic	Medtronic
Size of Monitor, Transmitter, and Sensor	Monitor: L 4.5" x W 2.3" x H 0.85" Display: 2" x 1.3" Transmitter and sensor: L 4.5" x W 2.3" x H 8.5"	Monitor: L 3.0" x W 2.0" x H 0.8"; display incorporated into the insulin pump Sensor: the size of a nickel Transmitter: about the size of a quarter	Monitor: L 3.2" x W 2.0" x H 0.77" Sensor: the size of a nickel Transmitter: about the size of a quarter
Probe Size and Gauge	Length of probe: 13 mm Gauge of sensor probe: 26 gauge	Length of probe: 13 mm Gauge of sensor probe: smaller than needle, which is 22 gauge	Length of probe: 13 mm Gauge of sensor probe: smaller than needle, which is 22 gauge
Range of Monitor to Transmitter	5 feet	6 feet	6 feet
Glucose Display	Displays new glucose value every 5 minutes with trend arrows and rate of change	Displays new glucose value every 5 minutes with trend arrows and rate of change	Displays new glucose value every 5 minutes with trend arrows and rate of change
Sensor Wear/Life	7 days	3 days	3 days

Source: adapted from Diabetes Health, 2010.[19]

Generally, glucose values vary greatly throughout the day in individuals with type 1 diabetes and even more so in children and adolescents with erratic schedules and changing bodies. RT-CGM is better able to capture this variability than traditional glucose monitoring methods. Additionally, for a parent caring for a young child or an adolescent who manages his/her own care, RT-CGM allows the user to make well informed decisions regarding diabetes management, both in realtime and after reviewing the data retrospectively. RT-CGM also helps diabetes clinicians better manage their patients. When data from the receiver are uploaded into a specific program, the clinician can see several days of CGM data and make appropriate adjustments based on these data. Diabetes clinicians can review patient data remotely by receiving CGM downloads via e-mail or fax or by signing into a web-based software system (in the case of Medtronic).[23,25]

A recent meta-analysis showed a clear decrease of HbA_{1c} levels from baseline in children and adolescents with the use of RT-CGM, which provides new and important insights about the advantages of this technology in younger patients.[7] This is in contrast to the first study of RT-CGM in children and adolescents with type 1 diabetes, which observed only a modest decrease in HbA_{1c} levels.[26] An important common finding of studies showing benefits from RT-CGM use is that patients need to use the realtime device consistently to fully benefit.[3,7,11,12,15] However, in practice, even if the RT-CGM device is only used one week per month, data will still provide some guidance for patients' diabetes management.

Checking blood glucose levels at least four to seven times a day, as recommended when performing SMBG, is a difficult task at any age. The pain caused by SMBG, especially in children, has been reported as a major reason for poor adherence to diabetes control.[27–29] In addition, finger-stick tests are a hassle and interrupt daily activities; no child wants to stop playing to check their blood glucose level. With the use of RT-CGM, the number of finger-sticks can potentially be decreased, while at the same time the number of glucose values collected greatly increases. It is important to note that finger-sticks are not completely eliminated with current RT-CGM devices. Finger-stick blood sugar levels must be measured at least twice a day to calibrate the RT-CGM system in order to keep it running properly and also verify hypoglycemia and hyperglycemia.

Hypoglycemia is a major concern for parents of children with type 1 diabetes. Studies have shown that RT-CGM reduces the time spent in hypoglycemia.[3,7,17] By using predictive and out-of-range glycemic alerts and regularly checking the readings on the device's receiver, a patient who may have hypoglycemia unawareness will be able to detect and treat a low blood sugar reaction sooner. For smaller children, the parent/care-giver can keep the receiver with them—data will be transmitted to it from the sensor as long as it is within 5–6 feet of the child—and look at it for glucose information to reassure themselves that the glucose level is in a safe range or see if treatment is needed.

A recent study found that RT-CGM also improves the epinephrine response in adolescents with type 1 diabetes and hypoglycemia unawareness. Using devices' alarms set to predetermined glucose levels was found to be a useful tool for avoiding hypoglycemia and therefore improving the counter-regulatory response to hypoglycemia in adolescents with hypoglycemia unawareness.[6]

Despite technological advances, alerts, and alarms, it is still difficult to recognize overnight hypoglycemia. It takes a significant amount of time for patients to wake up to RT-CGM alerts and alarms.[30] Parents have even smaller chances of hearing these alerts, since their children do not usually sleep in the same room as them. Some parents use a baby monitor so that they can hear the RT-CGM device should its alarm be triggered during the night.

Medtronic has developed two systems to help with these issues. The first is the Veo® System, a sensor-enabled insulin pump that will turn off the pump's basal rate for two hours if the sensor identifies hypoglycemia (glucose level below the threshold set by the patient or clinician) and the alert is not quickly acknowledged. The Veo System is available in Europe, Australia, and Canada but is currently unavailable in the US. The second system is mySentry®, a remote glucose monitor designed to ease parental concerns of hypoglycemia, especially at night. It was approved for use in the US in early 2012. The mySentry system consists of an

outpost that receives information from the child's sensor and a wirelessly connected (reach of up to 50 feet or more) monitor screen.[8] The outpost can be plugged in the child's bedroom while the monitor sits at the parent's bedside. This remote monitoring system is currently only available for use with the Guardian and Paradigm RT-CGM devices.

Lastly, satisfaction when using RT-CGM should be considered a benefit. Several studies have shown high ratings for overall satisfaction and ease of use of RT-CGM with pump therapy in children aged 3–15 years.[18,31]

Challenges to Using Continuous Glucose Monitoring in Children and Adolescents

Despite the obvious benefits that CGM provides, there are still challenges to using this technology in youth that need to be overcome. Many patients and/or their parents/care-givers are not keen to start using another device to manage their diabetes. Once they eventually start using RT-CGM, in many cases they do not use it consistently.[3,18] Their resistance to start using a CGM device may be due to a lack of knowledge or understanding of the technology, fear of the device, the belief that it is too big, reluctance to wear a second device (in the case of pump users), or the fact that they have spoken to someone who has had a less than favorable experience. These barriers and resistances must be overcome before beginning CGM therapy because, without motivation and dedication, there is a higher chance of discontinuation.

Some studies show insertion site issues—including pain at insertion, discomfort during wear, itching, redness—sensor size, and other concerns that challenge continuous use.[7,18] In children with sensitive skin or who are afraid of needles, these issues must be considered. In children and adolescents, pain may be a problem. While only 7 % of those wearing a sensor in the study by Ramchandani et al. discontinued RT-CGM use due to pain, up to 38 % reported experiencing pain.[18] Companies who develop and manufacture glucose sensors have been working to reduce the size of the needle and the size of the transmitter and to increase the number of approved days for wear, all factors that could influence a younger patient.

Many patients who start using RT-CGM stop shortly thereafter. Looking beyond pain and resistance to adopting the technology in the first place, reasons for discontinuation include intrusion of RT-CGM in patients' lives, problematic equipment, and inaccuracy issues.[18] Some pediatric patients would not even consider using RT-CGM; the most common reason they cite is that they are too busy to give the necessary attention to the sensor.[16] Other patients have reported that RT-CGM was stressful, annoying, and uncomfortable and that it interfered with their lives.[18]

Calibration is another obstacle. The Dexcom SEVEN PLUS sensor can be calibrated at any time. The Medtronic systems recommend calibrating the sensors only during periods of glycemic stability and not during periods of rapid glucose change. In children who are constantly eating and running around, this can be somewhat of a challenge. Additionally, the Medtronic systems require a second calibration six hours after the first, so the timing of sensor start needs to take that into consideration as well.

Lack of insurance coverage can also deter from using RT-CGM. In one study, 19 % of subjects reported insurance coverage problems with RT-CGM.[18] In practice, health insurance companies keep changing their minds about whether or not they should cover glucose sensors. Due to current financial constraints, some health insurance companies who previously covered sensor equipment are no longer paying for it. RT-CGM technology is not cheap; many patients who would potentially benefit from it and are interested in using it cannot financially afford to do so.

Safety

Based on study findings, other than some of the concerns discussed above, there are very few safety issues to take into account when considering the use of RT-CGM in children and adolescents. There are infrequent reports of skin abscess formation or cellulitis; ketoacidosis is a rare occurrence and the risk is comparable with that seen in cohorts not using RT-CGM.[4,11]

Future Directions

In research, CGM technology is a key component of the closed-loop system or artificial pancreas. The subcutaneously inserted sensor electrode measures interstitial glucose concentrations every minute and communicates with software (currently installed on a laptop computer, but soon to be mobile) that takes into account the current glucose level, rate of change, and amount of insulin on board to determine if more insulin needs to be given. If insulin does need to be given, the software sends a signal to an external insulin pump to deliver a bolus. CGM is also used in other research studies as an adjunct to therapy to better monitor the impact of the intervention.

Medtronic and Ford Motor Company have teamed up to develop a system using RT-CGM technology that may be particularly useful for new young drivers or any driver with diabetes. They have used a screen similar to a built-in global positioning system screen on the car's console and have turned it into the CGM device's receiver. The system displays CGM results on the dashboard in realtime. This could also be used to monitor a child in the back seat.[9] There has also been talk about the car not starting if the user's glucose is low, but for now these are just rumors.

The eventual goal is to combine the RT-CGM device with an insulin delivery device; the combined technologies would effectively manage diabetes almost entirely on their own, with very little user interference.

Conclusion

RT-CGM is a beneficial addition to diabetes care in all age groups. A recent stratified analysis of numerous studies showed results favoring CGM over SMBG for improved diabetes care consistently across different age groups and different levels of initial glycemic control. The concurrent meta-analysis of these studies showed a decrease of HbA_{1c} levels from baseline in children and adolescents with the use of CGM.[7] This is an important finding, because the results of the JDRF study in 2010 recommended CGM mainly in the adult population with type 1 diabetes.[3] More robust studies are under way to verify these findings of beneficial results of CGM in children and adolescents with type 1 diabetes.

There is also a high degree of satisfaction among parents whose children use glucose sensors. RT-CGM devices are useful in decreasing HbA_{1c}, decreasing time spent in hypoglycemia, and increasing glucose

information, while at the same time potentially decreasing the number of finger-stick tests and causes for concern. Using the information provided by RT-CGM, patients, parents/care-givers, and providers are able to make educated decisions and adjustments in diabetes management as well as gain confidence in those decisions.

CGM technology has improved over the years and research, including the artificial pancreas, is increasingly using it. Continued improvements are necessary to reduce the lag time between sensor glucose values and actual glucose values, increase sensor accuracy, and overcome the known barriers to CGM use—especially when trying to attract a younger population. With such advances, the consistent use of RT-CGM should increase among patients. Patients, parents/caregivers, and healthcare providers should be aware that benefits of CGM technology have been documented in children and adolescents with diabetes,[6–10] and its use should be encouraged. ■

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