Continuous Glucose Monitoring for Diabetes Management—Current Status and Future Perspectives

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Optimal glycemic control is essential to the management of patients with type 1 diabetes (T1D). This is best achieved by precise and accurate methods of delivering insulin, using multiple daily injection (MDI) and continuous subcutaneous insulin infusion (CSII), as well as monitoring blood glucose, either by self-monitoring of blood glucose (SMBG) and real-time continuous glucose monitoring (rtCGM). The recent COMISAIR study compared four treatment strategies, and concluded that the method of glucose monitoring is more important than the means of insulin delivery in reducing glycated hemoglobin (HbA1c) and hypoglycemia in adults with T1D. The use of rtCGM + MDI represents an equivalent but lower-cost alternative to sensor-augmented insulin pump therapy and is superior to treatment with SMBG + MDI or SMBG + CSII. The Dexcom G6 CGM device is one of the new generation of CGM devices and is designed to work with a range of insulin pumps, glucose meters, or other electronic devices used for diabetes management. This editorial is accompanied by an expert interview in which Kevin Sayer, of Dexcom, (Dexcom, San Diego, CA, USA) describes the unique features of the Dexcom G6 CGM.

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Diabetes, real-time continuous glucose monitoring, management, type 1 diabetes, COMISAIR study

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Despite significant advances in technologies for the management of patients with type 1 diabetes (T1D), outcomes remain suboptimal across all age groups.[1] Achieving glycemic control in patients with T1D requires precise and accurate methods of delivering insulin and monitoring blood glucose. The introduction of insulin analogues, with rapid and prolonged durations of action has allowed for different methods of insulin delivery, either as multiple daily injection (MDI) and continuous subcutaneous insulin infusion (CSII) therapies.[2] The two common glucose monitoring systems are self-monitoring of blood glucose (SMBG) and real-time continuous glucose monitoring (rtCGM). The limitation of SMBG is the potential for missing a spike or fall in blood glucose that occurred between two measurements. By contrast, rtCGM provides data every 5 minutes, allowing patients to respond promptly to changes and prevent hyper- and/or hypoglycemia.[3] One difference between the two methods is that rtCGM measures interstitial fluid (ISF) glucose concentration, while SMBG measures capillary blood glucose concentration. Although the two measurements correlate well, there is a lag of several minutes between ISF and plasma glucose concentration due to the transport between vascular and intracellular compartments.[4]

A 2012 Cochrane review concluded that, while there was limited evidence for the effectiveness of rtCGM in patients with poorly controlled diabetes, rtCGM was associated with improvements in glycemic control in combination with insulin pump therapy i.e., sensor-augmented insulin pump therapy.[5] Moreover, two randomized trials have demonstrated that rtCGM can also be effective in combination with MDI.[6,7] rtCGM technology has advanced, with improvements in accuracy, extended sensor life and lack of requirement for SMBG calibration measurements.[8,9] Therefore, we need clinical studies with the newer generation of CGM devices. Finally, prospective studies simultaneously comparing head-to-head the different combinations of insulin delivery and monitoring systems were lacking. Such a study would help to elucidate whether the observed benefit of sensor-augmented pump use is secondary to the rtCGM technology, the type of insulin delivery, or both.

The COMISAIR study is a clinical trial that compared four treatment strategies for patients with T1D.[10] This 3-year, non-randomized, prospective, real-world, study involved 94 participants with T1D, and investigated rtCGM + MDI (n=22), rtCGM + CSII (n=26), SMBG + MDI (n=21), and SMBG + CSII (n=25). The clinical end points were changes in glycated hemoglobin (HbA1c), time in range (70–180 mg/dL), time below range (<70 mg/dL), and glycemic variability. At the baseline all patients were monitored by professional CGM (iPro™2; Medtronic, Northridge, CA, USA) for 6 days.

Throughout the study, participants in two SMBG groups had professional CGM every 3 months. The CSII group wore one of two types of insulin pumps, the MiniMed™ Paradigm™ Veo™ (Medtronic) or the Animas® Vibe (Animas Corporation, West Chester, PA, USA), while those in the rtCGM-CSII subgroup used either the MiniMed Paradigm Veo System with Enlite sensors (Medtronic) or the Animas Vibe system with DexCom G4 sensors (Dexcom, San Diego, CA, USA). The subgroup of patients with MDIs and rtCGM used a DexCom G4 CGM system comprising a 7-day transcutaneous sensor, a transmitter, and a receiver. The patients were given a personal blood glucose meter (OneTouch® [LifeScan, Milpitas, CA, USA] or CONTOUR™ LINK [Bayer Diabetes Care, Basel, Switzerland]), which was used for diabetes self-management and calibration of CGM. All participants underwent a 4-day training program in the use of their devices, as well as the general principles of T1D management. Baseline characteristics were similar in the three groups.[10]

Recently, 3-year findings of this study have been released.[11] These have shown that there was no significant improvement in HbA1c in the SMBG + MDI group. There was slightly more improvement in the SMBG + CSII group; however, this improvement appeared after 1 year of follow-up and by 3 years there was no significant reduction of HbA1c. Patients with MDI + rtCGM had marked improvements in HbA1c, and the same was true of the final group of patients with CSII and rtCGM. At 3 years, the HbA1c levels in the two rtCGM groups (rtCGM + MDI and rtCGM + CSII) were 7.0%, (p=0.0002) and 6.9% (p<0.0001), respectively, compared with 7.7% (p=0.3574) and 8.0% (p=1.000) in the SMBG+CSII and SMBG+MDI respectively). Time in range was also improved in the rtCGM+MDI and rtCGM + CSII (48.7-69.0%, p<0.0001; and 50.9–72.3%, p<0.0001, respectively), and in the SMBG + CSII group (50.6–57.8%, p=0.0114). Significant reductions in time below range were only observed in the rtCGM subgroups (rtCGM + MDI, 9.4-5.5%, p=0.0387; and rtCGM + CSII, 9.0-5.3%, p=0.0235, respectively). A total of seven severe hypoglycemia episodes were reported: five in the SMBG groups and two in the sensor-augmented insulin regimens groups.[11] All of the CGM groups wore a sensor for more than 70% of the time, which was one of the prerequisites for inclusion in the trial. Compared with some other studies, participants in COMISAIR showed higher adherence to rtCGM, with 93% of patients completing all study visits, and rtCGM users wearing their sensors on average 88% of the time.[12,13] This is an important finding because sufficient sensor use is essential to the optimal outcomes with CGM.[14]

This study clearly shows that improvement in glycemic parameters with CGM is stable throughout 3 years, a very significant finding as this is the longest rtCGM trial to date. The authors concluded that the means of insulin delivery is less important than the way that patients monitor glucose.[11] An important limitation was the fact that this was a non-randomized trial; however, it reflects everyday practice. rtCGM + MDI can be considered an equivalent but lower-cost alternative to sensor-augmented insulin pump therapy and superior to treatment with SMBG + MDI or SMBG + CSII therapy.

These findings suggest that rtCGM should be the gold standard for patients with T1D. There are several barriers to using rtCGM, the most important is reimbursement in many countries. In addition, according to an interview with lead author of the COMISAIR study, Jan Šoupal of Charles University in Prague, Czech Republic, physicians are still not sufficiently skilled in the reading and interpretation of CGM, and unable to catch all typical patterns of rtCGM and address them during treatment.[15] Education and support to address these benefits and barriers may equip physicians with skills to address all the challenges of rtCGM use. ❑

An Expert Interview with Kevin Sayer

CEO, President and Executive Chairman, Dexcom, San Diego, CA, USA

Kevin Sayer

Mr Sayer is the Executive Chairman of the Board of Directors, President and Chief Executive Officer of Dexcom. He joined Dexcom as President and Chief Operating Officer in 2011. From April 2007 to December 2010, Mr Sayer served as Chief Financial Officer of Biosensors International Group, Ltd. ("Biosensors"), a medical technology company developing, manufacturing, and commercializing medical devices used in interventional cardiology and critical care procedures. Previously, Mr Sayer served as Chief Financial Officer of MiniMed, Inc. from 1994 until its acquisition by Medtronic, Inc. in 2001. He also has served as Executive Vice President and Chief Financial Officer of Specialty Laboratories, Inc., and as an independent healthcare and medical technology industry consultant. Mr Sayer received his master's degree in Accounting and Information Systems concurrently with a BA, both from Brigham Young University.

CGMs have become a standard tool for glucose control in patients with T1D.[16] Their use is associated with the reduction of glucose variability in patients undergoing MDI or CSII therapy,[17,18] and also results in less time in hypoglycemia.[18,19] The Dexcom G6 CGM device is the first CGM designed to work with a range of other compatible medical devices and electronic interfaces, such as insulin pumps, glucose meters, or other electronic devices used for diabetes management. Compared with previous models, the G6 eliminates the need for fingerstick calibration, can be worn for up to 10 days, has a thinner transmitter, and an alert that is activated when a glucose value ≤55 mg/dL (<3.1 mmol/L) is predicted within the next 20 minutes. In 2018, the Dexcom G6 received US Food and Drug Administration (FDA) approval for use in adults and children (aged ≥ 2 years) with diabetes. Approval was based on data from two 10-day clinical studies involving adults and children with diabetes.[20,21]

In an expert interview conducted at the 55th Annual Meeting of the European Association for the Study of Diabetes (EASD), which was held on September 16–20, 2019 in Barcelona, Spain, Kevin Sayer discusses the unique features of the Dexcom G6 CGM.

Q. What have recent clinical trial data taught us about the accuracy, utilization, and other benefits of the Dexcom CGM?

Much of the technology involved in the management of diabetes is starting to revolve around CGM. At this year's EASD, we have seen several studies in T1D where the outcome is statistical time in range, in other words, how long a patient's glucose levels are in a healthy range; and this data has to be obtained using CGM. In the COMISAIR study, which involves the intensive management of people with diabetes, the results continue to be strong.[11] Some of the data show that time out of range decreases dramatically with an accurate CGM, which allows intervention if glucose levels are high or low.[11] This technology is allowing people to be healthier, is saving lives, and is delivering data that we can use to evaluate new medical treatments and make better decisions. I think it is going to become the cornerstone of diabetes treatment over the coming years.

Q. What are the advantages of rtCGM?

rtCGM provides the patient with a much steadier stream of data than intermittent CGM. The Dexcom rtCGM system has a share feature which can be particularly useful for pediatric patients. They can sync their device with their phone while they are at school, and then share data with their parents. This allows parents to continually monitor their child's glucose and alert the school if an intervention is needed, sooner than the school nurse would otherwise be aware. This is real-time action and real-time prediction.

rtCGM also allows the patient to set personalized parameters, alerting them when their glucose levels reach the predetermined high or low points. A predictive algorithm gives a warning 20 minutes before the patient reaches one of these marks. This allows a much safer and more meaningful experience then intermittent CGM.'

Q. Could you tell us a little about the Tandem Control IQ-closed loop system?

Tandem Diabetes Care (San Diego, CA, USA) is one of our valued partners at Dexcom. The closed-loop system involves a Tandem pump that will delivers insulin based on readings from the Dexcom G6 sensor. The system will take some decisions out of the patients' hands and they will get automated control and strive for a better outcome without as much interface. We believe that this will provide an improved patient experience.

Q. In an increasingly competitive CGM market, what are the unique features of the Dexcom CGM?

For many years, our primary feature has been performance. Dexcom delivered the first device that could perform to the expectations of patients for managing glucose levels, and for the past several years we have provided meaningful data to patients. Our recent advances with the G6 system, with more convenience around the daily wear and the elimination of fingerstick calibrations because the system is so accurate, has taken our technology to a new level. As we look forward to the future, we will continue to focus on performance, as well as convenience for patients. What is going to become increasingly important over time, is scale. In order to reach millions of patients, capital investment is needed. Dexcom only produces CGMs and we have the resources to scale this business to serve the incredibly large population of people with diabetes.

Q. What do you expect to be the next major development in the Dexcom CGM?

Our next major development will be our next-generation system, the G7, which incorporates many of the features of G6 and more. It will be a fully disposable system and will remain interconnected with an extended wear. Another important future opportunity is our ability to be interoperable, to integrate with a number of devices and, in reality, to meet patients where they are. Patients will be able to get their glucose data where they want it. For example, if they want to use the Tandem pump, our CGM can integrate with it. If a patient wants one of the new Bluetooth-enabled insulin pens that are coming out, we can provide the data to allow the patient to make appropriate decisions. If a patient just wants the data, and to share it with others and manage their diabetes that way, we can provide that as well. CGM technology delivers an HbA1c benefit and health benefit that far exceeds any drug to have hit the marketplace, and this is the beginning of something very important. ❑

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