EDITORIAL

The Future of Glucose Monitoring

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IT WAS NEARLY FOUR DECADES AGO that many of us questioned the usability of the first glucose meter “glucometer.” Usual statements in the literature included who, why, when, etc. As expected, the Association of Clinical Pathologists questioned the accuracy of meters, perhaps due in part to their selfish motive of maintaining pathologists’ business. We saw how over the last four decades that self-monitoring of blood glucose (SMBG) became the standard of care and was used as an important tool in managing diabetes intensively in the Diabetes Control and Complications Trial study.¹ More recently, T1D Exchange data further confirm the importance of SMBG where higher frequency of testing was associated with lower A1c values.²

Similarly, continuous glucose monitors (CGMs) were first evaluated about two decades ago (MiniMed iPro[®] retrospective [Medtronic, Northridge, CA] system), followed by approval of the first real-time prospective relay of glucose data using reverse iontophoresis in the GlucoWatch[®] (then Cygnus, Redfield, CA, now Animas, West Chester, PA) in 1999.^{3,4} Because of the local side effects associated with the use of the GlucoWatch, it was not prescribed or used much in clinical practice, although this concept set the stage for future availability of several CGMs. Several companies (like DexCom, Inc. [San Diego, CA]) were even trying to come up with an implantable sensor that might convey glucose values continuously like CGMs for up to 1 year.⁵ Even though data were supportive of the concept up to 4–6 months, the implantation was a surgical procedure and did result in excessive subcutaneous reaction, which resulted in blunting of the glucose signal.

In the past decade, several models of CGMs have become available: the Medtronic MiniMed Enlite[™] 2 and 3, the Navigator[®] and Flash[®] by Abbott Diabetes Care (Alameda, CA), the DexCom STS[™], G4[®], and G5[®], and the Atos by Roche Diagnostics (Mannheim, Germany) (not yet available).^{6–13} I still remember measurements of mean absolute relative difference (MARD) of >20% in the earlier phases of development of several CGMs.¹² Nowadays, most CGMs boast of single digit MARDs, and some even do not require SMBG calibrations (Abbott’s Flash). Different systems are elegantly reviewed by David Rodbard in this supplement.¹⁴

Jeremy Pettus and Steve Edelman discuss the role of the rate of change of glucose depicted from CGM devices in diabetes

care in this supplement.¹⁵ Gary Scheiner reviews the further role of retrospective data analysis from CGM systems.¹⁶

CGM use in pediatrics has been challenging but most useful as these patients are more vulnerable to hypoglycemia. Lori Laffel discusses at length about issues in pediatrics and improved accuracy of CGMs in this vulnerable population.¹⁷ Similarly, patients with insulin-requiring diabetes are living longer—especially into their seventh, eighth, or ninth decades of their lives.^{18,19} These patients are at high risk of severe hypoglycemia partly due to age, longer duration of diabetes, and associated hypoglycemic unawareness.²⁰ Very little attention has been given to these emerging high-risk patients, and more work needs to be done in this area.

Various agents may interfere with glucose data from the CGM (e.g., acetaminophen, alcohol, vitamin C, etc.). New filters need to be developed so that such commonly used agents do not interfere with the glucose data. Basu et al.²¹ examine ways to overcome this issue in the supplement. Poor uptake of CGM devices so far may in part be due to poor reimbursement and cost as elaborated in this supplement by Lutz Heinemann and Hans DeVries.²² The lack of resources is another reason for poor uptake of CGMs.²³

For the best outcome (just like SMBG), CGM use should be on a continuous basis. However, intermittent use of CGM has been shown to improve glucose control and reduce hypoglycemia,²⁴ in both type 1 and type 2 diabetes patients. Another important hurdle in the use of CGM is the lack of standardization of the download reports, (like EKG). An attempt has been made to standardize reports,^{25,26} but most companies tout that their downloaded report is the best and do not collaborate with each other possibly for financial reasons. Most CGMs now relay data in real-time to Smart phones through a bluetooth. Perhaps in the future the data could be transmitted directly to the Smart phones (regulators might have issues with that)? The use of CGM will likely increase with significant benefits to providers, patients, and payors if a standard report is generated for the users. Is it possible that the Food and Drug Administration (FDA) and other regulatory agencies may mandate this in the future?

I expect some time in the next decade CGM to replace SMBG and be considered as a stand-alone entity. Lastly, improvements in CGM data (accuracy and lower MARD) have allowed scientists and researchers to close the loop—the

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artificial pancreas.^{27,28} Several companies and investigators are taking different approaches to a bionic pancreas (artificial pancreas).²⁹ The first version is already approved in the United States (Minimed 530G with threshold suspend), where insulin delivery is stopped for up to 2 h, indirectly allowing CGM data to act without confirming the glucose data by SMBG. In Western Europe and many other parts of the world the Minimed 640G is available where threshold suspend goes one step further: predictive algorithms stop insulin delivery via the pump 30 min before the anticipated hypoglycemic threshold. Several studies are ongoing to assess the safety and efficacy of hybrid closed-loop (Minimed 670G) and other systems for use at home. I am hopeful that some version of closed loop (single or dual hormone approach) will be available in the United States in the next 2 years. Jort Kropff and Hans DeVries also highlight future products and updates in this supplement.³⁰

I sincerely want to thank all of the contributors to this supplement and compliment them for their hard work and submitting their manuscripts on time to be made available at this ATTD 2016 meeting in Milan, Italy. I hope our readers will find this supplement helpful and allow them to offer new technologies to the patients they serve.

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