COMMENTARY

Is It Safe to Use “On-Demand” Continuous Glucose Monitoring During Pregnancy?

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PREGNANCIES COMPLICATED BY DIABETES are associated with numerous adverse maternal and fetal outcomes when glucose levels are not optimally controlled.^{1–3} Although the glycated hemoglobin A1C (A1C) level, point-of-care premeal blood glucose level, and point-of-care postmeal blood glucose level are used to define target goals during pregnancy,⁴ a body of evidence is emerging to suggest other indices of glucose control as targets.⁵ Some alternative indices are time spent in the time in range (TIR), hypoglycemic range, hyperglycemic range, and the coefficient of variation.⁵ Thus, continuous glucose monitoring (CGM) would be required to evaluate these other measures of glycemic control.

Previous studies evaluating CGM usage during pregnancy used devices that require patient calibrations, could be blinded or unblinded (real-time), and could be used with any type of diabetes treatment (diet-controlled, noninsulin hypoglycemic agents, insulin).⁶ Safety and efficacy of CGM usage during pregnancy have been shown in multiple studies.^{6–8} However, in earlier studies, the ultimate effect on maternal and fetal outcomes was suggestive of improvements with CGM usage, but not conclusive.^{9–11} The CONCEPT study was the first large-scale, multicenter, randomized controlled trial of CGM use compared with self-monitoring of blood glucose (SMBG) throughout pregnancies associated with T1D.¹² It found that A1C was only slightly reduced in the CGM group, but TIR was significantly increased. Rates of adverse fetal outcomes were lower with CGM usage than with SMBG alone, despite the very similar A1C results between groups. This gives further evidence that glycemic variability during and between days may have a large impact on health outcomes. However, one cannot decipher which elements of the CGM system most lend themselves to these improved outcomes, such as frequency of sensor glucose readings, real-time alerts/alarms for hypo- and hyperglycemia, and identification of sensor glucose trends.

In this issue of *DTT*, Scott et al. conducted a study in 13 UK and Austrian sites wherein blinded Flash glucose monitoring was worn by pregnant women with gestational diabetes mellitus (GDM), T1D, and T2D for up to 14 days.¹³ Sensor glucose results were compared with SMBG values. In addition,

a questionnaire assessing user acceptability of the Flash Libre device was administered. Of the 74 women evaluated, most had GDM ($n=39$, 52.7%). The ConEG analyses and overall mean absolute relative difference (MARD) were acceptable. Type of diabetes, treatment modality, age of gestation, and body mass index did not appear to significantly affect these parameters. The most impressive factors on the user acceptability questionnaire were the levels of agreement for the sensor being comfortable (97.3%), less stressful (98.4%), and less painful (100%) than a finger prick, and the ease of use (100%). All together, the authors showed that Flash glucose monitoring appears safe, reasonably accurate, and comfortable for pregnant women.

At present, there is inconsistency between guidelines for CGM use during pregnancy. Guidelines in the United Kingdom recommend that one considers CGM therapy for women using insulin during pregnancy who have severe hypoglycemia, “unstable blood glucose levels,” or to obtain a picture of glycemic variability.¹⁴ The medical associations in the United States have no specific recommendation about CGM use during pregnancy,⁴ recommend CGM use for patients with T1D (without specific mention during pregnancy),¹⁵ or state that CGM may be used as an educational or management tool in GDM.¹⁵ Thus, the role of such devices in general, and of the Flash system in particular, has yet to be standardized throughout gestation. It is, therefore, beneficial when studies like Scott’s are conducted, to provide evidence for guidelines committees to consider.

There are still some questions remaining when it comes to Flash glucose monitoring during pregnancy. This study did not evaluate women in the first trimester, when they are most prone to hypoglycemia, particularly severe hypoglycemia, requiring the assistance of a third party.^{16–18} Flash glucose monitoring has been shown to have more variability with hypoglycemia than real-time CGM in nonpregnant populations.¹⁹ In addition, real-time CGM performed better to reduce hypoglycemia in adults with T1D and impaired hypoglycemia awareness than Flash glucose monitoring in one randomized, open-label trial.²⁰ Thus, this device should be evaluated during early gestation when the risk of hypoglycemia is highest. Women with T1D experience the most glucose variability,^{21,22} but only about a third of the women

in this study had T1D ($n=24$, 32.4%), so the sample size was relatively small. It would be helpful to assess the performance of this device in a larger group of women with T1D and for longer duration.

This study did not allow women to view the glucose data until the final study visit. Hence, when used in an unblinded manner, it is still unclear whether the Flash monitoring would be comparable, better, or worse than SMBG alone or real-time CGM use throughout gestation. Some of the barriers to device use²³ would still exist for patients considering Flash glucose monitoring, although it has high user acceptability. Would the user acceptability be enough to overcome barriers when compared with SMBG testing alone? Flash glucose monitoring records sensor glucose readings every 15 min, which is less than the 5 min intervals with other CGM systems, and it does not provide alerts/alarms in real-time. Is the frequent access to data (scanning or receiver viewing to find out one's current sensor glucose) enough to reduce severe hypoglycemic events or is the real-time alarm more important during pregnancy?

Finally, although the recommendations for CGM use during pregnancy are variable, mention of the “on-demand” system during gestation is still absent. Scott et al.,¹³ like others,^{21,22,24} find that having glucose levels outside the target ranges occurs very frequently, irrespective of the type of diabetes a woman has or the mode of treatment (glucose <70 mg/dL: 2.42–3.43 h/day and glucose >140 mg/dL: 1.26–9 h/day). The frequency and duration of these episodes are much more difficult to capture with SMBG testing than with “on-demand” or CGM. Thus, CGM and CGM-like systems could, at the very least, assist patients and providers to identify glucose patterns throughout pregnancy. More studies are needed to determine whether the maternal outcomes, fetal outcomes, and cost-benefit analyses support the use of these systems during gestation and whether there are differences in these measures between the real-time and intermittent glucose monitoring systems.

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