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Counterpoint: Glucose Monitoring in Gestational Diabetes

Lots of heat, not much light

It was once fashionable for theological scholars to debate the number of angels that could dance on the head of a pin. The debates were quite heated, narrowly focused, and unencumbered by facts. They made for great controversy but solved no real problems (lots of heat, no light). In many respects, ongoing debates about the nuances of glucose monitoring for patients with gestational diabetes mellitus (GDM) are analogous to those past debates about dancing angels. The debates are heated, they are focused on very small nuances in the management of GDM that have minor if any impact on the outcomes of pregnancies complicated by GDM, and they are generally unencumbered by hard facts. While generating considerable heat, the debates shed very little real light on optimization of perinatal outcomes in pregnancies complicated by GDM. In this counterpoint, we briefly summarize the major limitations of such a narrow focus on the nuances of glucose monitoring and control in the antepartum management of GDM. We will address the topic at two levels: *1*) whether there really are optimal times to measure glucose levels in women with GDM, and *2*) whether all patients really need to perform glucose self-monitoring.

Among clinicians and investigators working in the field of GDM, the debate rages on whether pregnant patients should measure their glucose levels before or after meals and, if after, how long after eating. Ammunition in favor of one timing or another comes largely from analyses of correlations between maternal glucose levels and fetal outcomes, such as rates of macrosomic (>4,000 g at birth) or large-for-gestational-age (LGA) infants. The results have been quite inconsistent. Fasting glucose was most strongly correlated with outcomes in some studies and 1- or 2-h postprandial glucose levels in others. These varied results are not hard to understand. Preprandial and postprandial glucose concentrations are generally quite well correlated. In a given study, glucose concentrations at one time point or another may be the better predictor of perinatal outcomes, but the differences in predictive value are usually small. Treatments to lower glucose levels at one time point also lower glucose levels at other times as well. Selection of the best timing for glucose measurements should take into account not only potential efficacy but also convenience, which is so important for patient compliance and satisfaction. Why make patients monitor glucose levels at inconvenient times if the same perinatal outcome can be obtained by monitoring at more convenient times? So, the question becomes one of comparing perinatal outcomes between different glucose monitoring regimens. To our knowledge, only one randomized trial (1) has addressed this issue. That study used one relatively high glucose target for a preprandial monitoring group and one relatively low target for a postprandial monitoring group. The mean fasting glucose concentrations at study entry were in the range of overt diabetes (~140 mg/dl), much higher than fasting glucose levels in most women with GDM. By setting different degrees of control as targets in the two treatment groups, the researchers achieved a much greater reduction in HbA_{1c} (−3 vs. −0.6%) and better perinatal outcomes in the postprandial monitoring group. However, a 3% reduction in HbA_{1c} cannot be achieved when glycemia starts in the range that is common for GDM (at least not without a large amount of maternal hypoglycemia). Moreover, the perinatal outcomes would very likely have been better in the preprandial monitoring group if a relatively low glucose target had been set for them and a relatively high target had been set for the postprandial group. Indeed, our group eliminated the excess of LGA infants in women with mild GDM using a treatment program that focused on aggressive preprandial glucose targets (see below) (2). The bottom line: it is not only the timing of glucose monitoring that matters, but also the glycemic targets that are set. To our knowledge, there are no studies that have tested the general concept of preprandial versus postprandial glucose monitoring to achieve the lowest possible overall glycemia. The same deficiency of information holds for 1- vs. 2-h postprandial monitoring. In our clinical care and clinical research experience, aggressive glycemic targets can be used to reduce perinatal complications regardless of the timing of the glucose measurements. Thus, convenient and aggressive targets should be applied at convenient times for the patient.

The second level of debate is whether glucose self-monitoring is required at all in most women with GDM. Only a minority of women with GDM are at risk for a perinatal complication. More importantly, perinatal risks increase very slowly and quite continuously with increasing maternal glucose levels, regardless of the timing of glucose measurements. There is no threshold of glucose below which risks are low and above which risks increase rapidly. Clinical glycemic targets can be no more than arbitrary cut-points across a shallow continuum of risk to the fetus. Elimination of all excess risk using glucose levels alone requires treatment of many individuals at no risk whatsoever. Our group (2,3) has shown that relatively simple fetal measurements made by ultrasound can identify pregnancies in which growth-related morbidities are minimal in the absence of maternal glucose self-monitoring and insulin treatment. The approach worked best with women whose fasting glucose concentrations, measured every 1–2 weeks in the clinic, remained <105 mg/dl on diet therapy. This approach allows the majority of women with GDM to be managed with very accurate laboratory fasting glucose measurements at 1- to 2-week intervals. Women whose fasting glucose levels

monitored in this way exceed 105 mg/dl despite diet therapy have sufficient risk to warrant additional treatment, usually with insulin. Women with lower fasting glucose levels can be managed on diet therapy and without glucose self-monitoring up to ~30 weeks of gestation. If the fetal abdominal circumference (AC) is <70th percentile at that time, perinatal outcomes will be excellent with continued management on diet therapy and without glucose self-monitoring. The excess risk of macrosomia is limited to women with a fetal AC ≥70th percentile at 30 weeks. Those pregnancies will benefit from aggressive glucose lowering in the mother. It is in this setting that we used preprandial glucose targets of 60–80 mg/dl to eliminate the excess risk of LGA infants (2). Unlike approaches that rely solely on frequent (and often inaccurate) measures of each patient's glucose levels, the ultrasound guided approach takes into account the variety of maternal, placental, and fetal factors that can affect fetal growth in pregnancies complicated by GDM.

Maternal glucose levels in GDM are and forever will be relatively poor predictors of fetal development and, thus, of perinatal and long-term outcomes for the infant. Continued debates about the fine nuances of timing and levels of glycemia that are best for the management of GDM will be productive only in the setting of very well designed and randomized trials. These trials should test not individual time-target pairs, but the general concept of timing and targets that can best achieve the lowest possible glucose levels that are safe for the mother and beneficial for the infant. Even in this setting, a focus on maternal glycemia alone will leave us arguing about dancing angels, while nonglucose factors continue to influence fetal growth, development, and outcomes. Real light will be shed on the antepartum management of GDM only when the focus moves to development of *1*) a better definition of the phenotype of infants adversely affected by maternal GDM and *2*) better methods to detect that phenotype as it develops in utero, so that the most intensive therapies can be directed at the affected fetuses in time to minimize the perinatal and long-term consequences of GDM.

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