COMMENT ON LAW ET AL.

Suboptimal Nocturnal Glucose Control Is Associated With Large for Gestational Age in Treated Gestational Diabetes Mellitus. Diabetes Care 2019;42:810–815

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We were interested in the article by Law et al. (1), who reported that high nocturnal glucose, as recorded by continuous glucose monitoring (CGM), was associated with large for gestational age (LGA) newborns in women with gestational diabetes mellitus (GDM). The nocturnal hyperglycemia was not detected by fasting self-monitored blood glucose (SMBG), which argues for performing CGM in GDM.

The figure in the article nicely depicts how nocturnal hyperglycemia was missed by conventional SMBG: as underlined by the authors, the difference in nocturnal CGM glucose between mothers of LGA infants and those of normal-weight newborns was a peak displayed at 0200–0300 h, which then progressively declined to become nonsignificant when the women woke up. This 0200–0300 h glucose peak seems to be an important finding. For patients with type 1 or type 2 diabetes, CGM usually detects numerous hypoglycemias during this time interval (2), but this pattern may change at the end of pregnancy, when insulin resistance progresses. Accordingly, in a previous study that included pregnant women with type 1 or type 2 diabetes, Law et al. (3) reported declining nocturnal CGM glucose (nadir at 0400 h) in the first trimester of pregnancy and peaking nocturnal glucose in the second and third trimesters. They hypothesized that nocturnal hyperglycemia may result from diet, sedentary behavior, difficulty sleeping, or increased endogenous glucose production.

Whatever the mechanism, a nocturnal hyperglycemia peak in mothers of LGA infants has implications for the choice of second-line therapies. When SMBG targets were not reached by their patients through dietary and lifestyle advice, Law et al. (1) used metformin, which may help to reduce nocturnal endogenous glucose production, and/or insulin, but they did not report which long-acting insulins were injected in the evening.

Euglycemic clamp studies have shown that NPH insulin, in contrast to insulin glargine, has an action peak 4 h after injection (4), which may help to reduce the 0200–0300 h glucose as reported by CGM data in type 2 diabetes (5) and to reduce the risk of hypoglycemia later, when CGM glucose declined in mothers of LGA infants. To our knowledge, there is no concern about the safety of using glargine in women with GDM, but the peaking nocturnal glucose profiles as reported by Law et al. (1) argue for the injection of insulin NPH in the late evening if the aim is to correct the nocturnal hyperglycemia that may drive fetal growth acceleration.

The women who participated in the study by Law et al. (1) had a diagnosis of GDM at ~26 weeks' gestation, and the CGM was performed at 30–32 weeks' gestation. We can speculate that some of them were then still on first-line therapy and had to start second-line therapy based on SMBG results after their CGM glucose had been recorded. If women who later started evening insulin NPH or metformin had nocturnal high CGM glucose, this would argue for the use of these recommended therapies to correct the nocturnal high glucose. If not, this would argue for performing CGM before introducing an appropriate second-line treatment to better address nocturnal glucose control.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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