Obesity and no-call results: optimal timing of cell-free DNA testing and redraw

We thank the authors for their comments. Although cell-free DNA (cfDNA) testing has the highest detection rate among aneuploidy screening modalities, we agree that the reportedly high screening failure rates in women with obesity affects its use in this population. We also agree that the optimal aneuploidy screening option depends on the patient and her preferences.

Our study sought to determine the screening failure rate in women with obesity cases with an initial screen failure and to assess the increase in the fetal cfDNA fraction over time in the most obese women. We concluded that more than 80% of women weighing >400 lb received results between 9 and 12 weeks’ gestation and that approximately 94% of women weighing >400 lb received results between 13 and 18 weeks’ gestation. The no-call result rate owing to low fetal fraction is lower than previously reported, indicating that cfDNA screening is appropriate in women who desire aneuploidy screening with the highest detection rate and lower false-positive rates.

The authors’ screening algorithm does not address the limitations of other forms of aneuploidy screening in women with obesity. In particular, there may be a higher rate of unobtainable nuchal translucency and greater scanning time required for women with obesity.1,2 Studies have shown that targeted and standard sonography have higher failure rates and lower detection rates for soft aneuploidy markers in women with obesity.3,4 In addition, the higher false-positive rate in screening with ultrasound or serum analyte screening may lead to increased invasive testing, which can be technically more challenging in the most obese women. Therefore, we believe that cfDNA screening offers a viable aneuploidy screening option for patients with obesity with the appropriate pretest counseling.

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Gestational diabetes, metformin, and the risk of hypoglycemia

TO THE EDITORS: Picón-César et al1 published a study aimed at determining if metformin could reach the same glycemic control and other outcomes as insulin in patients with gestational diabetes not properly controlled with lifestyle changes. The authors concluded that metformin treatment was associated with a better postprandial glycemic control than insulin for some meals, a low risk for hypoglycemic episodes, less maternal weight gain, and a low rate of failure.

TO THE EDITORS: Picón-César et al1 published a study aimed at determining if metformin could reach the same glycemic control and other outcomes as insulin in patients with gestational diabetes not properly controlled with lifestyle changes. The authors concluded that metformin treatment was associated with a better postprandial glycemic control than insulin for some meals, a low risk for hypoglycemic episodes, less maternal weight gain, and a low rate of failure.
as isolated treatment. Most obstetrical and perinatal results were similar between groups.

The study team collected and analyzed a large amount of data, leading to an interesting and important debate, and we do not have any critical remarks about the study. Nevertheless, we would like to ask 2 questions related to hypoglycemia in the metformin study group. Hypoglycemic episodes were far more common in the insulin group; however, some episodes with relatively low glycemic levels (<54 mg/dL) also occurred in the metformin group (55.9% with insulin vs 17.7% with metformin treatment; odds ratio, 6.118; 95% confidence interval, 3.134–11.944; P = 0.000).

Metformin, as a drug targeting mainly insulin resistance, is considered to have a very low risk of hypoglycemia in patients with type 2 diabetes with a risk ratio for nonsevere hypoglycemia in a model-based meta-analysis of ~2 when compared with placebo. A relatively recent “real-world” study among patients with type 2 diabetes showed a >5-fold increased risk for hypoglycemia in patients treated with insulin compared with those treated with metformin, with the incidence of hypoglycemia being 4.39 per person-year for insulin and 0.76 per person-year for metformin.

Unfortunately, the patient-level factors, such as reduced dietary intake, increased physical activity, or alcohol consumption, which may contribute to the metformin-related hypoglycemia risk, are unknown because these factors are not usually recorded during the studies.

Because the study of Picón-César et al was conducted with great care, we would like to ask if detailed information about the circumstances during hypoglycemic episodes in the metformin group are available and primarily if the risk of hypoglycemia associated with the metformin dose. Such knowledge would enhance the understanding of the mechanism of metformin-related hypoglycemia and contribute to diminishing its risk.

Our second question is related to the mean duration of the treatment in the study because it was not clearly stated in the paper. This information would further enhance the study impact and enable the calculation of per person-year frequency of hypoglycemia and a comparison with such a number in patients with type 2 diabetes.

With great respect, we suggest considering these comments if study continuation is planned.

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Gestational diabetes, metformin, and risk of hypoglycemia

We appreciate the comments of Drs Jan Brož and Klára Brožová regarding our recent publication “Metformin versus insulin in gestational diabetes: glycemic control, and obstetrical and perinatal outcomes. Randomized prospective trial.”

Unfortunately, we did not record the exact circumstances in which the hypoglycemic episodes occurred, but, in both treatment groups, most hypoglycemic episodes happened in the period between breakfast and prelunch (Table 2 in the original article). By ruling out alcohol consumption and not having evaluated the factual carbohydrate intake (neither a possible concurrent emesis), we think that greater physical activity during these hours is the reason for this higher rate of hypoglycemia.

As you suggested, we have studied the possible relationship between the hypoglycemic episodes and the dose of metformin. At the prepartum visit (maximum metformin dose), patients who experienced any hypoglycemic episode had a mean metformin dose of 1540 ± 316 mg/d compared with 1421 ± 543 mg/d among women who did not experience hypoglycemia (P = 0.359). In the metformin-only group, 6 women