

Viewpoint on Diabetes

Oral Therapy for Gestational Diabetes



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During pregnancy, a variety of important changes occur in a woman's body that allow it to accommodate and nurture a developing fetus. Among these changes are alterations in how sugar is handled; early in pregnancy fasting sugar levels fall, while postprandial (after a meal) levels rise. By the end of the second trimester, most women experience a 50% reduction in the body's ability to respond to insulin, equal to what many people with type 2 diabetes experience. The vast majority of pregnant women, however, do not become diabetic, because their pancreatic beta cells are able to make more insulin than usual to keep up with increased demand. There are some women, however, who are unable to make sufficient insulin in the face of pregnancy-induced insulin resistance. These women develop high blood sugar, and are said to have "gestational diabetes". The good news for these women is that their blood sugar values will almost always fall back to normal after delivery. There are two bits of bad news, however. For one, these women are at increased risk of developing type 2 diabetes later in their lives. Of more immediate concern, however, is the fact that their babies are more likely to suffer certain adverse consequences than the babies of non-diabetic mothers. These complications are usually related to the fact that the infants of women with diabetes (gestational or otherwise) are usually larger than expected, which interferes with normal labor and delivery and can even lead to stillbirth.

The mainstay of therapy for women with gestational diabetes is dietary—by reducing caloric intake, blood glucose levels can usually be maintained in the normal range. It is critical that enough calories be consumed to support a growing fetus, however, and some women are unable to sufficiently reduce the amount of food they eat to maintain normal sugar levels. For these women, the standard therapy is insulin injections. Insulin works well, and because it is a natural hormone, there are few concerns about possible adverse effects on the fetus. Insulin injections can be difficult for some people, however, and this strategy greatly increases the cost and complexity of prenatal care.

Physicians have traditionally avoided giving oral antidiabetic medications during pregnancy for two reasons. First, the sulfonylurea drugs (until recently the only oral option in the United States) were shown to cross the placenta into the fetal circulation, where they increase fetal insulin levels in much the same way that they do in adults with type 2 diabetes. These elevated insulin levels lead to a greater chance of having a very large infant, with the attendant risks already mentioned. The second reason why oral agents have not been used in pregnancy is that they have been linked to birth defects, although to be fair, high blood sugar by itself can cause birth defects, which complicates the analysis of such studies.

Given this background, it was both surprising and exciting to read a study performed in Texas and published in the **October 19th edition of The New England Journal of Medicine**. In this study, 400 women with gestational diabetes were given either the usual therapy with insulin, or an oral sulfonylurea drug (glyburide, also called Micronase or Glynase). There were several important findings. First of all, the glyburide worked quite well. Only eight women (4%) receiving the drug couldn't maintain normal blood sugar levels, forcing them to switch to insulin. Secondly, no increase was seen in the rate of fetal complications with the oral drug. There was no increased risk of birth defects, no increase in the size of the fetus, and elevations in fetal insulin levels were not seen. In fact, the drug could not be detected at all in the circulation of the infants, despite being present at expected levels in the mother's serum. This represents a discrepancy from earlier data which showed that sulfonylureas can cross the placenta. The discrepancy is likely resolved by the fact that glyburide is a newer drug than the ones previously tested, with different chemical properties.

So, should women with gestational diabetes be treated from now on with oral agents such as glyburide instead of insulin? Certainly, there are caveats about this approach. For one, drugs other than glyburide were not tested, so that the use of other sulfonylureas, metformin (Glucophage), and thiazolidinediones (Avandia, Actos) can not be recommended during pregnancy. In contrast to glyburide, some of these drugs have in fact been shown to cross the placenta—their effects on the fetus are not well documented. Secondly, all the women in this study were given glyburide after the 11th week of gestation, when most organ formation has been completed. It would not be prudent, then, for women who already have type 2 diabetes before becoming pregnant to stay on their oral drugs during the first trimester. The majority of women with gestational diabetes, however, present in the second trimester. For these women, glyburide therapy would greatly simplify their prenatal care. When a finding as important as this is reported, it is certain that other studies will be rapidly performed to confirm the results. If these follow-up studies are in concordance with the original observations, then it is likely that glyburide therapy will become very common indeed in gestational diabetes.

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