

Diabetes, Insulin and Pregnancy

a report by

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High glucose levels during pregnancy increase the chance that a baby will be born with birth defects. High glucose levels have the most significant effect early in pregnancy, possibly before a woman knows she is pregnant. Therefore, if a woman with diabetes discovers she is pregnant, it is a medical emergency. Lowering her blood sugar is an immediate priority.

The situation is similar if a woman develops diabetes during her pregnancy (gestational diabetes). Although the risk of birth defects is decreased, there can be other complications such as stillbirth. There is also a higher chance of pre-eclampsia, pre-term delivery, and excess amniotic fluid around the baby. Mothers with diabetes, if in poor glycemic control, are also more likely to have large babies, some weighing more than 10lb.

When type 2 diabetic women become pregnant they are at a higher risk than type 1 diabetic women for complications. This observation is most likely due to the fact that the majority of type 2 diabetic women present for the first time during pregnancy, and thus during the time they are pregnant before care is initiated the fetus suffers from the severe untreated hyperglycemia. At least type 1 diabetic women receive some care in the non-pregnant state. Clues that a woman has undiagnosed type 2 diabetes include an elevated blood pressure, elevated body mass index (BMI), evidence of acanthosis nigricans, and an elevated glycosylated hemoglobin at the time of diagnosis.

Criteria vary from country to country on when to start therapy to normalize glucose levels. Ideally, anything above normal requires treatment in the diabetic pregnant woman.

The most powerful agent to control glucose is insulin, and with the recent recombinant DNA technology the development of insulin analogs has greatly improved the likelihood that patients will live longer and have a greater quality of life. Animal, human or synthetic insulin have been used for glucose control during pregnancy, although no insulin is specifically approved for use in pregnancy.

A pregnant woman with diabetes who may have been controlling her blood sugar with oral medication may be advised to switch to insulin as this is thought to better control glucose levels.

Rapid-acting insulin analogs are valuable because they best mimic normal physiological response to a meal. The first analog to become commercially available was insulin lispro, which is similar to normal insulin except for the switching of amino acids at positions B28 and B29 (lysine and proline). Insulin aspart was the second analog developed and has a single amino acid substitution at position B28, proline changed to aspartic acid. Both analogs have a maximum effect within 30 to 60 minutes, and in several trials they have been shown to control postprandial glucose better than regular human insulin.

The medical rationale for using a long-acting insulin analog is to mimic better the basal physiological insulin profile of normal individuals. A popular long-acting analog is glargine, with once-daily dosing providing a smooth, peakless action profile, which lowers risk of nocturnal hypoglycemic events, has better glycemic control, and has a safety profile similar to regular insulin. Another long-acting analog is detemir, which binds to serum albumin to prolong its circulation in the body for an extended duration of action.

The best glycemic control is obtained with the use of a rapid-acting insulin analog that optimises postprandial glycemic control in combination with a long-acting insulin analog that provides consistent basal insulin. However, there is no data on the use of long-acting insulin analogs during pregnancy and, although they are likely safe and effective, until clinical trial data becomes available they should be used cautiously.

Observations in diabetic and non-diabetic pregnant women may help lead to an understanding of diabetes and the path to treatment. The hormones of human pregnancy are instrumental in protecting the

fetal/placental unit from rejection. A phenomenon of apparent pancreatic rejuvenation has been observed during pregnancy in some type 1 diabetic women. These women show a rise in their C-peptide level and a drop in their insulin requirement. The C-peptide rise was in parallel with a rise in their pregnancy-related growth factors, specifically prolactin and human placental lactogen, and

diabetes. Replacement of this naturally-occurring hormone in people with type 2 diabetes appears to improve glucose tolerance and insulin production, reduce glucagons secretion and gastric emptying and suppress the appetite in many patients. Investigations are on-going as to whether women with gestational diabetes have reduced levels of GLP-1 during their pregnancy compared with after they deliver their

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pregnancy related immunosuppressive hormones, specifically cortisol and progesterone.

Glucagon-like peptide-1 (GLP-1) has received considerable attention as a treatment for type 2

baby, and also compared to non-diabetic pregnant women. If it can be shown that gestational diabetes is associated with a defect in GLP-1 production, the next step would be to propose treatment with GLP-1 during pregnancy. ■

Further Reading – Recent Articles of Interest by Lois Jovanovic

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