Diabetes Management and Exercise in Pregnant Patients With Diabetes

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Approximately 4% of pregnant women in the United States have diabetes. Eighty-eight percent of these women have gestational diabetes mellitus (GDM; 450,000 women per year), and the remaining 12% have either type 1 (12,000) or type 2 diabetes (50,000).[1]

Pregnancy is a diabetogenic condition characterized by insulin resistance with a compensatory increase in β-cell response and hyperinsulinemia.[2] The placental secretion of hormones (progesterone, cortisol, placental lactogen, prolactin, and growth hormone) is a major contributor to the insulin resistance, which likely plays a role in ensuring that the fetus has an adequate supply of glucose.[3]

Pregnancy in patients with diabetes is associated with an increased incidence of congenital anomalies for the fetus and spontaneous abortions in women with poor glycemic control. For both type 1 and type 2 diabetes, hemoglobin A_{1c} (A1C) values early in pregnancy are correlated with rates of spontaneous abortion and major congenital malformations.[4,5] The effect of the increased glucose levels on the rate of spontaneous abortion occurs at the time of conception. Normalizing blood glucose concentrations before and early in pregnancy can reduce these risks to levels of the general population.[6]

Treatment with close monitoring of glucose levels, oral agents (metformin and sulfonylureas), medical nutrition therapy, and insulin therapy if glucose levels are above goal may reduce maternal and fetal complications.

Monitoring Glucose Levels

Glucose is a potential for being a co-teratogen or teratogen surrogate because there is a correlation between A1C levels early in pregnancy and the predictive malformation risk for the fetus. However, there is a lack of a strong correlation between A1C and glucose levels by continuous glucose monitoring. This may indicate that plasma blood glucose levels vary significantly day by day, and A1C cannot adequately describe daily glucose profiles over an 8- to 10-week period.[7]

Self-monitoring of blood glucose is mandatory during pregnancy, especially for patients with type 1 diabetes. Poor glycemic control leads to increased maternal-fetal transfer of glucose and amino acids as well as fetal hyperinsulinemia. These metabolic changes contribute to the development of macrosomia and can lead to difficult delivery, an increased rate of cesarean section, and an increase in fetal morbidity. However, preventing hypoglycemia is just as important. An elevated first morning blood glucose value may reflect an episode of hypoglycemia during the early morning hours because pregnancy is associated with an exaggerated rebound from hypoglycemia. Performing glucose checks at bedtime, 3 a.m., and in the morning can assist in the discovery of nocturnal hypoglycemia.

The goal of self-monitoring is to detect glucose levels elevated to concentrations that increase perinatal mortality.[2] Blood glucose goals in pregnant patients with diabetes vary in the medical literature. The Fourth International Workshop-Conference on Gestational Diabetes Mellitus recommends maintaining capillary blood glucose values of preprandial glucose < 95 mg/dl, 1-hour postprandial glucose < 140 mg/dl, and 2-hour postprandial glucose < 120 mg/dl.[2,8] The American College of Obstetricians and Gynecologists (ACOG) guidelines are the same except that the 1-hour postprandial glucose value is considered acceptable at either 130 or 140 mg/dl.[8,9] Jovanovic-Peterson et al.[10] suggest guidelines that are a little stricter: fasting glucose < 90 mg/dl and 1-hour postprandial glucose < 120 mg/dl.[2,10] The authors believe that the tighter glucose control recommended by Jovanovic-Peterson et al. will become the more acceptable guideline in the future.

The 3-hour, 100-g glucose tolerance test is used to diagnose GDM. GDM is diagnosed if two or more plasma glucose

IN BRIEF

Pregnancy in patients with diabetes is associated with an increased incidence of congenital anomalies for fetuses and spontaneous abortions in women with poor glycemic control. Normalizing blood glucose concentrations before and early in pregnancy can reduce these risks to levels of the general population. To improve outcomes, pregnant women with type 2 diabetes should plan their pregnancies, maintain good metabolic control of their diabetes, exercise, and take folate daily.

levels meet or exceed the following thresholds: fasting glucose of 95 mg/dl, 1-hour glucose of 180 mg/dl, 2-hour glucose of 155 mg/dl, or 3-hour glucose of 140 mg/dl.[11]

Fetal complications of GDM include macrosomia, neonatal hypoglycemia, perinatal mortality, congenital malformation, hyperbilirubinemia, polycythemia, hypocalcemia, and respiratory distress syndrome.[11] Maternal complications associated with GDM include hypertension, preeclampsia, and an increased risk of cesarean delivery.[12]

Postprandial glucose also has a most important role in macrosomia. Simpson and Kast[13] suggest that maternal and neonatal outcomes in women with GDM are comparable to those in women without GDM when 2-hour postprandial glucose levels are maintained up to 144 mg/dl.

Oral Agents

When diet and exercise do not maintain glucose levels within goal, several studies have supported the use of sulfonylureas and biguanides. Recent studies have demonstrated the safety of glyburide use in pregnancy.[14] It has been used off-label after the first trimester. In addition, metformin is also being used off-label throughout pregnancy, especially if the agent was used to promote pregnancy.

Medical Nutrition Therapy

Medical nutrition therapy includes not only the total daily caloric intake and its carbohydrate content, but also the number of meals throughout the day. Generally, there is not an increased energy requirement during the first trimester, and a normal-weight woman will need an additional 300 kcal/day in the second and third trimesters.[1,15] Normal-weight women with GDM need a daily caloric intake of 30 kcal · kg^{-1} · day^{-1} based on their present pregnant weight.[2,16] The composition of the diet should be 40% carbohydrate, 40% fat, and 20% protein divided among three meals and three snacks.[16]

In addition, folate (400 μg) should be prescribed to all pregnant patients early in the first trimester to decrease the incidence of neural tube defects. Ideally, folate should be given in the preconception phase. Women with a previously affected infant with a neural tube defect and those taking anticonvulsant medications need folate 4 mg/day.

Obese women and women with type 2 diabetes are characterized by insulin resistance that is aggravated during pregnancy. Insulin resistance has been associated with pregnancy complications.[17] Maternal overweight and obesity in normoglycemic women is associated with an increased rate of complications (stillbirth, operative delivery, hypertensive complications, and congenital malformations).[17,18] For obese women (BMI > 30 kg/m^2), a 30–33% calorie restriction (to ~ 25 kcal · kg actual $weight^{-1}$ · day^{-1}) has been shown to reduce hyperglycemia and plasma triglycerides with no increase in ketonuria.[15] Restriction of carbohydrate to 35–40% of calories has been shown to decrease maternal glucose levels and improve maternal and fetal outcomes.[19]

Insulin Therapy

Insulin requirements vary during pregnancy. There is an increase in requirement during weeks 3–7, a decreased need during weeks 7–15, and then an increase again during weeks 15–40. The total daily insulin requirement for type 1 diabetes during pregnancy is 0.7 units/kg in the first trimester, progressing over time to 1.0 units/kg as the patient nears term. Pregnant type 2 diabetic patients may need higher doses (1–2 units/kg) to deal with insulin resistance and the requirements of the pregnancy. Avoiding excessive weight gain and incorporating an exercise program can improve glycemic control and decrease insulin resistance.

Exercise

ACOG recommends that pregnant women perform 30 minutes or more of moderate exercise daily. The American Diabetes Association recommends starting or continuing a program of moderate exercise in women without medical or obstetrical contraindications[8] (Table 1).

Recommended forms of exercise include walking, stationary bicycling, low-impact aerobics, and swimming.[20] Each exercise session should begin with a 5- to 10-minute warm-up period involving some flexibility exercises (stretching) to reduce the risk of musculoskeletal injury during the workout, followed by a cool-down period. In sedentary women who decide to exercise during pregnancy, ACOG recommends that exercise heart rates should not exceed 140 bpm (~ 60–70% of VO_{2max}).[21]

Exercise increases insulin sensitivity of muscle glucose transport and also enhances insulin action in extramuscular tissues.[22] The three most important endocrine responses to exercise include *1*) a decrease in plasma insulin, *2*) an increase in sympathethic nervous activity causing changes in insulin counterregulatory hormones, and *3*) hormones affecting sodium and water balance. The autonomic nervous system cannot adjust the plasma insulin concentration in patients with type 1 diabetes and relies on the pharmacodynamics of the injected insulin. There are changes in metabolism resulting from exercise in these patients based on the dose of insulin taken.

There is a potential increase in insulin levels during exercise (because of an increase in the absorption of insulin) causing inhibition of the normal increase in hepatic glucose production and increased muscle glucose

Table 1. Absolute Contraindications to Exercise During Pregnancy[23]

- Preterm labor
- Premature rupture of membranes
- Incompetent cervix
- Persistent second- or third-trimester bleeding
- Intrauterine growth reduction
- Placenta previa beyond week 26
- Pregnancy-induced hypertension

uptake. Both of these effects can result in hypoglycemia.

For patients with type 2 diabetes, there is some insulin secretory capacity, so these patients do not have the same metabolic risks for hypoglycemia with exercise as their type 1 diabetic counterparts. Even though these patients have insulin resistance, exercise-mediated glucose uptake is not reduced. This means that diet-treated individuals are able to perform prolonged mild to moderate exercise and still have a marked reduction in hyperglycemia.

Before initiating a regular exercise program, all patients with diabetes should undergo a medical evaluation, be educated on the benefits and risks of exercise, and understand the potential effects exercise can have on their glucose levels (the interaction between food, insulin, and exercise). During any physical activity, muscles consume glucose at a rate of 2–3 mg · kg of body wt^{-1} · minute of $exercise^{-1}$. An exercise program should be started only when glucose levels are adequately controlled.

Exercise regimens differ for each type of diabetes and according to patients' preconception exercise habits. Type 1 diabetic patients need to be watched closely for exercise-induced hypoglycemia. If they were exercising regularly before pregnancy, they should be able to continue an exercise program during pregnancy. Type 2 diabetic patients may either start or continue an exercise program depending on their preconception exercise habits. Sedentary individuals who wish to start exercising should do so after being evaluated by a physician. They should start on a low-intensity program, progressing in intensity and duration slowly and as tolerated.[23] The progression should not exceed a 10% increase per week. Patients need to be advised of the warning signs to stop exercising and seek medical attention (Table 2). Appropriate exercises during pregnancy and the postpartum period include low-impact aerobics, swimming, stationary bicycling, walking, 65-cm Swiss ball exercises, yoga, light weights, and resistant band exercises.[23]

Programs of moderate physical exercise have been shown to lower maternal glucose concentrations in women with GDM. The impact of exercise on any neonatal complications awaits clinical trials. The beneficial glucose-lowering effects of exercise warrant the encouragement of women without medical or obstetrical contraindications to start or continue a program of moderate exercise as a part of their treatment for GDM.[9] Patients should be taught to palpate their uterus during exercise to detect contractions and to discontinue the exercise if contractions occur.[2]

Physiological changes of pregnancy produce an alteration in the point of gravity (lordosis), an increase in elastin (joint and ligament laxity), and an accumulation of interstitial fluids (edema). These changes increase the risk for soft tissue injuries during exercise.[21] The exercise prescription should take into account these potential injuries and be designed to prevent them as well as to strengthen other areas, such as the abdominal and lower back muscles. To prevent aortocaval compression and hypotension, exercises should be avoided in the supine position after the first trimester. Exercise heart rates should not exceed 140 bpm or 60–70% of VO_{2max}.[21]

During exercise there is preferential carbohydrate utilization, and this is most noticeable in non–weight-bearing exercises (bicycling and swimming). Exercise is safe when the glucose levels are between 90 and 140 mg/dl. The exercise program should be for < 45 minutes, and a meal should be consumed 1–3 hours before the exercise. Ideally, insulin should be given in the abdomen and should not be injected into active muscles (extremities). The insulin injection should occur ~ 1 hour before exercise. In addition, one should decrease the bolus insulin if its peak activity is going to coincide with the exercise period. Over time, the basal insulin may need adjustment.

Table 2. Warning Signs to Stop Exercising and Seek Medical Evaluation[23]

- Vaginal bleeding
- Faintness
- Decreased fetal activity
- Generalized edema
- Low back pain

Patients should avoid exercising at the time their insulin is peaking. It is imperative to monitor glucose levels, checking the level before exercise (if < 100 mg/dl, then take a supplemental snack), during exercise (if > 45 minutes), and after exercise (being aware of post-exercise hypoglycemia). If the glucose level is > 250 mg/dl, then the urine should be checked for ketones. If the urine is positive for ketones, exercise should be delayed until the glucose is better controlled and ketones have resolved. If ketones are negative but the glucose level is > 300 mg/dl, then be cautious with exercise.[22] Some authors recommend avoidance of exercise with hyperglycemia. Volume depletion from osmotic diuresis may cause orthostatic changes and predispose patients to injury. Patients should always carry some readily digestible carbohydrate and injectable glucagon in case of hypoglycemia.

Preconception Counseling

Because the planning of a pregnancy and early admittance for antenatal care are associated with a reduction in complications,[17] every woman with diabetes in the reproductive age group must be counseled about contraception and family planning. At each office visit, these women should be asked if there is the slightest chance they could be pregnant. They should be counseled before becoming pregnant (preconception counseling) about optimizing metabolic control and planning their pregnancy. They should be aware of the risks of spontaneous abortion and birth defects associated with poor metabolic control. Despite the risks involved, women of reproductive age with diabetes can become pregnant and give birth to healthy infants.

Table 3. Risk Factors for GDM at the Initial Visit[11]

- Marked obesity
- Personal history of GDM
- Glucose intolerance or glycosuria
- Strong family history of type 2 diabetes

In addition, patients should be screened for risk factors for GDM at their initial visit (Table 3).

Summary

To improve outcomes, pregnant women with type 2 diabetes should plan their pregnancy, maintain good metabolic control of their diabetes, exercise, and take folate daily. Ideally, an interdisciplinary team approach with centralized care offers the best outcomes.[17]

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