



Council for the Advancement of Diabetes Research and Education

MISSION STATEMENT

CADRE is a nonprofit organization committed to reducing the devastating complications of both type 1 and type 2 diabetes mellitus (DM) through achievement of tight metabolic control. To achieve this goal, CADRE provides health care professionals with scientific information and educational programs to enable them to manage and empower their patients with DM.

CADRE'S "DIABETES TACTICS"

CADRE's "Diabetes Tactics" are case studies presenting challenging diabetes treatment scenarios that practitioners are likely to encounter. These brief case studies explore controversies or dilemmas in diabetes management and offer practical suggestions for dealing with management challenges. CADRE is pleased to partner with *Insulin* to provide these educational cases to readers of this journal.

ACHIEVING OPTIMAL GLYCEMIC CONTROL IN A PREGNANT WOMAN WITH TYPE 2 DIABETES MELLITUS AND POLYCYSTIC OVARY SYNDROME

This issue's "Diabetes Tactics" discussion is provided by CADRE Advisory Board member Lois Jovanovič, MD, FACE, Chief Executive Officer and Chief Scientific Officer, Sansum Diabetes Research Institute, Santa Barbara, California; Clinical Professor of Medicine at the University of Southern California–Keck School of Medicine, Los Angeles; and Adjunct Professor of Bioscience and Engineering at the University of California–Santa Barbara. Scientific writing assistance was provided by Julie Martin, MS.

CASE PRESENTATION

A 36-year-old white woman visits the clinic 2 days after discovering she is pregnant through use of a home pregnancy test. The patient received a diagnosis of polycystic ovary syndrome (PCOS) 4 years earlier, when she and her husband sought medical evaluations after a year of infertility. Three years ago she learned that she had type 2 diabetes mellitus (DM) and was started on metformin treatment; glyburide was added to her regimen 2 years ago. No evidence of retinopathy or other known complications of diabetes has been detected. Last year she started taking lisinopril, an angiotensin-converting enzyme (ACE) inhibitor, for mild hypertension.

The patient's pregnancy is confirmed with a serum pregnancy test. Based on the start date of her last menstruation, she is at 3 weeks' gestation. Her current medications include metformin 1000 mg twice daily, glyburide 5 mg twice daily, lisinopril 10 mg daily, and folate 400 µg daily. Her fasting glucose is 118 mg/dL, her glycosylated hemoglobin (A1C) level is 6.7%, and her blood pressure is 115/68 mm Hg. Her height is 62 inches; her weight of 206 lb (body mass index, 38 kg/m²) reflects a weight loss of 10 lb since her clinic visit 3 months earlier. The patient states that she has been seeing a dietitian to improve her diet and has been walking 1 to 2 miles daily to lose weight and improve her glycemic control. She performs self-monitoring of blood glucose (SMBG) every morning before breakfast and occasionally 2 hours after eating. She and her husband still yearn to have a child—she experienced a spontaneous abortion early in the first trimester 3 years ago and is highly motivated to do whatever is needed to improve her chances of having a healthy baby.

Analysis

Although this patient's A1C is below the standard goal of <7.0% recommended by the American Diabetes Association, this is not an acceptable goal during pregnancy. To reduce the risks of spontaneous abortion and congenital malformations, this patient needs to rapidly improve her glycemic control, with an A1C goal of <5.0%. In the first 6 to 7 weeks of pregnancy, hyperglycemia increases the risk of severe birth defects (eg, congenital heart malformations, musculoskeletal deformities, central nervous system abnormalities). Although this patient has been working to change her diet and lifestyle to improve her glycemic control, ideally she should have had more complete preconception planning to adjust her diabetes therapy for tighter control and discontinue the lisinopril. Fortunately, this patient identified her pregnancy early and sought medical care immediately.

The best method to quickly improve glycemic control is to start insulin therapy. Discontinuation of this patient's glyburide and metformin is recommended—although glyburide has been used safely in pregnancy, it will not be needed if insulin therapy is initiated, and controversy exists regarding use of metformin in pregnant women with PCOS complicated by type 2 DM. Metformin has been shown to reduce the risk of spontaneous abortion, but the literature suggesting that metformin does so in women who have PCOS does not report the glucose concentrations in these women during the first trimester. Because the risk of gestational diabetes is >25% in this high-risk group of women, the spontaneous abortion rate is most likely related to the degree of glucose control with metformin versus no metformin therapy. Because metformin crosses the placenta, further research is needed before it can be approved in the United States for use during pregnancy. ACE inhibitors are contraindicated during pregnancy; therefore, this patient must stop taking lisinopril.

Recommendations

The patient was agreeable to starting insulin therapy, increasing her SMBG to at least 8 times daily, and meeting with a dietitian for further diet education. It was determined that this could be achieved with outpatient teaching, which was started at this visit.

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The patient was started on a basal-bolus insulin regimen using a rapid-acting insulin (insulin lispro or insulin aspart) before meals and 3 injections of neutral protamine Hagedorn (NPH) insulin daily (before breakfast, before dinner, and at bedtime). She was instructed on the use of insulin injections and how to prevent and treat hypoglycemia. Her total insulin need was assessed as 0.7 unit/kg of actual body weight for the first trimester (her insulin need is expected to increase to 0.8 unit/kg and 1.0 unit/kg in the second and third trimesters, respectively, due to increasing insulin resistance); thus, she was estimated to need a total of 66 units of insulin daily (current weight of 93.6 kg \times 0.7 unit/kg) to achieve ideal metabolic control. Of this total, ~50% will be used as basal insulin (NPH) and the rest as rapid-acting insulin. Because the patient was prescribed 3 equal doses of NPH insulin, each dose was easily calculated as 1/6 of the total insulin need (11 units). The same is true of the premeal insulin doses for this patient, although some patients require more insulin at breakfast and less at the later meals. The patient was instructed to inject 11 units of NPH insulin and 11 units of rapid-acting insulin before breakfast, 11 units of rapid-acting insulin before lunch, 11 units of NPH insulin and 11 units of rapid-acting insulin before supper, and 11 units of NPH insulin before going to bed.

The diabetes educator explained that frequent SMBG will be the best method of monitoring her metabolic control, because it will take many weeks for her A1C level to show improvement. She was instructed to perform SMBG before each meal, with a goal of 60 to 90 mg/dL, and 1 hour after the start of each meal, with a goal of <120 mg/dL. Additional testing at bedtime and 3 AM was also recommended. She was told to record her results and to look for patterns. In addition, she was given a sphygmomanometer and instructed on its use and the need to maintain her blood pressure below 120/80 mm Hg.

The patient also met with the dietitian, who recommended that she eat <40% of her calories as carbohydrates. She was given a meal plan with suggestions for each meal and snack. She was encouraged to continue the walking program, and her calories were adjusted to maintain her weight.

The patient was told to stop taking her glyburide, metformin, and lisinopril. She was instructed to start methyldopa 250 mg every 6 hours to treat her hypertension. The dose could be increased to 500 mg every 6 hours if needed. If this proved to be ineffective, hydralazine 25 mg every 6 hours could also be prescribed, up to a maximum dose of 50 mg every 6 hours. Finally, the patient was scheduled for weekly clinic follow-up visits and instructed to call daily for insulin, diet, and hypertension medication adjustments.

Rationale

In this case, the patient was already pregnant when she presented to the clinic and immediate action was indicated to improve her metabolic control. If this patient's blood glucose was less well controlled, if she was not as motivated or able to learn on an outpatient basis, or if this teaching was not available at her doctor's office, hospitalization might have been indicated. Close follow-up was required for this patient to ensure that she was controlling her blood glucose level and not experiencing frequent or serious hypoglycemic events.

When choosing insulin for use in pregnancy, it is important to use an insulin that is not immunogenic. Although insulin itself does not cross the placenta, maternal anti-insulin antibodies bind to insulin; the insulin is then carried across the placenta, where it may contribute to fetal hyperinsulinemia. NPH insulin was chosen as the basal insulin for this patient because of insufficient clinical data to recommend the new long-acting insulin analogues (detemir and glargine) in pregnancy. Rapid-acting insulin was chosen over regular insulin because research has shown that it causes fewer hypoglycemic events and achieves better postprandial glucose levels. Insulin lispro and insulin aspart have both been studied in pregnancy and have acceptable safety profiles; they are not immunogenic, and they do not cross the placenta. Because no clinical trials have been published on the use of insulin glulisine in pregnant women, more research is required before it can be recommended in this patient population.

Improved metabolic control to a nondiabetic level (A1C <5.0%) is the best way to decrease the risks of spontaneous abortion and birth defects and increase the chances of delivering a healthy baby.

Outcome

This patient was successful with her pregnancy, even though her A1C at the end of the first trimester was 5.2% (slightly higher than the goal). At her final visit before delivery, her total insulin requirement was 1.1 unit/kg. She delivered a healthy female infant weighing 8 lb 4 oz at 39 weeks' gestation.

Key Messages

- Preconception care should be strongly encouraged for women with PCOS, type 2 DM, or both conditions, to improve glycemic control and begin counseling before conception.
- Pregnant women with diabetes can reduce the risks of spontaneous abortion and severe birth defects if they achieve metabolic control before conception or within the first 6 to 7 weeks of gestation.
- Intensive insulin therapy and rigorous SMBG are recommended during pregnancy for women with type 2 DM.
- When a pregnancy is confirmed, it is important to check all medications to ensure that they are safe for the fetus.

RECOMMENDED READING

- Gabbe SG, Carpenter LB, Garrison EA. New strategies for glucose control in patients with type 1 and type 2 diabetes mellitus in pregnancy. *Clin Obstet Gynecol.* 2007;50:1014–1024.
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