CASE REPORT

Basal Insulin Requirements after Progesterone Treatment in a Type 1 Diabetic Pregnant Woman

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Abstract

We herein report the case of a 37-year-old type 1 diabetic pregnant woman treated with an insulin pump. Although the patient’s glycemic control deteriorated following progesterone treatment for the prevention of preterm delivery and miscarriage, it was improved by adjusting the basal insulin rate on the days of progesterone treatment. Excess progesterone is known to impair both insulin sensitivity and secretion. The present case is the first report to evaluate deterioration of glycemic control induced by progesterone treatment and to determine the dose of insulin required in a type 1 diabetic pregnant woman whose insulin secretion was completely depleted.

Key words: progesterone, type 1 diabetes, insulin pump therapy, basal insulin

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Introduction

It is very important for pregnant women with and without diabetes to maintain normoglycemia during pregnancy. Elevated glucose levels are associated not only with the development of diabetic complications, such as nephropathy and retinopathy, but also with the development of complications during pregnancy, such as congenital malformations, preterm delivery, preeclampsia, macrosomia, shoulder dystocia, cesarean delivery and maternal mortality (1). Several studies have shown the beneficial effects of improved glycemic control on fetal outcomes in pregnant women with pregestational diabetes (2-4). The American Diabetes Association has published recommendations for target blood glucose levels for premeal, bedtime and overnight (60-90 mg/dL for each) and for peak postmeal (1 to 2 hours after the beginning of a meal, 100-129 mg/dL) (5).

Glycemic control in fertile type 1 diabetic women is known to be affected by physiological fluctuations of sex hormones such as progesterone and estrogen during the menstrual cycle and increases in placental hormones, including placental lactogen, human chorionic somatomammotropin, cortisol, estrogen and progesterone, during pregnancy (6-9). Among these hormones, progesterone has been reported to impair the insulin suppression of hepatic glucose production, insulin sensitivity in muscle and adipose tissue and insulin secretion from the pancreas (10-15). It has recently been reported that progesterone treatment for the prevention of recurrent preterm delivery increases the incidence of glucose intolerance and gestational diabetes (16, 17). However, there have been few reports evaluating the influence of progesterone treatment on glucose tolerance in diabetic pregnant women. Furthermore, no reports have evaluated the effects of progesterone treatment in view of insulin sensitivity in type 1 diabetic pregnant women whose insulin secretion is completely depleted. In this case report, insulin resistance induced by progesterone treatment was successfully controlled by increasing the basal insulin rate in a type 1 diabetic pregnant woman whose insulin secretion was completely depleted.

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A 37-year-old type 1 diabetic Japanese woman was referred to our hospital for glycemic control during pregnancy. She had been diagnosed with type 1 diabetes at 3 years of age and was treated with an insulin (Lispro) pump using carbohydrate counting. Her carbohydrate-to-insulin ratio was (8-10-1) g/U (breakfast-lunch-supper). Her insulin sensitivity factor was 50 mg/dL/U and her total daily insulin dose (TDD) was 30-35 units. She was impregnated through in vitro fertilization and embryo transfer (IVF-ET), then treated with 125 mg of 17-hydroxyprogesterone caproate (17-OHPC) per week via intramuscular injection until the eighth week of pregnancy. However, her glycemic control instantly deteriorated on the day of progesterone treatment. One day following progesterone treatment, the hyperglycemia lasted for one day following progesterone treatment.

Recent studies have shown a correlation between high progesterone levels and glucose intolerance (14, 16-23). Exogenous progesterone decreases insulin sensitivity with the subsequent development of hyperglycemia in rodents (14, 20), and the use of 17-OHPC to prevent recurrent preterm delivery is associated with an increased risk of developing glucose intolerance and gestational diabetes mellitus in humans (16, 17). In addition, the levels of homeosta-

**Case Report**

In this report, we presented the case of a 37-year-old type 1 diabetic pregnant woman whose glycemic control deteriorated due to progesterone treatment and improved by adjusting the basal insulin rate. To our best knowledge, the present case is the first report to evaluate deterioration of glycemic control following progesterone treatment and to determine the insulin requirements in a type 1 diabetic pregnant woman whose insulin secretion was completely depleted.

Progesterone is a steroid hormone involved in the female menstrual cycle, pregnancy and embryogenesis. The use of progesterone and its analogues has many medical applications. It has recently been reported that administration of 17-OHPC not only prevents recurrent preterm delivery in association with a higher pregnancy rate, but also reduces the incidence of several complications in infants (18, 19). The present patient was impregnated through IVF-ET and treated with 17-OHPC injections to prevent preterm delivery and miscarriage until the eighth week of pregnancy. However, her glycemic control instantly deteriorated on the day of progesterone treatment, and the hyperglycemia lasted for one day following progesterone treatment.

**Discussion**

In this report, we presented the case of a 37-year-old type 1 diabetic pregnant woman whose glycemic control deteriorated due to progesterone treatment and improved by adjusting the basal insulin rate. To our best knowledge, the present case is the first report to evaluate deterioration of glycemic control following progesterone treatment and to determine the insulin requirements in a type 1 diabetic pregnant woman whose insulin secretion was completely depleted.

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sis model of insulin resistance (HOMA-IR) increase during the luteal phase of the menstrual cycle in association with increases in the serum progesterone levels in humans (23). Therefore, increases in both exogenous and endogenous progesterone deteriorate glucose tolerance. Several studies have suggested possible mechanisms by which glucose tolerance is deteriorated by progesterone. Acute administration of progesterone reduces the ability of insulin to suppress endogenous hepatic glucose production in rats (10). In addition, female progesterone receptor knockout mice have larger pancreatic islets and show lower fasting glucose levels with higher insulin levels on glucose injection (14). These findings demonstrate that progesterone affects not only insulin sensitivity, but also insulin secretion. In the present patient, insulin secretion was completely depleted. This suggests that the deterioration of glycemic control induced by progesterone treatment in the present case was primarily caused by the development of insulin resistance.

Hepatic glucose release into the bloodstream is primarily regulated by insulin from the pancreas and affects the fasting and postmeal levels of blood glucose. Therefore, the basal insulin rate in patients with insulin pump therapy regulates hepatic glucose production and is set to maintain the blood glucose levels during the fasting state (24). In the present case, both the patient’s premeal and postmeal glucose levels increased immediately following progesterone treatment, and the hyperglycemia lasted for one day after progesterone treatment. Furthermore, the TDD increased to approximately 1.7 times the ordinary dose. Therefore, we attempted to increase the basal insulin rate, but not the amount of bolus insulin, in proportion to the ordinary dose by 1.7 times on the day of progesterone treatment. As a result, the patient’s premeal and postmeal blood glucose levels were controlled within the target range. These results suggest that the insulin resistance induced by progesterone treatment in this case was primarily due to elevated hepatic glucose production. In addition, considering the half-life (t1/2: 10 days) and time of maximum concentration (Tmax: 1.6 hours) of 17-OHPC (25), it is possible that there is a threshold level affecting glycemic control. We assume that when the serum progesterone level is above the threshold, the basal insulin dose should be increased. Furthermore, it is interesting that the effects of progesterone on glycemic control are different from those of prednisolone, one of the most well-known drugs known to cause a deterioration in insulin sensitivity, in that it primarily causes postmeal hyperglycemia and increases in bolus insulin.

In conclusion, the number of type 1 diabetic patients who are on progesterone treatment to prevent preterm delivery and miscarriage will be increased in the future. The present case is a pilot report to determine the dose of insulin required for progesterone treatment in type 1 diabetic pregnant women.

The authors state that they have no Conflict of Interest (COI).

References

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