Chronic Disease and Pregnancy Care: Requisites for Permissible Pregnancy and Timing of Shift to Obstetric Management

Nagayasu TOYODA
Professor, Department of Obstetrics and Gynecology, Mie University School of Medicine

Abstract: Very-low-calorie therapy was performed in a patient with severe obesity, diabetes mellitus, and hypertension who was on antihypertensive therapy, oral antidiabetic therapy, and insulin therapy and who had been advised by her doctor to avoid becoming pregnant. Since the blood glucose level and blood pressure normalized without medication, the patient was given permission to conceive, and ovulation induction and artificial insemination with her husband's semen were performed because of sterility. As a result, the patient conceived and gave birth to a healthy baby. Requisites for permissible pregnancy should always be subject to reconsideration as perinatal medical care advances. Attempts to conceive have recently increased in patients with chronic diseases that used to preclude them from conceiving. However, when giving permission for pregnancy, it is necessary for doctors to provide patients with relevant medical information and to base decisions on the individual case, while respecting the patient's right to self-determination based on the information given on possible risk. To optimize obstetric management of a patient with chronic disease, the patient should be referred to an obstetrician prior to conception, so that an optimal environment for pregnancy can be prepared beforehand.

Key words: Diabetes mellitus; Hypertension; Prepregnancy management; Requisites for permissible pregnancy

Introduction

This article discusses chronic disease and pregnancy care, with particular attention to requisites for permissible pregnancy and timing of the shift to obstetric management. However, since it is impossible to discuss all chronic diseases, a patient with a typical lifestyle-related disease will be described as an example.
Case Report

Patient: A 31-year-old woman.
Chief complaints: Obesity, diabetes mellitus, hypertension, desire to have a baby.
Present illness: The patient has been on treatment for obesity, diabetes mellitus, and hypertension under her internist since 1992, when she was 27 years old. For the treatment of diabetes, dietary instructions, oral antidiabetic therapy, and insulin therapy (since 1996) have been employed. A Ca antagonist and a β-blocker have been used for the treatment of hypertension.

The patient married when she was 24 years old, and because of lack of pregnancy, she visited an obstetrics and gynecology clinic at the age of 26 years and another clinic at 28 years, with the desire to have a baby. At these clinics, she received ovulation induction therapy and artificial insemination with her husband’s semen, which ended in failure. On November 6, 1996, she visited another obstetrics and gynecology clinic with the desire to have a baby, but was referred to the department of obstetrics and gynecology of our hospital on November 13 because of complications such as diabetes mellitus and hypertension. She had been told by her doctor to avoid conceiving because her blood pressure was high (190/110 mmHg), and thus discontinuation of antihypertensive drug therapy would be dangerous.

Family history: Diabetes mellitus (−). The patient’s mother and brother were obese.
Menstrual history: Menstruation cycle, 28–30 days; duration, 6 days.
Physical examination: The patient was 167 cm tall and weighed 102 kg. Blood pressure was 132/62 mmHg on the first examination and 161/89 mmHg on the second examination. There were no other particular abnormalities on physical examination.

Major laboratory findings:
Blood biochemistry
Glu 194 mg/dl ↑, HbA1c 9.0% ↑, GOT 331U/l, GPT 441U/l, and serum creatine 0.6 mg/dl. No other abnormalities were noted.

Urinalysis
Urinary protein 7 mg/dl, urinary trace albumin 122.7 mg/day ↑.

Endocrinology
PRL 71.8 ng/ml ↑, LH 2.40 mIU/ml, FSH 2.10 mIU/ml, T 47.2 ng/dl

Funduscropy
Fukuda’s classification AI.

Diagnoses: Obesity, diabetes mellitus, suspected diabetic nephropathy, diabetic retinopathy, hypertension, infertility, and hyperprolactinemia.

Concept of Permissible Pregnancy in the Present Case

1. Blood glucose control in the initial stage of pregnancy and permissible pregnancy

A variety of perinatal complications may occur in pregnant women with diabetes. Poor blood glucose control in the early stage of pregnancy elevates the incidence of congenital malformation. Because congenital malformation cannot be prevented if blood glucose control is initiated after the patient has conceived, it is important to pursue planned pregnancy after strict blood glucose control has been achieved. There is a correlation between the glycosylated hemoglobin (HbA1c) level in the early stage of pregnancy and the incidence of congenital malformation. Values not more than mean ±4SD denote low risk, whereas moderate risk is denoted by values corresponding to mean ±6SD to 10SD, and high risk by those exceeding mean ±10SD to 12SD (Table 1). The HbA1c value was 9.0% (normal range 4.3–5.8%) in the present case. This value corresponds to mean ±10SD, with the mean value and SD set at 5.0% and 0.39, respectively. The risk level of this patient was, thus, moderate to high. This level of risk may be assessed by the patient herself as high or low depending on her interpretation of the incidence of congenital malformation of 2–4% in healthy pregnant
and continuation or artificial termination of the pregnancy will be determined by a doctor designated under the Mother’s Body Protection Law, on the basis of discussion with the patient herself and her husband and ophthalmologist. Because rapid normalization of the blood glucose level may aggravate retinopathy, it is desirable for the patient to conceive after the blood glucose level has been adequately controlled.

### 2. Presence of diabetic retinopathy and permissible pregnancy

Pregnancy is one of the factors that causes worsening of diabetic retinopathy. If there is preproliferative or proliferative retinopathy, the patient is permitted to conceive after the prepregnancy blood glucose level has been improved and after retinopathy has been relieved by ophthalmic treatment including photocoagulation therapy of the retina. If the patient conceives while proliferative retinopathy is present, she will be informed of the risk of losing her eyesight as well as the success rates of photocoagulation and vitreous surgery, and continuation or artificial termination of the pregnancy will be determined by a doctor designated under the Mother’s Body Protection Law, on the basis of discussion with the patient herself and her husband and ophthalmologist. Because rapid normalization of the blood glucose level may aggravate retinopathy, it is desirable for the patient to conceive after the blood glucose level has been adequately controlled.

### 3. Diabetic nephropathy and permissible pregnancy

Currently, diabetic nephropathy accompanied with atherosclerotic cardiac disease is a contraindication of pregnancy. Patients with this condition should avoid conceiving because the vital prognosis of the mother is poor. Gestational toxicosis frequently occurs among pregnant women with diabetic nephropathy. Patients with decreased renal function (CCr 30 ml/min or less, serum creatinine 3–5 mg/dl...
or more) often fail to maintain pregnancy to the terminal stage. Such patients should be advised to conceive after the initiation of dialysis or kidney transplantation. However, it should be noted that the probability of achieving a live birth on dialysis is low. For patients with kidney transplantation, it is preferable that pregnancy occur 2–5 years after kidney transplantation, the period in which the patient usually is most stable.

Whether pregnancy deteriorates the natural course of diabetic nephropathy is controversial. Some reports claim no effects, whereas others indicate the possibility that pregnancy reduces the length of time until the introduction of dialysis. The present case was in the early stage of diabetic nephropathy, which does not constitute a reason for inhibiting pregnancy.

4. Oral antidiabetic drugs and permissible pregnancy
   As a general rule, oral antidiabetic drugs are replaced by insulin before the patient becomes pregnant. However, it has been reported that the use of oral antidiabetic drugs is a useful means particularly in developing countries because these drugs are not associated with an increase in congenital malformation and because drug-induced neonatal hypoglycemia can be prevented by changing them to insulin at the time of delivery. In the present patient, oral antidiabetic medication was discontinued and switched to insulin monotherapy, which is known to be safe for the fetus.

5. Hypertension and permissible pregnancy
   Women with chronic hypertension have a high potential to bear a healthy baby if there is no complication; however, the result worsens if the patient develops toxemia of pregnancy. Toxemia of pregnancy is apt to develop when there is accompanying renal disease or severe hypertension (160/110 mmHg or higher).

   Currently, \( \beta \)-blockers, \( \alpha/\beta \)-blockers, and Ca antagonists are also in clinical use. ACE inhibitors, however, are contraindicated because of their possible adverse effects on the fetus. Not a few drugs, particularly new drugs, are described as contraindicated for pregnant women on package inserts merely because of the lack of experience with their use in pregnant women.

   The present patient was on antihypertensive drug therapy without established safety, and was at high risk of developing gestational toxicosis, which would have made the pregnancy a challenge if it had occurred under the existing circumstances. The possibility existed that the patient’s hypertension might improve with treatment of obesity, and the patient had four years until she would reach 35 years of age, when a decrease in the pregnancy rate becomes apparent. Taking all this into consideration, the strategy that pregnancy be attempted after treatment of obesity was adopted, as the patient agreed to it.

Course of Illness in This Patient

Outpatient treatment
   The patient received treatment for diabetes and obesity at our outpatient clinic as well as continuing antihypertensive treatment at the office of her own doctor. Diet therapy (1,500 kcal/day) was initiated with the assistance of dietitians in our hospital. Intensive insulin therapy was begun, while oral antidiabetic therapy was discontinued.

   In June 1997, although the HbA1c value decreased to 6.6% and body weight to 96.5 kg, her blood pressure remained at 163/96 mmHg, an insufficient decrease on antihypertensive therapy. Her condition began to worsen around this period, and the values of HbA1c, body weight, and blood pressure increased to 7.0%, 102.5 kg, 172/99 mmHg, respectively, in March 1998. Since the patient claimed that she was reaching the limits of her effort, a very-low-calorie diet (VLCD) program was attempted.
Very-low-calorie diet (VLCD)

The patient underwent a VLCD program in the Third Department of Internal Medicine of our hospital from April 9 to June 27, 1998, in which caloric intake was reduced to 420 kcal/day. Her body weight and HbA1c value were 104.5 kg and 8.1%, respectively, on admission. After 20 days of hospitalization, her blood glucose level and blood pressure were normalized in the absence of insulin and antihypertensive drugs. Her body weight, blood pressure, and HbA1c value were improved to 85.5 kg, 113/49–133/96 mmHg, and 5.6%, respectively, at the time of discharge.

Course of pregnancy and delivery

Since the blood glucose level and blood pressure were normalized without medication, the patient was permitted to conceive. She underwent four sessions of ovulation induction by hMG-hCG with administration of bromocriptine and artificial insemination with the husband’s semen at our infertility clinic. As a result, the patient conceived in December 1998. The HbA1c value increased to 7.0% during pregnancy, and therefore insulin therapy was resumed. During pregnancy, weight gain was 12 kg, and values of urinary protein, blood pressure, and HbA1c varied within ranges of 12–33 mg/day, 136/80–156/95 mmHg, and 5.0–7.0%, respectively. On August 30, 1999 (39 weeks, 0 day), the patient underwent cesarean section because bradycardia was noted on a fetal nonstress test (fetal cardiotocography), and she gave birth to a healthy male baby weighing 3,074 g.

Discussion

1. Concept of the requisites for permissible pregnancy

The requisites for permissible pregnancy should always be subject to reconsideration as perinatal medical care advances. According to Davison et al., perinatal mortality due to pregnancy complicated by severe renal dysfunction as indicated by a serum creatinine level of 2.8 mg/dl or higher has improved dramatically over time: from 100% in the 1950s, to 91% in the 1960s, 56% in the 1970s, 53% in the 1980s, and 10% in the 1990s.

Thus, patients with chronic disease, in whom pregnancy would not have been permitted in the past, have a greater chance of conceiving. However, such pregnancies remain a challenge, and should be attempted only in a hospital fully equipped with a perinatal care center.

Medical ethics have also changed in Japan, with more respect given to the patient’s own wishes as to treatment policy, even when this may threaten the patient’s life, as exemplified by the lawsuit regarding blood transfusion to followers of Jehovah’s Witnesses. In this sense, the term “permission to conceive” suggest paternalism on the part of the doctor and should be reconsidered.

In assessing whether patients with chronic diseases should conceive, the doctor must provide the patient with as much currently available information as possible, fully explain the risks to the patient under the current level of medical care, and make assessments on the basis of the individual case while respecting as much as possible the patient’s right to self-determination.

2. Timing of shift to obstetric management: Need for prepregnant obstetric management

Patients with chronic disease should be referred to an obstetrician prior to pregnancy, so that they can conceive under optimal circumstances, as is clear from the present case. If the patient is referred to obstetric care after conception has occurred, a difficult decision as to the propriety of artificial termination of the pregnancy may be necessary. In extreme cases, the internist in charge of the patient may provide an explanation of artificial termination of the pregnancy before referring the patient to an obstetrician. Such explanations involve delicate legal issues and can only be given by doc-
tors designated to do so under the Mother’s Body Protection Law.

The management of pregnant women with chronic disease represents an area of patient care that is difficult for both internists and obstetricians, and appropriate management is often not provided. Specialists who have sufficient knowledge and experience in this border zone are thought to be indispensable. For instance, at Mie University, almost all management of pregnant women with diabetes, including insulin therapy, is carried out from the prepregnant stage by a diabetic treatment team of obstetricians. Another possible option is medical management of the pregnant woman by a maternity physician in a hospital that has a department of maternity medicine. In any case, in the management of pregnant women with chronic disease, it is important to provide team care from prepregnancy to postpartum, based on close cooperation among the departments of obstetrics and internal medicine, related departments, and co-medical areas.

**Conclusion**

The concepts of prerequisites for permissible pregnancy, importance of prepregnancy management, and need for cooperation among relevant departments have been discussed with an illustrative example case of pregnancy in a woman with chronic disease.

**REFERENCES**