Note

A Case of Obesity, Diabetes and Hypertension Treated with Very Low Calorie Diet (VLCD) followed by Successful Pregnancy with Intrauterine Insemination (IUI)

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Abstract. The patient was a 32-year-old obese woman with a history of type 2 diabetes and hypertension for 6 years. Although she was treated with antihypertensive agents and intensive insulin therapy, her hyperglycemia was difficult to control. She wanted to have a baby but pregnancy was not recommended because her diabetes was under poor control and the use of antihypertensive medication. To achieve good control of obesity, diabetes and hypertension, she was admitted to our clinical department for weight reduction using very low calorie diet (VLCD). During VLCD she had a 19.8 kg reduction in body weight and her blood glucose and blood pressure were in good control without the use of drugs. Five months later, she became pregnant after the fourth trial of intrauterine insemination (IUI) and gave birth to a female baby under insulin therapy. This is the first report that showed the usefulness of VLCD for prepregnant control of glucose metabolism and blood pressure in an obese hypertensive patient with type 2 diabetes mellitus.

Key words: Obesity, Type 2 diabetes mellitus, Hypertension, Very low calorie diet, Pregnancy

(Endocrine Journal 47: 787-791, 2000)

Previous studies have shown the usefulness of very low calorie diet (VLCD) for morbid obese patients with type 2 diabetes mellitus or hypertension [1-3]. It has been reported that VLCD is more effective for short-term treatment of obesity than routine diet restriction [4].

In general, patients with sterility are older than normal women; they also have generally a strong desire to have a baby as soon as possible. We expected that VLCD would be useful for prepregnant control of blood glucose and blood pressure in obese hypertensive patients with type 2 diabetes mellitus.

In this case report, we show an obese hypertensive patient with type 2 diabetes who became free from insulin therapy and antihypertensive agents after VLCD, followed by successful pregnancy.

Case Report

The patient was a 32-year-old woman. She had a family history of diabetes mellitus and had obesity since primary school. At age 26, her body weight was 95 kg and she was diagnosed as suffering from type 2 diabetes mellitus and hypertension at a local clinic. At age 28, antihypertensive agents (imidapril hydrochloride 5 mg/day, amlodipine besilate 5 mg/day) and oral hypoglycemic agent (glibenclamide
2.5 mg/day) were initiated because of hypertension (150~170/90~100 mmHg), but her blood sugar was in poor control (HbA1c: 8.0~10.0%).

At age 31, she consulted a local obstetrician because of sterility for 7 years. Her ovulation did not occur regularly and she was referred to the Department of Obstetrics and Gynecology of our hospital for further examination. She was found to have a latent hyperprolactinemia as demonstrated by TRH loading test. At that time, pregnancy was not recommended because her diabetes was in poor control and because of the use of antihypertensive medication. The patient was subjected to intensive insulin therapy (multiple injection of insulin combined with self-monitoring of blood glucose [SMBG]; regular insulin; 16-4-14 units before every meal, NPH insulin; 4 units before breakfast and 4 units before sleep) and dietary treatment (1500 kcal/day). However, the patient could not follow the dietary regimen well. Thus her body weight did not change and her hyperglycemia was difficult to control. She was also found to have proliferative diabetic retinopathy and photocoagulation therapy was started. She was then referred to our clinical department for weight reduction and for control of her hyperglycemia and hypertension. Because of her age and strong desire to have a baby she was subjected to weight reduction therapy using VLCD.

On admission, she weighed 103.2 kg and a body mass index (BMI) of 36.6. Her blood pressure was 127/87 mmHg under antihypertensive therapy. Fasting plasma glucose level was 225 mg/dl and HbA1c level was 8.1%.

After admission, her dietary calorie was gradually reduced from 1320 to 420 kcal/day (salt 7 g/day) in 11 days (Fig. 1). VLCD was performed using Optifast™ (420 kcal/day, Taiyo Kagaku Co., Ltd., Mie, Japan) for 6 weeks. During VLCD, she had a 19.8 kg reduction in body weight. Body fat reduction as measured by the impedance method using TBF-101 (Tanita, Tokyo, Japan) was 18.9 kg. At the beginning, she received insulin at a daily dose of more than 60 units, but thereafter this dose was reduced and insulin administration became unnecessary during the course of VLCD. Antihypertensive agents also became unnecessary.

Evaluation of the body fat distribution by computed tomography at umbilical level revealed a decrease in visceral (235.3~163.1 cm²) and subcutaneous fat areas (316.3~262.2 cm²), reduction in visceral fat being predominant (visceral fat, 30.7%...
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reduction; subcutaneous fat, 17.1% reduction) [5]. Hyperleptinemia also improved (13.0-4.3 ng/ml) after treatment.

Insulin resistance was evaluated by euglycemic hyperinsulinemic clamp technique (goal of blood glucose levels, 95 mg/dl; insulin levels, 200 μU/ml) using artificial pancreas (NIKKISO STG-22, Tokyo, Japan) [6, 7]. Mean dose of glucose administered during the last 30 min of clamp study was defined as the glucose infusion rate (GIR). This was taken as the index of insulin sensitivity. GIR improved from 4.3 to 7.9 mg/kg/min, but it was still lower than the normal values (n=12; age, 40.0±6.9 years old; sex, M/F=10/2; BMI, 22.3±2.0; GIR, 11.2±1.2 mg/kg/min; mean±SD).

In order to evaluate insulin secretion we performed the 75 g-oral glucose tolerance test (OGTT) after VLCD. Blood was taken at 0, 30, 60 and 120 min. Insulin secretion in the early phase (0 min: 8.3; 30 min: 20.3; 60 min: 66.5; 120 min: 87.5 μU/ml, the ratio of increment of serum insulin from 0 to 30 min [ΔI₃₀] to increment of plasma glucose from 0 to 30 min [ΔG₃₀]: [ΔI₃₀/ΔG₃₀], 0.19) was lower than that in normal subjects (0 min: 8.7±5.1; 30 min: 76.9±39.9; 60 min: 65.9±34.7; 120 min: 41.3±10.3 μU/ml, ΔI₃₀/ΔG₃₀, 2.2±3.3). Decreased insulin sensitivity and insulin secretion in the early phase suggested the necessity of insulin injection during pregnancy.

After discharge, her ovulation did not occur regularly and she was treated by intrauterine insemination (IUI) with ovarian stimulation using hMG and hCG under bromocriptine medication. Five months later, she became pregnant after the fourth trial of IUI. During the course of pregnancy, she was treated by dietary therapy (1440 kcal/day, salt 7 g/day). However, to achieve strict glycemic control required during pregnancy, an intensive insulin therapy was instituted (Fig. 2). Although the dose of insulin was gradually increased (~15th week of gestation: regular insulin 16~18 units/day, NPH insulin 10 units/day; 16~27th week of gestation: regular insulin 18~34 units/day, NPH insulin 10~16 units/day; 28~35th week of gestation: regular insulin 34~41 units/day, NPH insulin 16~26 units/day; 36~39th week of gestation: regular insulin 41 units/day, NPH insulin 26 units/day) her hyperglycemia was well controlled (~15th week of gestation; HbA₁c 6.2±0.3%, blood glucose at the second hour after meal [postprandial glucose] 106.5±9.9 mg/dl; 16~27th

![Fig. 2. Clinical course during pregnancy.](image)

Blood pressure was also under control without anti-hypertensive agents. Insulin R: regular insulin; Insulin N: NPH insulin. Data are mean±SD.
week of gestation: HbA1c 5.3, 5.5%, postprandial glucose 93.0±7.9 mg/dl, 28~35th week of gestation: HbA1c 5.3%, postprandial glucose 112.5±8.0 mg/dl; 36~39th week of gestation: HbA1c 5.5%, postprandial glucose 106.2±14.1 mg/dl).

Her blood pressure was under control without antihypertensive agents. Her body weight increased by about 10 kg during pregnancy. On the 39th week of pregnancy, she underwent Cesarean section because of fetal distress. A female baby (3074 g) was born and neither mother and baby had any complications. Proliferative diabetic retinopathy treated with photocoagulation therapy before VLCD did not change throughout VLCD, pregnancy and delivery.

**Discussion**

Appropriate control of obesity, diabetes and hypertension is prerequisite for successful pregnancy, but, in practice, it is not easily achieved by routine diet restriction and exercise. In such a situation, VLCD is a therapy of choice. This obese hypertensive patient with type 2 diabetes mellitus received VLCD therapy that resulted in withdrawal from anti-hypertensive agents and insulin, and she subsequently became pregnant and delivered a baby under strict control of blood sugar.

She showed marked improvement in insulin resistance and decrease in visceral fat area after VLCD. The decrease in visceral fat may have contributed to the improvement of insulin resistance.

Previous studies have demonstrated that elevated plasma concentrations of leptin are associated with obesity and essential hypertension [8, 9]. Although the exact mechanism is not clear, increased circulating leptin has been suggested to contribute to hypertension in obesity by cardiorenal action and by activation of the sympathetic nervous system [10, 11]. In this patient, improvement in hyperleptinemia was associated with normalization of arterial hypertension. The arterial hypertension observed in this patient was probably in part due to hyperleptinemia.

After becoming pregnant, her blood pressure was well controlled without any intensive antihypertensive treatment. Good control of glycemia during pregnancy as well as weight reduction by VLCD might have contributed to the good control of blood pressure.

This report showed that VLCD is useful for prepregnant control of hyperglycemia and blood pressure in an obese hypertensive patient with type 2 diabetes mellitus. Even under therapy with insulin and antihypertensive agents, pregnancy and delivery may have a normal course if prepregnant weight reduction by VLCD and strict control of blood glucose during pregnancy are achieved.

**References**


