Troglitazone in Progesterone Derivative-induced Impairment of Glucose Tolerance

To the editor: Medroxyprogesterone acetate (MPA) is a derivative of 17-medroxyprogesterone with strong progestational activity and is used for the treatment of advanced breast cancer and endometrial cancer. Other than progestational activity, medroxyprogesterone acetate has a weak glucocorticoid-like effect (1) and it is known to induce impairment of glucose tolerance and hyperglycemia when given at high doses (2). Oral hypoglycemic agents such as sulphonylurea, biguanide, and α-glucosidase inhibitor are often ineffective in the treatment of steroid-induced diabetes, and insulin therapy is required. We report two type 2 diabetic patients with MPA treatment whose deterioration of

Figure 1. Clinical course of case 1 (upper) and case 2 (lower). Dashed line indicates the change of HbA1c measurement. Measurement of HbA1c changed from both unstable and stable content fractions (normal range, 5.0–6.5%) to stable HbA1c only (normal range, 4.3–5.8%) in 1996.
glucose tolerance was notably improved by troglitazone, a thiazolidinedione derivative.

The first case involved a 70-year-old woman who was diagnosed as having type 2 diabetes at the age of 64. She underwent a hysterectomy for endometrial cancer in September 1994 at 65 years of age. Before the operation, her height was 146 cm, weight was 58 kg, and her HbA1c was 7.9%. After surgery, she was prescribed 600 mg per day MPA. Her blood glucose control deteriorated after MPA administration (Fig. 1, upper set). In January 1997, glibenclamide was prescribed and HbA1c decreased to 9.1%, but her blood glucose increased again. Because she could not tolerate α-glucosidase inhibitors, metformin was added in December 1997, but it was not effective. In June 1998, her body weight was 56.5 kg and HbA1c was 13.2%. Her urinary C-peptide immunoreactivity (CPR) was 73.6 μg/day, and fasting serum immunoreactive insulin (IRI) was 9 μU/ml. Troglitazone was prescribed at a dose of 400 mg per day. Her HbA1c subsequently decreased. Her blood glucose and serum level of IRI increased again after discontinuation of troglitazone, and these changes were improved when MPA therapy was complete.

The second case involved a 64-year-old woman who was diagnosed as having type 2 diabetes at the age of 58. A hysterectomy was performed for endometrial cancer in May 1995 at 60 years of age. She was treated with diet therapy alone and her hemoglobin A1c was 6.4% before surgery. After the hysterectomy, 600 mg a day of MPA was prescribed. Her blood glucose control subsequently deteriorated (Fig. 1, lower set). In February 1997, her height was 161 cm, weight was 62 kg, HbA1c was 9.8%, urinary CPR was 81.2 μg/day, and serum IRI was 7 μU/ml. Metformin and voglibose were prescribed and HbA1c was decreased to 6.8% in May, but the effect of these drugs was temporary. In November, HbA1c was 8.6% and troglitazone was added. Her HbA1c decreased. Her HbA1c increased again when troglitazone was discontinued, but it was improved when MPA administration was discontinued.

These two patients showed deterioration of blood glucose control after MPA administration. The effects of sulphonylurea, biganide, and α-glucosidase inhibitor were insufficient. During treatment with MPA, side effects due to glucocorticoid activity have been reported, including weight gain, moon face, hypertension, fluid retention, and hyperglycemia (1). Steroid-induced diabetic patients often require insulin treatment. Regarding the glucocorticoid-induced insulin resistance, troglitazone prevented the decrease in insulin-stimulated glucose disposal, namely the development of peripheral insulin resistance, and not the hepatic glucose output in dexamethasone-treated rats (3).

Although the effect of troglitazone in steroid-induced diabetes differs among patients, it may be useful for steroid-induced diabetics who do not have complications of other inflammatory diseases as in these two cases.

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References

