OBSERVATIONS

Sitagliptin Improves Postprandial Hyperglycemia by Inhibiting Glucagon Secretion in Werner Syndrome With Diabetes

Werner syndrome (WS) is a typical progeria syndrome and often leads to diabetes (1). Here, we report a case in which sitagliptin, a dipeptidyl peptidase-4 inhibitor, normalized the postprandial glucagon secretion and improved postprandial blood glucose levels.

A 54-year-old female was admitted to our hospital. She developed bilateral cataracts at 35 years of age. Thereafter, at 44 years of age, because of her progeria-like face, she underwent genetic testing and was diagnosed with WS (mutation 4/6, compound heterozygote). At 49 years of age, she developed diabetes. Her height was 144 cm, weight 30.4 kg, and BMI 14.6 kg/m^2. Her visceral fat area was 124.8 cm^2. At the time of the hospitalization, she was prescribed 30 mg pioglitazone daily. The initial examination presented the following results: fasting blood glucose levels, 93 mg/dL; 2-h postprandial blood glucose levels, 207 mg/dL; and HbA_{1c} levels, 5.9%. For an understanding of the mechanism of pathogenesis of postprandial hyperglycemia in this case, pioglitazone administration was ceased for 7 days and the changes in the hormone levels were analyzed after consumption of a test meal. The meal was Calorie Mate (500 g; calorific level: carbohydrate: fat:protein = 60:26:14).

The respective results at 0, 15, 30, 60, and 120 min after the meal were as follows: 95, 131, 195, 240, and 216 mg/dL for blood glucose levels; 17.7, 132.4, 113.6, 259, and 390 IU/mL for insulin levels; 67, 95, 99, 80, and 68 pg/mL for glucagon levels; and 7.4, 41.7, 10.3, 9.2, and 2 pmol/L for levels of active forms of glucagon-like peptide-1 (GLP-1). The areas under the curve were 24,390 for blood glucose levels, 28,029 for insulin levels, 9,795 for glucagon levels, and 1,386 for GLP-1 levels.

Sitagliptin (50 mg/day) was then initiated, and the same examination was repeated after 4 days. We obtained the following results: 82, 86, 170, 182, and 202 mg/dL for blood glucose levels; 21.7, 17.3, 143.1, 189.1, and 539 IU/mL for insulin levels; 56, 64, 69, 63, and 57 pg/mL for glucagon levels; and 5.1, 5.6, 18.4, 16.4, and 19.9 pmol/L for GLP-1 levels. The following were the area under the curve values: 19,980 for the blood glucose levels, 28,321 for the insulin levels, 7,477 for the glucagon levels, and 1,871 for GLP-1 levels.

These results indicated an improvement in the postprandial hyperglycemia without any changes in the total amount of secreted insulin; moreover, an increase in GLP-1 levels and an inhibition of glucagon secretion after the meal were observed.

Although the patients with WS are insulin resistant (2,3), it has been suggested that only those who have impaired insulin secretion develop overt diabetes (4). In this study, we revealed the paradoxical pattern of postprandial glucagon secretion in WS with diabetes. We have recently reported that a single dose of sitagliptin was well tolerated in a WS patient with diabetes (5). This study showed that sitagliptin improved postprandial glucose along with its inhibitory effects on glucagon secretion. Therefore, sitagliptin is certain to become the primary treatment option for WS with diabetes.

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