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# Substitution of Chronic Insulin Therapy with Dipeptidyl Peptidase-4 Inhibitors and Sodium-Glucose Co-transporter-2 Inhibitors

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Insulin is a very useful and widely used treatment for diabetes. Temporary insulin therapy improves glucose toxicity due to improved  $\beta$ -cell function of the pancreas. Upon achieving glycemic control, insulin treatment could be discontinued and substituted with oral hypoglycemic agents. Nevertheless, insulin therapy is associated with side effects such as hypoglycemia, allergic reactions, and angioneurotic edema. Over this past decade, there have been rapid advances in diabetes treatment, including the introduction of Dipeptidyl peptidase-4 (DPP-4) inhibitors and Sodium-glucose cotransporter-2 (SGLT2) inhibitors. We present here the case of a patient with type 2 diabetes who discontinued insulin therapy after more than 20 years by switching to oral hypoglycemic agents including a DPP-4 inhibitor and a SGLT2 inhibitor.

A 64-year-old man with type 2 diabetes was being treated with Lispro Mix 50 insulin twice daily. He was started on subcutaneous insulin 20 years ago. He also has hypertension and hyperlipidemia, and visits the home clinic once a month. He consulted the clinic because he strongly wanted to discontinue insulin therapy due to his work situation. At the time, he was taking Lispro Mix 50 insulin twice daily (morning: 10U, evening: 6U) and his HbA1c was 7.3%. His body weight was 47.0 kg, height was 160 cm, and body mass index was 18.4 kg/m<sup>2</sup>. His blood pressure was 118/68 mm Hg and his pulse rate was 72 beats per minute. After evaluation of his condition, insulin therapy was discontinued and oral therapy consisting of glimepiride 1 mg/day, teneligliptin 20 mg/day, and canagliflozin 100 mg/day was started. Serum C-peptide and HbA1c were 0.9 ng/ml and 7.3% respectively three months later.

In theory, the dose of insulin should be reduced gradually when oral hypoglycemic agents are added and insulin therapy is being discontinued. However, the patient demanded immediate discontinuation of insulin therapy. Since his insulin dose was relatively low, 0.3 U/kg, insulin was discontinued, and oral hypoglycemic agents were started at once after a comprehensive review of the risks and benefits of a sudden change in therapy.

Early introduction of short-term insulin therapy is more protective for the beta cells of pancreas than oral hypoglycemic therapy in patients with type 2 diabetes. Surprisingly, in the present case, although the duration of insulin therapy was over 20 years, serum C-peptide, an indicator of insulin secretion, was 0.9 ng/ml, which is not too low. This may be explained by the following: 1) glimepiride increases insulin release from the  $\beta$ -cells of the pancreas, and

2) DPP-4 inhibitors increase incretin levels, which suppresses glucagon release, thereby increasing insulin secretion and decreases blood glucose levels.

SGLT2 inhibitors reduce hyperglycemia by increasing urinary glucose excretion independent of insulin secretion or action. In addition, it has been reported that SGLT2 inhibitors increase glucose-dependent insulin secretion by improving  $\beta$ -cell function of the pancreas.<sup>1</sup>

Based on the empiric evidence, DPP4 inhibitors and SGLT2 inhibitors are effective in patients who secrete less insulin after long-term insulin therapy since they do not have a direct effect on insulin secretion.

**CONFLICTS OF INTEREST:** None.

#### **CONSENT**

The patient has provided the informed written consent for this case to be published.

#### **REFERENCE**

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