Efficacy of Additional Canagliflozin Administration to Type 2 Diabetes Patients Receiving Insulin Therapy : Examination of Diurnal Glycemic Patterns Using Continuous Glucose Monitoring (CGM)

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Introduction

The efficacy of administering a sodium-glucose cotransporter 2 inhibitor during insulin therapy has not been established.

In this study, we examined its effects based on diurnal glycemic patterns using continuous glucose monitoring (CGM).

Material

The subjects were 15 patients who had received insulin therapy for 1 year or more.
A CGM device was attached to all subjects for 1 week.
The administration of canagliflozin at 100 mg was started 4 days after attachment.

Method

The mean glucose concentrations, standard deviation (SD), mean amplitude of glycemic excursions (MAGE), mean of daily difference of blood glucose (MODD), and area under the curve (AUC)(≥180, <70) after the start of administration were compared with the pretreatment values.

In addition, we compared changes in the unit number of insulin between basal and bolus insulin.

Furthermore, we investigated the influence of canagliflozin on oxidative stress markers and cytokines using 8-hydroxy-2'-deoxyguanosine (8-OHdG), tumor necrosis factor-α (TNF-α), and adiponectin as parameters.

Clinical characteristic of the subjects

Number (Male/Female)	15 (10/5)
Age (years)	52.9 ± 14.4
Body mass Index (kg/m ²)	28.8 ± 4.5
Body weight (kg)	75.4 ± 15.4
Diabetic duration (years)	6.6 ± 6.7
Insulin therapy duration (years)	1.3 ± 2.6
HbA1c (%)	10.5 ± 2.5
eGFR (ml/min/1.73m ²)	91.6 ± 2.5
Insulin doze (IU/day)	26.3 ± 16.0
Insulin therapy, n (%)	
Basal pulus bolus	10 (66.7)
Basal alone	1 (6.6)
Bolus alone	4 (26.7)
Glucose-lowering therapies, n (%)	
Metformin	2 (13.3)
Sulfonylureas	1 (6.6)
Dipeptidyl peptidase-4 inhibitors	3 (20.0)
Glucagon-like peptide-1 agonists	1 (6.6)

Date are mean ± SD

Results

Fig. 1

Fig.1 Glycemic Control

The graph shows the mean glucose consentrations of all subjects obtained on CGM.
The table shows the mean daily blood glucose level, SD, MAGE, MODD, AUC(≥180, <70).

These parameters decreased from Day 4.
In addition, the data were compared between Days 1 and 7.
The SD, MAGE, MODD, and AUC (≥180) significantly decreased.

Fig. 2

Fig.2 Doze of Insulin

The total amount of insulin in all patients was divided into basal and bolus regimens to show changes from Days 1 to 7.

It decreased from 394 to 230 units.
The number of basal insulin units markedly decreased from 128 to 76 units, and that of bolus insulin decreased from 266 to 154 units.

Fig. 3

Fig.3 Oxidative Stress Markers

The changes in the 8-OHdG, TNF-α, and adiponectin levels on Days 1 and 7 of CGM are expressed as box and whiskers plots. The data are expressed as the median and interquartile range.

Between days 1 and 7, the 8-OHdG level significantly decreased, and the TNF-α level slightly decreased.
Furthermore, the adiponectin level significantly increased.

Discussion

Combination therapy with SGLT2 inhibitors is useful in insulin-receiving patients whose body weight tends to increase.
Furthermore, in this study, the unit number of insulin units could be markedly reduced, suggesting the blood glucose-lowering effects of canagliflozin cover a decrease in the dose of insulin.
The antioxidant effects of SGLT2 inhibitors may involve weight loss-related anti-inflammatory effects, blood pressure-lowering actions, an improvement in the lipid profile, and a decrease in the uric acid level.
Thus, the favorable effects of SGLT2 inhibitors other than blood glucose-reducing actions are consistent with recent diabetes treatment emphasizing not only blood glucose control but also comprehensive risk management.

Conclusion

Canagliflozin improved blood glucose changes in type 2 diabetes patients using insulin.
In addition, the results suggest its antioxidant effects.
It may be useful as a second-choice drug for type 2 diabetes patients using insulin.