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# Enhanced renal protective effects of Tirzepatide in type 2 diabetes people

**S. Kaneko**, A. Nakasaki, T. Hirobata;
Japanese Red Cross Wakayama Medical Center, Wakayama, Japan.

**Background and aims:** In Japan, 1/400 diabetes people undergo hemodialysis. Chronic Kidney Disease (CKD) can lead to cardiovascular events (CVs). Therefore, early detection and protection against renal failure is paramount. Recent clinical trial research has revealed glucagon-like peptide-1 receptor agonist (GLP-1RAg) provides renal protection and decreases CVs in Type 2 Diabetes (T2D) people. However, the effects of glucose-dependent insulinotropic peptide (GIP), another incretin hormone, on renal function are unknown. This study analyzed whether Tirzepatide (Tir), GIP/GLP-1R dual agonist, has enhanced renal protection compared to GLP-1RAg therapy alone in real-world long duration applications.
**Materials and methods:** Retrospective univariate and multivariate analyses regarding HbA1c, eGFR, body weight and age were performed on all three groups, A) eGFR >60, B) eGFR 59~30, and C) eGFR <30, of the T2D cases receiving Tir or GLP1RAg for 12 months or more from 04/2023. In addition, statistical analysis regarding eGFR took into account changes in body weight. Adverse events were monitored.
**Results:** Of 367 T2D cases new to Tir (male 209, age 66.8±14.4, starting HbA1c 8.0±1.5%), 267 were analyzed (male 150, age 62±15, BMI 25.9±7.2, starting HbA1c 8.2±3.4%) and achieved HbA1c 6.7±2.4 % ($P<0.01$) over more than 1 years. In group B (70 cases/male 50, HbA1c 7.9 ± 1.5%, eGFR 42.2 ± 7.4), 43 improved significantly (eGFR 50 ± 8.7 was 50.1 ± 11.4 ($P < 0.01$)), 3 were unchanged and 24 worsened (eGFR 50 ± 8.7 was 5.1 ± 11.4 ($P < 0.01$)). When weight changes are taken into account, Tir eGFR provided significant favorable changes compared to semaglutide injections (Sema), GLP-1RAg alone ($P<0.01$). Group A (187 cases/male 92, HbA1c 8.1±1.6%, eGFR 85.5±18.1) and C (16 cases/male 11, HbA1c 8.7±1.3%, eGFR 20.9±6.6) had no significant changes. Side effects included excessive weight loss, appetite loss or nausea/vomiting and were cited as reasons for discontinuation, occurring at a similar rate for both medicines. Regarding Group B, Body weight changes for both Tir and Sema treated people showed no significant difference. Therefore, changes in body weight were factored out of the analysis. More cases of slower deterioration of eGFR or improvement in eGFR were observed in Tir treated people, compared to that of the Sema treated people. This suggests additional positive effects of GIP on GLP1RAg on renal protection which may possibly result in an end-stage renal disease population decrease. Tir therapy may also lead to comparable reductions in CVs.
**Conclusion:** This study suggests GIP/GLP-1R dual agonist signaling, Tir, enhances reno-protective effects and prevents renal impairment more than that of GLP1RAg alone without serious side effects. Overall positive effects of Tir could result in greater general well-being and immense medical cost savings. Longer observations in larger numbers are needed.
Clinical Trial Registration Number: N/A
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