Clinical Effects of Sodium Glucose Transporter Type 2 Inhibitors in Patients with Severe Insulin Resistance

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Background: Severe insulin resistance syndromes including lipodystrophy and pathogenic variants in the insulin receptor (INSR) lead to diabetes that is challenging to control. Oral antidiabetic agents have been used to control hyperglycemia, however the efficacy of these treatments has not been studied systematically. This study explores safety and efficacy of sodium glucose cotransporter 2 inhibitors (SGLT2i) in these patients.

Methods: This was a retrospective chart-review assessing safety (N=31) and efficacy (N=18) of SGLT2i use in patients with clinically or genetically confirmed diagnosis of lipodystrophy or INSR pathogenic variants at our institute.

Results: HbA1c did not significantly change after 1 year of SGLT2i (baseline 9.5±2.5 [80.3±27.7]; 12 months 8.8 ±2.3% [72.6±25.3 mmol/mol]; p=0.093), or across all time points (p=0.11). However, most patients (83%) were taking insulin, and SGLT2i treatment led to 35% reduction in total daily dose of insulin after 12 months (baseline 186 [100,1010]; 12 months 120 [75,260] units/day; p=0.07) and across all visits (p=0.035), which may have mitigated the reduction in HbA1c. Reduction in HbA1c was significant after adjustment for changes in insulin dose over time (p=0.0498). No significant change was noted in C-peptide, however fasting insulin decreased after 12 months (p=0.021) and across all visits (p=0.005). Urinary glucose excretion increased greater than 5-fold after 12 months of SGLT2i, to over 80 grams per day after 1 year (p=0.04). Adverse effects occurring in >1 subject included hypoglycemia, fungal infections, and extremity pain.

Conclusions: SGLT2i reduced insulin dose, insulinemia, and insulin dose-adjusted HbA1c in patients with severe insulin resistance, with a similar safety profile compared to type 2 diabetes. SGLT2i use may lead to overall better glycemic control and should be considered as part of the treatment armamentarium for these rare forms of diabetes, but larger trials are needed to confirm these findings.

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