SUMMARY (Clinical) 6/13/25 ciT1zen science

Adjunct-to-Insulin Therapy Using SGLT2 Inhibitors in Youth with Type 1 Diabetes
ciT1zen science summary

Source: Excerpts from "Adjunct-to-insulin therapy using SGLT2 inhibitors in youth with type 1 diabetes: a randomized controlled trial | Nature Medicine" (Published: 06 June 2025)
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I. Executive Summary

The ATTEMPT (Adolescent Type 1 Diabetes Treatment with SGLT2i for Hyperglycemia and Hyperfiltration Trial) study, a 22-week, double-blind, randomized, placebo-controlled trial, investigated the efficacy and safety of dapagliflozin as an adjunct to insulin therapy in youth aged 12–21 years with Type 1 Diabetes (T1D). The trial found that dapagliflozin significantly reduced measured glomerular filtration rate (mGFR), improved glycemic control (lower HbA1c and increased time in range), and led to body weight reduction without significantly affecting total daily insulin dose. The treatment was considered safe when combined with ketone monitoring and diabetic ketoacidosis (DKA) risk mitigation education, with only one mild DKA case reported in the dapagliflozin group.

II. Main Themes and Key Findings

This study addresses the critical need for effective adjunct therapies for youth with T1D, particularly focusing on renal health and glycemic control.

A. Impact on Glomerular Filtration Rate (mGFR)

- **Significant Reduction in mGFR:** The primary outcome demonstrated a substantial reduction in mGFR. "Dapagliflozin reduced mGFR by 8.8 ml min−1 1.73 m−2 when compared to placebo (95% confidence interval (CI): −12.7 to −4.8; $P < 0.0001$)."
- **Greater Attenuation with Higher Baseline mGFR:** Participants who began the trial with higher mGFR levels experienced a more pronounced reduction with dapagliflozin. This relationship showed a strong negative correlation: "participants with higher baseline mGFR experienced greater attenuation with dapagliflozin (r: −0.58; $P < 0.0001$)." This finding is particularly significant given that renal hyperfiltration often precedes chronic kidney disease in T1D.

B. Glycemic Control Improvements

- **HbA1c Reduction:** Dapagliflozin led to a statistically significant decrease in HbA1c, a key marker of long-term glycemic control. "HbA1c decreased by 0.47% (95% CI: −0.66 to −0.28)."
- **Increased Time in Range (TIR):** The percentage of time glucose levels remained within the target range (70–180 mg dl−1, 4–10 mmol L−1) improved. "time in range (glucose levels 70–180 mg dl−1, 4–10 mmol L−1) increased by 9.0% (95% CI: 3.8–14.3)." This indicates more stable glucose levels.

C. Body Weight Management

- **Weight Reduction:** Participants receiving dapagliflozin experienced a notable decrease in body weight. "Body weight decreased by 2.8 kg (95% CI: −3.7 to −2.0) with dapagliflozin." This is a beneficial side effect, as overweight and obesity are common comorbidities in adolescents with T1D and can contribute to complications.

D. Insulin Dosing and Safety Profile

- **No Change in Total Daily Insulin Dose:** Despite improvements in glycemic control and weight, the study found no significant alteration in insulin requirements. "No differences were observed with respect to total daily insulin dose (U kg−1)." This suggests that dapagliflozin works synergistically with existing insulin regimens without requiring adjustments in overall insulin quantity.
- **Adverse Events and DKA Risk:** The safety profile of dapagliflozin was comparable to placebo when proper mitigation strategies were in place. "Adverse events were similar between groups, with one mild DKA case in the dapagliflozin group." This highlights the importance of "ketone monitoring and diabetic ketoacidosis (DKA) risk mitigation education" as crucial components of this adjunctive therapy.

III. Implications and Significance

- **Potential for Renal Protection in Youth with T1D:** The reduction in mGFR is a crucial finding, as SGLT2 inhibitors are known to reduce the risk of chronic kidney disease progression in Type 2 Diabetes. This study extends that potential benefit to youth with T1D, a population at risk for early onset of kidney complications.
- **Improved Metabolic Outcomes:** Beyond renal effects, the improvements in HbA1c and time in range, along with weight reduction, suggest a multifaceted benefit of dapagliflozin in managing T1D in adolescents.
- **Feasibility and Safety with Mitigation:** The study demonstrates that dapagliflozin can be safely incorporated into T1D management in youth, provided that patients and caregivers are educated on and comply with DKA risk mitigation strategies, including ketone monitoring.
- **Contribution to Clinical Practice:** This trial provides strong evidence supporting the use of dapagliflozin as an adjunctive therapy for youth with T1D, potentially altering future treatment guidelines for this population.

IV. Study Design and Participants

- **Trial Name:** ATTEMPT (Adolescent Type 1 Diabetes Treatment with SGLT2i for Hyperglycemia and Hyperfiltration Trial)
- **Design:** 22-week, double-blind, randomized, placebo-controlled trial.
- **Participants:** Ninety-eight participants (12–21 years of age, 53% female).
- **Intervention:** Participants were randomly assigned to receive either dapagliflozin 5 mg or a placebo, alongside ketone monitoring and DKA risk mitigation education.
- **Primary Outcome:** Change in measured glomerular filtration rate (mGFR) using iohexol clearance.

V. Limitations/Considerations

- **Duration:** The study duration was 22 weeks. While providing valuable short-term data, longer-term studies would be beneficial to fully understand the sustained renal and glycemic benefits and the long-term safety profile, especially regarding DKA risk.
- **Data Availability:** "Due to confidentiality reasons (that is, limitations of informed consent and ethics board approval), the datasets used in this study are not publicly available." However, qualified researchers can request de-identified data for academic purposes.
- **Generalizability:** The study focused on youth (12-21 years). While this is a critical demographic, further research might explore the applicability to younger children or older adults with T1D.

VI. Conclusion

The ATTEMPT trial provides compelling evidence that dapagliflozin, when used as an adjunct to insulin therapy and coupled with appropriate DKA risk mitigation, offers significant benefits for youth with Type 1 Diabetes. These benefits include favorable effects on kidney function (reduced mGFR), improved glycemic control, and weight reduction, without increasing overall insulin requirements. This research marks a significant step forward in optimizing treatment strategies for this patient population.