College of Human Medicine
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GLP-1 vs SGLT2 for Type 2 Diabetics on metformin

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Clinic Scenario

- Many patients asked about GLP-1 Receptor Agonists
- Overweight individual with diabetes on metformin asked about GLP-1 Receptor Agonists
- For this patient, would another weight loss medication for Type 2 diabetes work better?
- Are GLP-1 Receptor Agonists superior to SGLT2 inhibitors for HbA1C Control for uncontrolled Type 2 Diabetics on metformin?

Background & Significance

- Type 2 Diabetes Mellitus is a chronic condition where the body resists insulin or fails to produce enough[1]
- 462 million people globally are affected with Type 2 Diabetes[1]
- Family history, obesity, age, and lack of exercise increase risk of Type 2 Diabetes Mellitus[23]
- Symptoms include increased thirst, frequent urination, and fatigue. Diagnosed with HbA1c > 6.5%[3]
- Managed with lifestyle changes, metformin, insulin, GLP-1 Agonists, and SGLT2 inhibitors[1]
- Good prognosis and ability to live a long life if properly treated[3]

- **PICO**: In patients with Type 2 Diabetes Mellitus on metformin, does the use of GLP-1 Receptor Agonists provide greater reductions in Hba1c and weight loss compared to the use of SGLT2 inhibitors?

Search Strategy

- Utilized Pubmed advanced search engine
- Search Query:
- ((((Semaglutide) OR (exenatide)) AND (SGLT2 inhibitor)) AND (type 2 diabetes)) AND (metformin)) AND (adult)
- Limits/filters: Randomized control trials, population and outcomes measured and access to studies

Search Results

- 3 RCTs identified that adequately answered study question
- Two studies identified significantly greater Hba1c reduction with GLP-1 Receptor agonists compared with SGLT2 inhibitors
- All three studies identified significantly greater weight reduction with GLP-1 Receptor agonists compared with SGLT2 inhibitors

Study ID	Aim/Hypothesis	Study Design	Population	Intervention details	Outcomes measured	Strengths/Limitations
Mcrimmon, 2020[5]	To compare the effects of once-weekly semaglutide vs once-daily canagliflozin on body composition (fat mass, lean mass, visceral fat) in adults with type 2 diabetes on a daily dose of metformin.	Double-Blind RCT	Adults ≥18 with uncontrolled T2DM (A1c 7.0–10.5%) on stable metformin; eGFR ≥60; N = 178	Semaglutide 1.0 mg subcutaneous once weekly. Vs. Canagliflozin 300 mg orally once daily.	Change in total fat mass. No statistically significant decrease in fat mass from semaglutide vs canaglifozin	Directly answers the PICO question and statistically significant, but small population size
Lingvay, 2019[6]	To compare the efficacy and safety of once-weekly semaglutide vs once-daily canagliflozin as add-on therapy to metformin in patients with uncontrolled T2DM	Double blind RCT	Adults ≥18 yrs with T2DM, HbA1c 7.0–10.5%, on stable metformin monotherapy; N = 788 randomized	Semaglutide 1.0 mg subcutaneous once weekly vs. Canagliflozin 300 mg orally once daily.	Hba1c and body weight Significantly decreased weight loss and Hba1c reduction in semiglutide vs canagliflozin	Large sample size, good methods, answers my PICO question
Jabbour, 2018[7]	To evaluate the long-term safety and efficacy of exenatide once weekly + dapagliflozin versus either agent alone in patients with T2DM inadequately controlled on metformin.	Double blind RCT	Adults ≥18 yrs with T2DM; HbA1c 8.0–12.0%; on ≥1500 mg/day metformin; N = 695 randomized	Exenatide 2 mg subcutaneous weekly + dapagliflozin 10 mg oral daily. Vs. 1) Exenatide + placebo 2) Dapagliflozin + placebo	Change in HbA1c at 28 weeks, body weight. Significantly greater reduction in Hba1c in the in combined group compared to controls.	Larger Randomized control trial, but only checked weight loss, not HbA1c

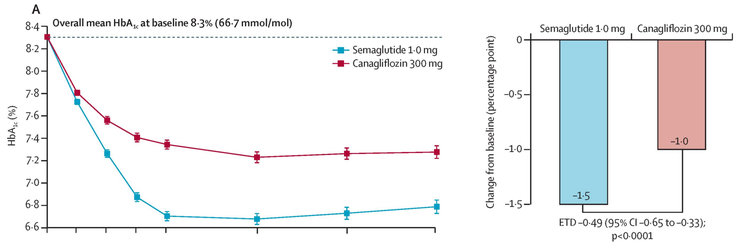


FIGURE 1. Mean Reduction in HbA1c on Semaglutide (GLP-1 Receptor Agonist) Compared to those on canagliflozin (SGLT2 inhibitor).[6]

Conclusion

Based on the randomized controlled trials reviewed, GLP-1 receptor agonists demonstrated greater reductions in HbA1c compared to SGLT2 inhibitors when used as add-on therapy.[5 6 7] Mcrimmon et al. showed significantly greater HbA1c and weight reduction with semaglutide versus canagliflozin, and Lingvay et al. demonstrated substantial glycemic improvement with GLP-1–based therapy. While Jabbour et al. did not show significant differences in body composition, overall glycemic outcomes consistently favored GLP-1 receptor agonists.

Because obesity is a common comorbidity of Type 2 Diabetes Mellitus,[2] medications that can effectively treat both are useful. This project supports that GLP-1 receptor agonists should typically be used over SGLT2 inhibitors for management of Type 2 Diabetes in adults that is uncontrolled on metformin. Overall, I was impressed with how well studied this PICO question was. Additionally, I was surprised to see that articles more frequently used weight as a measure of success compared to Hba1c. Limitations to this project included utilizing only studies I had access to, and one study only focused on body weight rather than testing for HbA1c. Future research should explore how treatments affect male versus female diabetic populations, and further research should explore long term effectiveness (>5 years) for treatment.

References

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