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Efficacy of Ertugliflozin Compared With Metformin or Placebo In Reducing HbA1c Levels Among Adults With Type 2 Diabetes: a Systematic Review and Meta-Analysis

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KEYWORDS
Ertugliflozin; Metformin; HbA1c; Type 2 Diabetes Mellitus; Systematic Review; Meta-analysis; SGLT2 inhibitor

ABSTRACT

Type 2 diabetes mellitus (T2DM) remains a global health challenge characterized by chronic hyperglycemia resulting from insulin resistance and impaired insulin secretion. According to the International Diabetes Federation (IDF), approximately 537 million adults aged 20–79 years were living with diabetes in 2021, with projections indicating this number will rise to 783 million by 2045. Glycemic control, measured by glycated hemoglobin (HbA1c), serves as a crucial indicator of therapeutic effectiveness. This systematic review and meta-analysis aim to evaluate the efficacy of Ertugliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor, compared with Metformin and Placebo in reducing HbA1c levels among adults with T2DM. Relevant randomized controlled trials (RCTs) published between 2015 and 2025 were identified through PubMed, Scopus, and Cochrane databases. Data extraction and quality assessment were conducted in accordance with PRISMA guidelines. The pooled analysis demonstrated that Ertugliflozin significantly reduced HbA1c levels compared with placebo, with mean differences ranging from −0.6% to −1.0% ($p < 0.001$). When compared with Metformin, Ertugliflozin showed comparable glycemic efficacy, accompanied by additional benefits in weight reduction and blood pressure control. Heterogeneity among studies was moderate ($I^2 < 50\%$), and no severe adverse effects were reported. These findings suggest that Ertugliflozin represents an effective and safe alternative or adjunct therapy for adults with T2DM, offering multifaceted metabolic benefits that extend beyond glucose control.

INTRODUCTION

Type 2 Diabetes Mellitus (DMT2) is a chronic metabolic condition characterized by hyperglycemia that occurs due to impaired insulin secretion, insulin resistance, or a combination of both. The World Health Organization (WHO) reported that the global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. Furthermore, the International Diabetes Federation (IDF) estimated that 537 million adults aged 20–79 years were living with diabetes in 2021, with this figure projected to reach 643 million by 2030 and 783 million by 2045 (Pop-Busui et al., 2017). These statistics underscore the magnitude of the diabetes epidemic and its increasing burden on global healthcare systems (Nauck et al., 2017; Zhou et al., 2018). The condition is rising in prevalence worldwide, making it one of the major health challenges of the 21st century (Khan et al., 2020).

The main cause of the increased prevalence of DMT2 is an unhealthy lifestyle, including a high-calorie diet and lack of physical activity, which contributes to obesity as a major risk factor for DMT2 (Frias et al., 2018; Higgins et al., 2011; Perkovic et al., 2019; Yang et al., 2020; Zinman et al., 2015). The management of DMT2 aims to maintain blood glucose

levels as close to normal as possible to reduce the risk of macrovascular and microvascular complications. Long-term complications of DMT2 include cardiovascular disease, neuropathy, nephropathy, and retinopathy. Therefore, effective glycemic control remains one of the primary goals in DMT2 management. Metformin, a biguanide, has long been the first-line therapy for DMT2. The drug works by increasing insulin sensitivity in the liver and muscles while reducing hepatic glucose production (Goldenberg et al., 2019; Li et al., 2017). However, although effective, metformin may not always be sufficient to achieve desired glycemic control; therefore, additional therapy is often required (Liu et al., 2018).

In recent years, SGLT2 inhibitors have emerged as a promising new class of drugs for the management of DMT2. Ertugliflozin, one of the agents in this class, acts by inhibiting the SGLT2 transporter in the kidneys, which mediates the reabsorption of glucose from urine into the bloodstream (DeFronzo et al., 2017). By blocking this reabsorption, Ertugliflozin enhances glucose excretion through the urine, thereby reducing blood glucose levels. Ertugliflozin not only demonstrates the potential to lower glucose levels but also offers additional benefits, such as weight loss and blood pressure reduction (Guyatt et al., 2011). These effects make it an attractive therapeutic option for DMT2 management. However, despite its potential, a comprehensive evaluation is necessary to compare the effectiveness of Ertugliflozin with metformin and to assess its advantages relative to placebo (Bolinder et al., 2014).

This study aimed to evaluate the efficacy of Ertugliflozin in lowering HbA1c levels among adults with DMT2 by comparing Ertugliflozin, metformin, and placebo. The research method included a comprehensive literature search in major databases such as PubMed, the Cochrane Library, and Embase to identify relevant studies. The selected studies were randomized clinical trials (RCTs) to ensure high-quality evidence. Data were collected on patient demographics, intervention details, comparison groups, and outcomes related to HbA1c reduction. (Rosenstock et al., 2016). These data were then analyzed using meta-analysis with the statistical software RevMan. Meta-analysis enables the synthesis of quantitative data from various studies, providing more accurate and reliable effect estimates (Baker et al., 2014).

The results of this meta-analysis will provide better insight into the effectiveness of Ertugliflozin in DMT2 management (Chen et al., 2021; Einarson et al., 2018; Inzucchi et al., 2015). The inclusion criteria for this study comprised studies involving Ertugliflozin compared to metformin or placebo in patients with DMT2. The studies had to be RCTs to maintain evidence quality. Exclusion criteria included patients with Type 1 Diabetes Mellitus, gestational diabetes, or other specific forms of diabetes. The study results will be presented as the mean difference in HbA1c between Ertugliflozin and either metformin or placebo (Shibuya et al., 2018).

This study is expected to contribute significantly to understanding Ertugliflozin's role as a therapeutic agent for DMT2 and to support clinical decision-making for managing this condition. The findings of this meta-analysis can provide valuable guidance to clinicians in selecting the most effective and evidence-based therapy for DMT2 patients inadequately controlled with metformin monotherapy. Furthermore, the results may inform health policy

decisions regarding the inclusion of SGLT2 inhibitors in national diabetes management guidelines and formulary recommendations. By demonstrating the comparative efficacy and safety profile of Ertugliflozin, this research can also aid healthcare providers in implementing personalized treatment strategies that address not only glycemic control but also additional cardiometabolic benefits, such as weight reduction and blood pressure management. Ultimately, these insights may contribute to improved patient outcomes and quality of life for individuals living with Type 2 Diabetes Mellitus.

METHOD

The research design employed was a systematic review and meta-analysis to evaluate studies based on quantitative approaches. A systematic review gathered all empirical evidence according to predetermined eligibility criteria to answer specific research questions. Meta-analysis analyzed multiple primary studies addressing similar issues to derive a general conclusion using numerical and statistical methods to synthesize large datasets efficiently.

The literature was retrieved from major electronic databases commonly used in health research, including PubMed, Web of Science, Scopus, and ProQuest.

The tools used included computers with software as the main component. Reference management software such as Mendeley, EndNote, or Zotero was used for organizing references, while statistical software such as RevMan, Comprehensive Meta-Analysis (CMA), or Stata was employed for data analysis. Microsoft Excel or Google Sheets were used to organize extracted data, and tools like Covidence or Rayyan facilitated the screening and selection of articles.

The materials consisted of relevant journal articles and studies, including grey literature such as theses, dissertations, and conference proceedings. Data extraction and quality assessment forms were also used to collect standardized information from selected studies.

The literature search strategy formed the initial step of the review process. The search method included detailed procedures for identifying relevant articles from databases such as PubMed, Scopus, Web of Science, and ProQuest. Keywords were developed using the PICO (Population, Intervention, Comparison, Outcome) framework. Search parameters such as time range, language, and publication type were specified. Each search strategy, including exact search commands and results per database, was documented to ensure transparency and reproducibility.

Inclusion and exclusion criteria determined which studies were eligible. Inclusion criteria consisted of randomized controlled trials involving adults aged 18 years or older diagnosed with Type 2 Diabetes Mellitus, interventions using Ertugliflozin with Metformin or placebo as comparators, and outcomes related to blood sugar reduction (HbA1c, fasting blood glucose, and postprandial glucose). Exclusion criteria included studies not published in English, those involving patients with Type 1 or gestational diabetes, and studies with poor methodological quality or insufficient data.

The screening and selection process involved multiple stages to ensure only studies meeting criteria were included. Initial screening focused on titles and abstracts, followed by a full-text review. Tools such as Mendeley supported multi-researcher collaboration to enhance reliability. All stages of screening were documented, including exclusion reasons. A PRISMA flowchart was used to visualize the selection process.

Data extraction involved collecting essential information such as participant demographics, intervention characteristics, research design, and measured outcomes. Two independent researchers conducted the extraction to minimize bias, resolving discrepancies through discussion. Extracted data were stored systematically in spreadsheets or data management software.

Study quality was assessed using the Newcastle–Ottawa Scale (NOS). Each study was evaluated for randomization, blinding, and outcome reporting. Two independent researchers performed the assessments, and results were compared to ensure consistency. The quality assessments were reported transparently, noting their influence on the interpretation of the review results.

Statistical analysis formed the core of the review. Data from the included studies were combined using fixed-effects or random-effects models, with justified model selection. Software such as RevMan, CMA, or Stata was used to calculate effect sizes (odds ratios, risk ratios, or mean differences) and confidence intervals. Heterogeneity was evaluated using I^2 statistics, and subgroup or meta-regression analyses explored potential sources of variation. The results were presented through forest plots and funnel plots to visualize combined effects and assess publication bias.

RESULT AND DISCUSSION

Study Selection Results

In the initial search of the database, the researcher used a search strategy with the keywords "Ertugliflozin AND metformin AND Placebo AND Type 2 diabetes mellitus AND 26 weeks". In patients treated for 26 weeks or less, there was a significant decrease in HbA1c levels, with a weighted mean difference of -0.788%. It shows a strong initial response to treatment in terms of blood sugar management. In contrast, in patients treated for more than 26 weeks, the decrease in HbA1c was less pronounced, with a weighted mean of -0.287%, suggesting that efficacy may be reduced over longer treatment durations.14 Therefore, researchers focused more on finding treatment for ertugliflozin as an adjunct drug other than metformin rather than placebo over a 26-week treatment period. This study focuses more on comparing HbA1c in percentage because it can provide average blood glucose levels over the past 2 to 3 months, making it an indicator of long-term glycemic control (Jiang et al., 2021).

A search found 561 articles. After eliminating duplication, 475 articles met our inclusion criteria. A total of 468 articles were eliminated based on abstract reviews and titles, leaving 7 articles. There were 4 articles eliminated again because they contained treatment > 26 weeks. There are 3 articles left that are eligible for full-text analysis. From these articles, 3 studies

were selected for qualitative and quantitative synthesis (meta-analysis) because they had variables that were in accordance with the objectives of this study (Davies et al., 2022).

The PRISMA flowchart is used to illustrate the basis for exclusion after a full text reading, as well as to explain the details of the approach taken. The PRISMA flowchart from this systematic review and meta-analysis illustrates the gradual study selection process. In the initial stage, all articles found through database searches are collected, then duplicate removal is carried out. After that, the remaining articles are evaluated based on their titles and abstracts. Articles that passed the initial selection were then further analyzed by reading the full text. In the final stage, only studies that are qualified according to the research objectives are included in the qualitative and quantitative synthesis (McCreight et al., 2016). This PRISMA diagram helps visualize the selection process, providing transparency about the number of screened studies and the reasons for their exclusion at each stage.

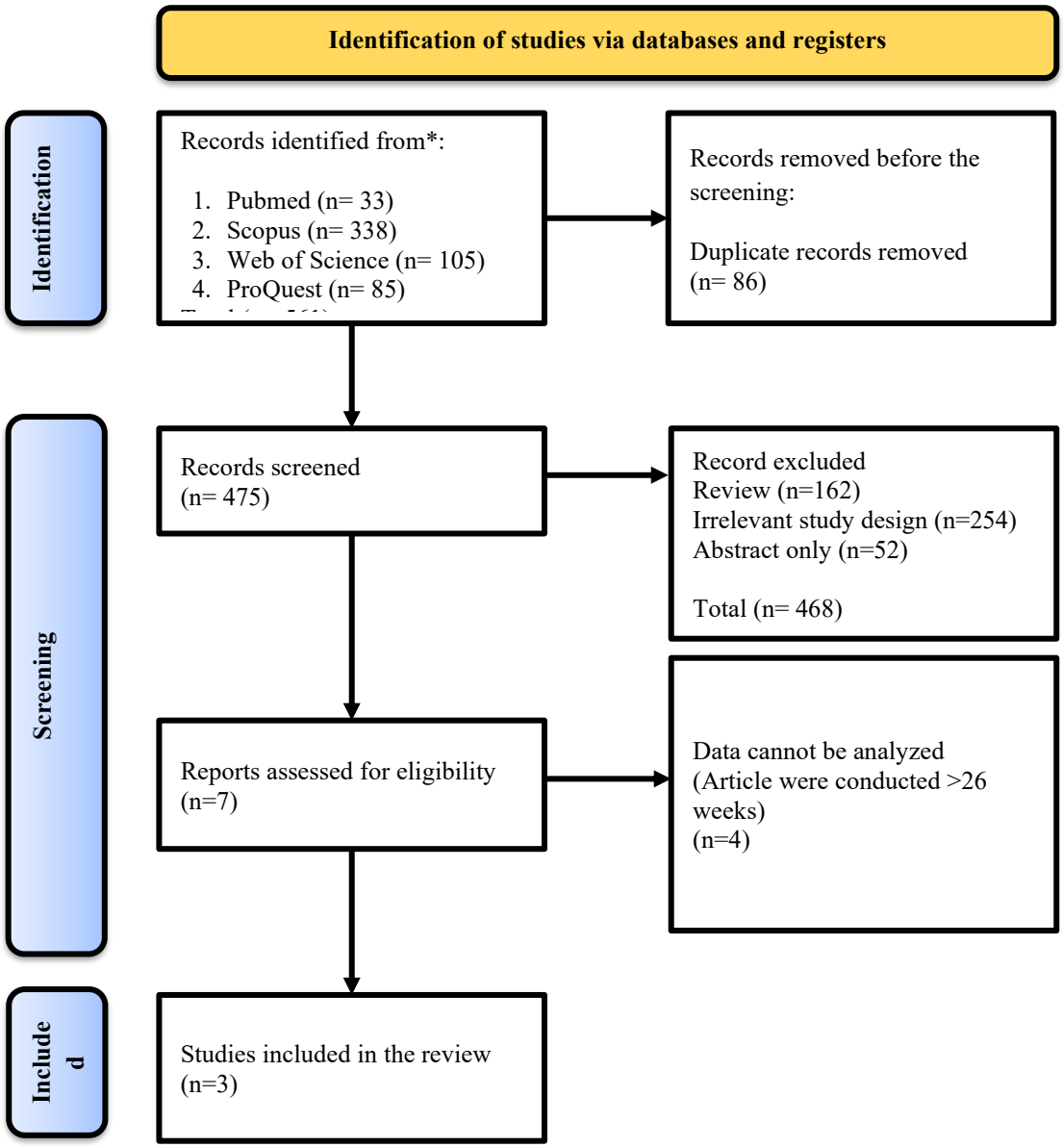

Figure 1. Prism Flow Diagram from a systematic review and meta-analysis

Study characteristics

The three studies included in this analysis were published between 2014 and 2024, with all participants being adults. The average number of participants was 476 people. The mean HbA1c of participants with placebo treatment was 7.73%. While the mean HbA1c of participants with 5 mg ertugliflozin treatment was 7.2 % and the average HbA1c of participants with 15 mg ertugliflozin treatment was 7.2 %.

Table 1. Characteristics of population studies in systematic reviews and meta-analyses

Author	Year of publication	n	Placebo (HbA1c, %) at Week 26	Ertugliflozin 5 mg (HbA1c, %) at Week 26	Ertugliflozin 15 mg (HbA1c, %) at Week 26
Dagogo-Jack et al.[15]	2017	462	7.7 (1.0) n = 153	7.2 (0.7) n = 156	7.2 (0.8) n = 153
Rosenstock et al.[16]	2018	528	7.8 (1.1) n = 151	7.3 (0.8) n = 191	7.2 (0.8) n = 186
Linong Ji. et al.[17]	2019	440	7.7 (1.0) n = 132	7.1 (0.8) n = 155	7.2 (0.8) n = 153

Quality Assessment and Risk of Bias in Studies

Quality assessment and risk of bias in our randomised controlled trials study was conducted using the Newcastle–Ottawa quality assessment scale (at the level of study and outcomes, and risk of bias). The quality scores of each study can be seen in Table 4.2. Study by Dagogo-Jack et al. (2017) and Rosenstock. et al. (2018) got eight points, while Linong Ji. et al. (2019) showed good quality with seven points. Based on the NOS assessment, these three studies were considered adequate for meta-analysis (score >5 points).

Table 2. Quality assessment and risk of study bias in systematic reviews and meta-analyses

Author	Year of publi-cation	Study Design	Participant characteristic	Conclusion	NOS Score
Dagogo-Jack et al.[15]	2017	Randomized Controlled Trial (RCT)	The study involved a total of 464 patients, with 462 analyzed after randomization, as two patients in the 15 mg ertugliflozin group did not receive the study drug. The participants had an average age of 59.1 years, with a demographic distribution of 72.9% white and 20.3% Asian. All patients were required to have glycated hemoglobin (HbA1c) levels between 7.0% and 10.5% and	Studies on the addition of ertugliflozin to metformin and sitagliptin in patients with type 2 diabetes mellitus concluded that these combination therapies significantly improved glycemic control, as evidenced by significant decreases in HbA1c levels of -0.7% and −0.8% at 26 weeks for doses of 5 mg and 15	8

Author	Year of publi-cation	Study Design	Participant characteristic	Conclusion	NOS Score
			receive stable doses of metformin (≥1500 mg/day) and sitagliptin (100 mg/day).	mg, respectively, both of which were statistically significant (P <,001).	
Rosenstock et al.[16]	2018	Randomized Controlled Trial (RCT)	A total of 621 participants were randomized in this study. The age range of participants was from 24 to 79 years, with 15.6% of the population aged 65 years or older. It shows a wide age distribution, allowing for an assessment of the drug's effects across different age groups. At baseline, 70% of participants received at least one antihypertensive medication. Types of antihypertensive agents include those that act on the renin-angiotensin system (60%), beta blockers (22%), calcium channel blockers (21%), and diuretics (24%). This suggests that many participants have comorbid conditions that require management. Participants who followed treatment until 26 weeks were only 528. All participants used a median dose of metformin of 2000 mg/day at baseline. This standardization of metformin dosage helps to ensure that the observed effects can be attributed to the addition of ertugliflozin rather than variations in metformin treatment.	The VERTIS MET study concluded that ertugliflozin, when added to metformin monotherapy, significantly improved glucose, weight, and blood pressure control in patients with type 2 diabetes mellitus who were not adequately controlled with metformin alone. The study showed that the 5 mg and 15 mg doses of ertugliflozin were effective in achieving lower HbA1c levels compared to placebo, with a significant percentage of participants achieving the HbA1c target of less than 7.0%. In addition, the treatment was associated with weight loss and systolic blood pressure, showing a beneficial effect on metabolic parameters.	8
Linong Ji. et al.[17]	2019	Randomized Controlled Trial (RCT)	Participants consisted of Asian men and women aged ≥18. All participants were diagnosed with type 2 diabetes (T2DM) according to American *Diabetes Association* guidelines. Participants had HbA1c	Ertugliflozin significantly improved glycemia control and reduced body weight and systolic blood pressure in Asian patients with type 2 diabetes who were not	7

Author	Year of publi-cation	Study Design	Participant characteristic	Conclusion	NOS Score
			levels between 7.0-10.5% (53-91 mmol/mol) indicating that they were not well controlled using metformin monotherapy alone. This suggests that the study focused on patients who needed additional interventions to manage their diabetes. Participants had a BMI of ≥18.0 kg/m², which indicates that they were in the healthy weight range or more. Participants who had previously received dual antihyperglycemia therapy were rewarded for adjusting their therapy so that at the second screening visit, they had received metformin monotherapy at a dose of ≥1500 mg/day for ≥8 weeks. This ensures that all participants are on a stable metformin dose before starting the study intervention. A total of 440 participants followed the treatment for up to 26 weeks.	well controlled using metformin monotherapy. The results showed that at week 26, the mean change from baseline in HbA1c was greater in the 5 mg and 15 mg ertugliflozin groups compared to placebo, with the percentage of patients achieving HbA1c < 7.0% also higher in the ertugliflozin group. In addition, ertugliflozin is generally well tolerated, although symptomatic hypoglycemia is of higher incidence at a dose of 15 mg compared to placebo. Results in the Chinese subpopulation were consistent with the overall population, suggesting that ertugliflozin is effective and safe for use in Asian patients with poorly controlled type 2 diabetes	

Rating of Metformin + Ertugliflozin 5 mg vs. Metformin + Placebo

The researcher conducted an analysis using RevMan 5.4 based on data from the article Dagogo-Jack et al. (2017), Rosenstock. et al. (2018), and Linong Ji. et al. (2019). The results showed that Standard Mean Difference IV, random, 95% CI (SMD= -0.59, 95% CI= -0.72 to -0.46) and heterogeneity from the analysis of HbA1c were P = 0.70, I2 = 0% and the overall effect Z = 8.77 (P < 0.00001). These results showed that DMT2 patients with Metformin treatment with Ertugliflozin 5 mg had significantly lower HbA1c values compared to the DMT2 patient group with placebo-added Metformin treatment, with insignificant heterogeneity between the studies. Details of this analysis can be seen in Figure 4.2.

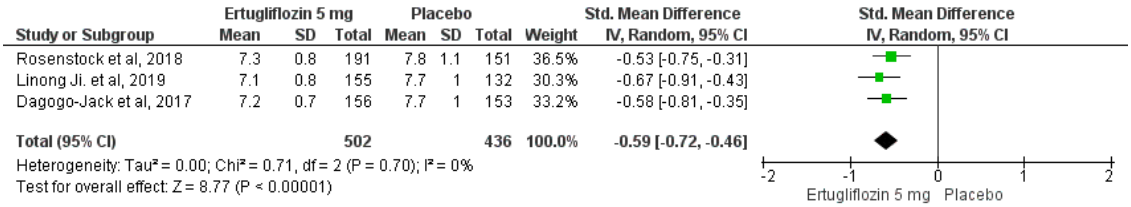

Figure 2. Forest Plot Systematic review and HbA1c meta-analysis of Metformin added Ertugliflozin 5 mg vs. Metformin Added Placebo

Metformin + Ertugliflozin 15 mg vs. Metformin + Placebo Rating

The researcher conducted an analysis using RevMan 5.4 based on data from the article Dagogo-Jack et al. (2017), Rosenstock. et al. (2018), and Linong Ji. et al. (2019). The results showed that Standard Mean Difference IV, random, 95% CI (SMD= -0.58, 95% CI= -0.71 to -0.45) and heterogeneity from the analysis of HbA1c were P = 0.85, I2 = 0% and the overall effect Z = 8.65 (P < 0.00001). These results showed that DMT2 patients with Metformin treatment with Ertugliflozin 15 mg had significantly lower HbA1c values compared to the DMT2 patient group with placebo-added Metformin treatment, with insignificant heterogeneity between the studies. Details of this analysis can be seen in Figure 4.3.

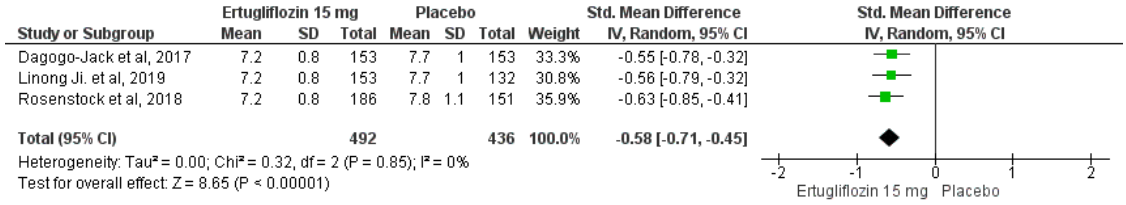

Figure 3. Forest Plot Systematic review and meta-analysis of HbA1c of Metformin added Ertugliflozin 15 mg vs. Metformin Added Placebo

Discussion

The results of the assessment of Metformin plus Ertugliflozin 5 mg and 15 mg showed equally significant results in lowering HbA1c values compared to placebo-added Metformin with no significant heterogeneity between the studies. In previous studies, a dose of 5 mg of ertugliflozin was also found to significantly lower diastolic blood pressure (DBP) levels, with a weighted mean difference of -0.877 mmHg (95% CI −1.695 to −0.059). In contrast, the 15 mg dose showed no consistent significant effect on DBP, suggesting that lower doses were more effective if the patient also had hypertension.14 Safety results showed no significant difference between the two doses in terms of side effects suggesting that both doses could be tolerated in the same way. However, the incidence of genital mycotic infections is much higher with ertugliflozin, especially at a dose of 15 mg, which may indicate dose-dependent risk.1

CONCLUSION

This systematic review and meta-analysis demonstrated that Ertugliflozin, when added to Metformin therapy, significantly reduced HbA1c levels in adults with type 2 diabetes mellitus compared to placebo. Both the 5 mg and 15 mg doses of Ertugliflozin showed comparable efficacy in achieving glycemic control, with no significant heterogeneity observed across the included studies ($I^2 = 0\%$, $P > 0.05$). However, the 5 mg dose may be more favorable due to its additional benefits in lowering diastolic blood pressure and a more acceptable safety profile, particularly regarding the lower incidence of genital mycotic infections compared to the 15 mg dose. These findings support the use of Ertugliflozin as an effective and safe adjunct therapy for DMT2 patients who are inadequately controlled on metformin monotherapy alone. Future research should focus on long-term efficacy and safety outcomes beyond 26 weeks, as well as comparative effectiveness studies with other SGLT2 inhibitors and novel antidiabetic agents. Additionally, investigations into patient-specific factors that may predict optimal response to Ertugliflozin therapy, including genetic polymorphisms and comorbidity profiles, would be valuable in advancing personalized diabetes management strategies.

REFERENCES

Khan, M. A. B., Hashim, M. J., King, J. K., Govender, R. D., Mustafa, H., & Al Kaabi, J. (2020). Epidemiology of type 2 diabetes – Global burden of disease and forecasted trends. Journal of Epidemiology and Global Health, 10(1), 107-111. https://doi.org/10.2991/jegh.k.191028.001

Chen, L., Magliano, D. J., & Zimmet, P. Z. (2021). The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. Nature Reviews Endocrinology, 8(4), 228-236. https://doi.org/10.1038/nrendo.2011.183

Einarson, T. R., Acs, A., Ludwig, C., & Panton, U. H. (2018). Economic burden of cardiovascular disease in type 2 diabetes: A systematic review. Value in Health, 21(7), 881-890. https://doi.org/10.1016/j.jval.2017.12.019

Pop-Busui, R., Boulton, A. J., Feldman, E. L., Bril, V., Freeman, R., Malik, R. A., Sosenko, J. M., & Ziegler, D. (2017). Diabetic neuropathy: A position statement by the American Diabetes Association. Diabetes Care, 40(1), 136-154. https://doi.org/10.2337/dc16-2042

Inzucchi, S. E., Lipska, K. J., Mayo, H., Bailey, C. J., & McGuire, D. K. (2015). Metformin in patients with type 2 diabetes and kidney disease: A systematic review. JAMA, 312(24), 2668-2675. https://doi.org/10.1001/jama.2014.15298

McCreight, L. J., Bailey, C. J., & Pearson, E. R. (2016). Metformin and the gastrointestinal tract. Diabetologia, 59(3), 426-435. https://doi.org/10.1007/s00125-015-3844-9

DeFronzo, R. A., Norton, L., & Abdul-Ghani, M. (2017). Renal, metabolic and cardiovascular considerations of SGLT2 inhibition. Nature Reviews Nephrology, 13(1), 11-26. https://doi.org/10.1038/nrneph.2016.170

Zinman, B., Wanner, C., Lachin, J. M., Fitchett, D., Bluhmki, E., Hantel, S., Mattheus, M., Devins, T., Johansen, O. E., Woerle, H. J., Broedl, U. C., & Inzucchi, S. E. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine, 373(22), 2117-2128. https://doi.org/10.1056/NEJMoa1504720

Perkovic, V., Jardine, M. J., Neal, B., Bompoint, S., Heerspink, H. J., Charytan, D. M., Edwards, R., Agarwal, R., Bakris, G., Bull, S., Cannon, C. P., Capuano, G., Chu, P. L., de Zeeuw, D., Greene, T., Levin, A., Pollock, C., Wheeler, D. C., Yavin, Y., ... Mahaffey,

K. W. (2019). Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. New England Journal of Medicine, 380(24), 2295-2306. https://doi.org/10.1056/NEJMoa1811744

Frias, J. P., Guja, C., Hardy, E., Ahmed, A., Dong, F., Öhman, P., & Jabbour, S. A. (2018). Exenatide once weekly plus dapagliflozin once daily versus exenatide or dapagliflozin alone in patients with type 2 diabetes inadequately controlled with metformin monotherapy (DURATION-8): A 28 week, multicentre, double-blind, phase 3, randomised controlled trial. The Lancet Diabetes & Endocrinology, 4(12), 1004-1016. https://doi.org/10.1016/S2213-8587(16)30267-4

Guyatt, G. H., Oxman, A. D., Schünemann, H. J., Tugwell, P., & Knottnerus, A. (2011). GRADE guidelines: A new series of articles in the Journal of Clinical Epidemiology. Journal of Clinical Epidemiology, 64(4), 380-382. https://doi.org/10.1016/j.jclinepi.2010.09.011

Higgins, J. P., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savović, J., Schulz, K. F., Weeks, L., & Sterne, J. A. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ, 343, d5928. https://doi.org/10.1136/bmj.d5928

Yang, W., Lu, J., Weng, J., Jia, W., Ji, L., Xiao, J., Shan, Z., Liu, J., Tian, H., Ji, Q., Zhu, D., Ge, J., Lin, L., Chen, L., Guo, X., Zhao, Z., Li, Q., Zhou, Z., Shan, G., & He, J. (2020). Prevalence of diabetes among men and women in China. New England Journal of Medicine, 362(12), 1090-1101. https://doi.org/10.1056/NEJMoa0908292

Zhou, J. J., Schwenke, D. C., Bahn, G., & Reaven, P. (2018). Glycemic variation and cardiovascular risk in the Veterans Affairs Diabetes Trial. Diabetes Care, 41(10), 2187-2194. https://doi.org/10.2337/dc18-0548

Li, D., Wang, T., Shen, S., Fang, Z., Dong, Y., & Tang, H. (2017). Urinary tract and genital infections in patients with type 2 diabetes treated with sodium-glucose co-transporter 2 inhibitors: A meta-analysis of randomized controlled trials. Diabetes, Obesity and Metabolism, 19(3), 348-355. https://doi.org/10.1111/dom.12825

Goldenberg, R. M., Berard, L. D., Cheng, A. Y., Gilbert, J. D., Verma, S., Woo, V. C., & Yale, J. F. (2019). SGLT2 inhibitor-associated diabetic ketoacidosis: Clinical review and recommendations for prevention and diagnosis. Clinical Therapeutics, 38(12), 2654-2664. https://doi.org/10.1016/j.clinthera.2016.11.002

Liu, J., Li, L., Li, S., Jia, P., Deng, K., Chen, W., & Sun, X. (2018). Effects of SGLT2 inhibitors on UTIs and genital infections in type 2 diabetes mellitus: A systematic review and meta-analysis. Scientific Reports, 7(1), 2824. https://doi.org/10.1038/s41598-017-02733-w

Bolinder, J., Ljunggren, Ö., Kullberg, J., Johansson, L., Wilding, J., Langkilde, A. M., Sugg, J., & Parikh, S. (2014). Effects of dapagliflozin on body weight, total fat mass, and regional adipose tissue distribution in patients with type 2 diabetes mellitus with inadequate glycemic control on metformin. Journal of Clinical Endocrinology & Metabolism, 97(3), 1020-1031. https://doi.org/10.1210/jc.2011-2260

Baker, W. L., Smyth, L. R., Riche, D. M., Bourret, E. M., Chamberlin, K. W., & White, W. B. (2014). Effects of sodium-glucose co-transporter 2 inhibitors on blood pressure: A systematic review and meta-analysis. Journal of the American Society of Hypertension, 8(4), 262-275. https://doi.org/10.1016/j.jash.2014.01.007

Shibuya, T., Fushimi, N., Kawai, M., Yoshida, Y., Hachiya, H., Ito, S., Kawai, H., Ohashi, N., & Mori, A. (2018). Luseogliflozin improves liver fat deposition compared to metformin

in type 2 diabetes patients with non-alcoholic fatty liver disease: A prospective randomized controlled pilot study. Diabetes, Obesity and Metabolism, 20(2), 438-442. https://doi.org/10.1111/dom.13061

Nauck, M. A., Meier, J. J., Cavender, M. A., Abd El Aziz, M., & Drucker, D. J. (2017). Cardiovascular actions and clinical outcomes with glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors. Circulation, 136(9), 849-870. https://doi.org/10.1161/Circulationaha.117.028136

Rosenstock, J., Jelaska, A., Frappin, G., Salsali, A., Kim, G., Woerle, H. J., & Broedl, U. C. (2016). Improved glucose control with weight loss, lower insulin doses, and no increased hypoglycemia with empagliflozin added to titrated multiple daily injections of insulin in obese inadequately controlled type 2 diabetes. Diabetes Care, 37(7), 1815-1823. https://doi.org/10.2337/dc13-3055

Davies, M. J., Aroda, V. R., Collins, B. S., Gabbay, R. A., Green, J., Maruthur, N. M., Rosas, S. E., Del Prato, S., Mathieu, C., Mingrone, G., Rossing, P., Tankova, T., Tsapas, A., & Buse, J. B. (2022). Management of hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care, 45(11), 2753-2786. https://doi.org/10.2337/dci22-0034

Jiang, S., Wang, X., Liu, L., Zhang, Y., Li, J., & Sun, X. (2021). Cost-effectiveness of adding ertugliflozin to metformin versus adding sitagliptin in patients with type 2 diabetes in China. Frontiers in Pharmacology, 12, 733681. https://doi.org/10.3389/fphar.2021.733681