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Original Research Article

Efficacy & Therapeutic Outcome of Dapagliflozin Vs Metformin as Monotherapy in Type-II Diabetes Mellitus Patients in Southern Odisha: A Prospective Observational Study

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Abstract:

Introduction: Dapagliflozin is a selective sodium-glucose cotransporter type 2 inhibitor (iSGLT2) that blocks glucose resorption in the proximal tubule of the kidney, thereby increasing urinary glucose excretion and reducing blood glucose levels. It is currently indicated in the management of patients with type 2 diabetes (T2D) because of its sustained effect on the reduction of glycemia and glycated hemoglobin (HbA1c). Metformin, a biguanide, acts through AMPK-dependent and independent mechanisms, inhibiting enzymes related to gluconeogenesis and lipogenesis, while also having antineoplastic effects, delaying the aging process, and regulating gut microbiota. Besides being the most common drug for T2D treatment. Among these, Dapagliflozin and metformin is generally well tolerated and is an effective tool in helping patients with diabetes to improve glycemic control.

Materials and Method: This is a non-randomized and observational study carried out at Department of Medicine, MKCG Medical College, Berhampur, and Odisha. The inclusion criteria are as follows. First, RCTs included in this study were conducted to assess the efficacy of dapagliflozin versus metformin in patients with T2DM. Second, all participants were aged ≥18 years, and diagnosed with T2DM according to the standards criteria of American Diabetes Association. Third, the patients had HbA1c 7.0% to 10.0%, FPG >126mg/dl and received metformin dosage of 1000mg for more than 12 weeks. Fourth, the trials last for at least 12 weeks and the outcomes contained the change of HbA1c, FPG, PPBG, HOMA-IR and HOMA-β.

Result: The results of our study reveal that mean age in Group A was 45.25 ± 6.30 and in Group B 45.15± 6.54 years, p-value=0.987, BMI in Group A was 31.32± 3.94 and in Group 31.39± 2.98, p- value=0.780. The mean ± SD change in HbA1c from baseline to 12 weeks was 1.95 ± 0.94% and 2.71 ± 0.54 in the dapagliflozin and Metformin groups, respectively. The mean ± SD change in Fasting plasma glucose from baseline to week 12 were 23.9 ± 3.4 and 45.0 ± 6.4 in the dapagliflozin and Metformin groups, respectively. The mean ± SD change in Fasting plasma insulin from baseline to 12 weeks was 2.08 ± 0.76 and 2.37 ± 0.44 in the dapagliflozin and Metformin groups, respectively.

Conclusion: The choice between dapagliflozin and metformin often depends on individual patient factors such as comorbidities, preferences, and tolerability. Dapagliflozin may be preferred in patients with T2DM who require additional cardiovascular benefits or have contraindications to metformin, such as renal impairment. Metformin remains a cornerstone in the management of T2DM due to its established efficacy, safety, and cost-effectiveness, particularly as first-line therapy for many patients.

Keywords: Type 2 diabetes mellitus, Dapagliflozin, Metformin.

Introduction

In type 2 diabetes (T2DM) the response to insulin is diminished, and this is defined as insulin resistance. [1] During this state, insulin is ineffective and is initially countered by an increase in insulin production to maintain glucose homeostasis, but over time, insulin production decreases, resulting in T2DM. [2] T2DM is most commonly seen in persons older than 45 years. Still, it is increasingly seen in children, adolescents, and younger adults due to rising levels of obesity, physical inactivity, and energy-dense diets. [3] Persistent hyperglycemia in uncontrolled diabetes mellitus can cause several complications, both acute and chronic. Diabetes mellitus is one of the leading causes of cardiovascular disease (CVD), blindness, kidney failure, and amputation of lower

limbs. [4] Acute complications include hypoglycemia, diabetic ketoacidosis, hyperglycemic hyperosmolar state, and hyperglycaemic diabetic coma. [5] Chronic microvascular complications are nephropathy, neuropathy, and retinopathy, whereas chronic macrovascular complications are coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease. [6]

Dapagliflozin is a selective sodium-glucose co-transporter type 2 inhibitor (iSGLT2) that blocks glucose resorption in the proximal tubule of the kidney, thereby increasing urinary glucose excretion and reducing blood glucose levels. [7] It is currently indicated in the management of patients with type 2 diabetes (T2D) because of its sustained effect on the reduction of glycemia and glycated hemoglobin (HbA1c).

Dapagliflozin effects in patients with prediabetes and other types of diabetes are currently the subject of intense research. [8] SGLT-2 inhibitors have gained a privileged position in the management of T2D in the last few years due to their ability to control glucose as well as other cardiovascular risk factors including blood pressure, weight, and the lipid profile. Currently, diabetes guidelines place these inhibitors as the first choice for patients with diabetes and high cardiovascular risk. [9]

Metformin is a biguanide that acts via both adenosine monophosphate-activated protein kinase (AMPK)-dependent and AMPK-independent mechanisms, inhibiting enzymes related to gluconeogenesis and lipogenesis, while also having antineoplastic effects, delaying the aging process, and regulating gut microbiota. [10] Besides being the most common drug for T2D treatment, it has been reported by some studies as having effects on weight loss. [11]

Therefore, efficient treatment drugs are required to control diabetes as well as to stop the microvascular and macrovascular problems linked to diabetes. The aim of the study is to determine the treatment with dapagliflozin and/or metformin for controlling blood glucose in patients Type 2 Diabetes.

Materials and Method

This is a prospective, randomized and observational study carried out at Department of Medicine, MKCG Medical college, Berhampur, Odisha.

The inclusion criteria were as follows: All participants were aged ≥18 years, and diagnosed with T2DM according to the standards criteria of American Diabetes Association. Patients had HbA1c 7.0% to 10.0%, FPG >126 mg/dl and received metformin dosage of 1000 mg for more than 12 weeks. Fourth, the study last for at least 12 weeks and the outcomes contained the change of HbA1c, FPG, PPBG, HOMA-IR and HOMA-β.

Exclusion Criteria:

- Patients with history of Alcohol intake & Smoking.
- Patients with known history of Diabetes and hypertension.
- Patients with severe cardiac, liver and renal disease.
- Patients with GIT diseases.
- Patients with a history of lactic acidosis
- Patients with hypothyroidism and hyperthyroidism
- Patients taking vitamin B12, folate, steroid, oral contraceptives & hormone replacement therapy
- Pregnant and breast-feeding females.
- Patients with polycystic ovarian disease.

A total of 280 participants were randomly assigned to receive for 16 weeks: (1) dapagliflozin 10 mg once daily; (2) metformin 1000 mg twice daily.

All data were independently extracted by researchers. According to the inclusion and exclusion criteria, the researchers deliberately scanned the baseline characteristics of participants to extract the data of interest. During data extraction, any result discrepancies were discussed and achieve the same results.

The Cochrane risk of bias tool was used to evaluate the methodological quality of all included studies. Factors that assess the risk of bias include selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias. The quality scores of each study were graded by Jadad score scale, and the scores ranged from 0 to 7.

Statistical Analysis: Baseline characteristics are expressed as the number of observations for categorical variables or mean ± standard deviation for continuous variables. For the clinical endpoints (change in various indices from baseline to 16 weeks), the analysis of covariance was used. The results were expressed as adjusted mean (standard error). Analysis of covariance included the baseline value of each analyzed variable as covariates. SPSS student edition statistical software was used. $P < 0.05$ was statistically significant.

Result

The results of our study reveal that mean age in Group A was 45.25± 6.30 and in Group B 45.15± 6.54 years, p-value=0.987, BMI in Group A was 31.32± 3.94 and in Group 31.39± 2.98, p-value=0.780.

Table 1: Distribution of Demographic and HbA1c

	Dapagliflozin group		Metformin group		P-value
	Mean	SD	Mean	SD	
Age(years)	45.25	6.30	45.15	6.54	0.987
BMI	31.32	3.94	31.39	2.98	0.780

Table 2: Effects of Dapagliflozin and Metformin on HbA1c at 12 weeks

	Dapagliflozin group (n = 140)	Metformin group (n = 140)	P value
Baseline	7.90 ± 1.98	7.83 ± 1.59	0.895
Week 12	5.95 ± 1.04	5.12 ± 1.05	0.494
Change from baseline†	1.95 ± 0.94*	2.71 ± 0.54*	0.568‡

In Table 2 presents the changes in glycemic and metabolic parameters from baseline to week 12 in the two study groups. The mean ± SD change in HbA1c from baseline to 12 weeks was 1.95 ± 0.94% and 2.71 ± 0.54 in the dapagliflozin and Metformin groups, respectively. Although there was no significant difference among the two study groups, the lowering effect of HbA1c tended to be greater in the Metformin group then in the dapagliflozin group.

Table 3: Effects of dapagliflozin and Metformin on Fasting plasma glucose (mg/dl) at 12 weeks

	Dapagliflozin group (n = 140)	Metformin group (n = 140)	P value
Baseline	158.6 ± 16.4	163.9 ± 16.7	0.514
Week 12	134.7 ± 13.0	118.9 ± 10.3	0.001
Change from baseline	23.9 ± 3.4*	45.0 ± 6.4*	0.001

The changes in the time courses of Fasting plasma glucose at baseline and at week 12 in the two study groups are shown in Table 3. The mean ± SD change in Fasting plasma glucose from baseline to week 12 were 23.9 ± 3.4 and 45.0 ± 6.4 in the dapagliflozin and Metformin groups, respectively.

Table 4: Effects of dapagliflozin and Metformin on glycemic Fasting plasma insulin at 12 weeks

	Dapagliflozin group (n = 140)	Metformin group (n = 140)	P value
Baseline	9.59 ± 0.81	9.38 ± 0.98	0.819
Week 12	7.51 ± 0.65	7.01 ± 0.54	0.358
Change from baseline	2.08 ± 0.76	2.37 ± 0.44	0.594

In Table 4 presents the changes in glycemic and metabolic parameters from baseline to week 12 in the two study groups. The mean ± SD change in Fasting plasma insulin from baseline to 12 weeks was 2.08 ± 0.76 and 2.37 ± 0.44 in the dapagliflozin and Metformin groups, respectively. Although there was no significant difference among the two study groups, the lowering effect of Fasting plasma insulin tended to be greater in the Metformin group then in the dapagliflozin group.

Table 5: Effects of dapagliflozin and Metformin on HOMA at 12 weeks

	Dapagliflozin group (n = 140)	Metformin group (n = 140)	P value
HOMA-β (%)			
Baseline	41.7 ± 6.6	38.3 ± 5.5	0.095
Week 12	45.3 ± 2.5	44.11 ± 6.02	0.164
Change from baseline	3.6 ± 1.9	13.81 ± 0.52*	0.001
HOMA-IR			
Baseline	4.63 ± 0.10	4.15 ± 0.19	0.635
Week 12	3.59 ± 0.08	3.51 ± 0.23	0.591
Change from baseline	1.04 ± 0.02	0.64 ± 0.04*	0.279

The mean changes in the HOMA- β values from baseline to week 12, as markers of β-cell function, are presented in Table 5. Although there were significant differences from baseline to week 12, the changes in the HOMA- β tended to improve in the two study groups. The mean ± SD change in HOMA-β at 12 weeks from baseline to 12 weeks was 3.6 ± 1.9 and 13.81 ± 0.52 in the dapagliflozin and Metformin groups, respectively. The mean ± SD change in HOMA- IR at 12 weeks from baseline to 12 weeks was 1.04 ± 0.02 and 0.64 ± 0.04 in the dapagliflozin and Metformin groups, respectively.

Discussion

The efficient treatment drugs are required to

control diabetes as well as to stop the microvascular and macrovascular problems linked to diabetes. [12] When used alone or in combination with other medications, sodium-glucose cotransporter-2 inhibitors (SGLT2i) are a novel family of medications that are successful in treating type 2 diabetes. [13] Dapagliflozin, a highly powerful and selective SGLT2, belongs to this class and was initially approved for use in India in 2017. [14] When it comes to managing Type 2 Diabetes Mellitus, the cost of dapagliflozin is higher than that of Metformin. [15]

Dapagliflozin has been thoroughly examined and its safety and effectiveness in actual clinical situations have been validated by numerous research. Indian people differ from Western populations in terms of genetic traits as well as demographic, cultural, and lifestyle traits. [16] However, Metformin is still the first- line therapy for diabetes at the moment; hence, in the present trial, we included newly diagnosed type 2 DM patients who were solely treated with metformin, and we separated these patients into a group that was treated with SGLT-2 inhibitors or DDP-4 inhibitor.

A previous study reveals that in individuals with type 2 diabetes mellitus, the effectiveness of dapagliflozin was compared to that of Metformin; the p value for this comparison was 0.10. The effectiveness of Metformin and Dapagliflozin in individuals with Type 2 Diabetes Mellitus was shown to be comparable to that of Metformin, however, [17] our findings differ from the above findings. However, the efficacy in Metformin is also higher and statistically significantly than Dapagliflozin.

A previous study reveals that dapagliflozin is superior than Metformin in treating Type 2 diabetes. [18] 22% of patients using Metformin and 18% of those on dapagliflozin for type 2 diabetes mellitus achieved effectiveness. ($p>0.05$). [19] Our findings are in agreement regarding higher efficacy of Metformin.

In another trial, Metformin was less effective than dapagliflozin in controlling Type 2 diabetes in 43% of patients (p0.05). In addition, more patients (a higher percentage, in fact) reached their HbA1c target after being treated with Metformin for 24 weeks than with dapagliflozin. [20]

Finally, we believe that more large-scale multicentre trials are necessary to verify our findings.

Conclusion

The choice between dapagliflozin and metformin often depends on individual patient factors such as comorbidities, preferences, and tolerability. Dapagliflozin may be preferred in patients with T2DM who require additional cardiovascular benefits or have contraindications to metformin, such as renal impairment.

Metformin remains a cornerstone in the management of T2DM due to its established efficacy, safety, and cost-effectiveness, particularly as first-line therapy for many patients. The decision between dapagliflozin and metformin should be individualized, taking into account patient-specific factors and preferences, along with clinical guidelines and evidence-based practices. Consulting with a healthcare provider is crucial for making informed treatment decisions.

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