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Original Research Article

An observational study on dapagliflozin as an add-on therapy in type-2 diabetes mellitus patients in a tertiary care teaching hospital

Venugopal Reddy M.[1]*, Christina Sahayaraj[1], Shaik Haseena Begum[1], Sharon Sonia S.[2], Vijayabhaskar Reddy Y.[1]

[1]Department of Pharmacology, Kurnool Medical College, Kurnool, Andhra Pradesh, India
[2]Department of Pharmacology, Government Medical College, Anantapur, Andhra Pradesh, India

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***Correspondence:**
Dr. Venugopal Reddy M.,
Email: drvenugopal23@gmail.com

ABSTRACT

Background: Diabetes mellitus is one of the prevalent morbid conditions all over the world and no exception for India. Day by day, increase in its prevalence is attributed to lifestyle derangements. To treat this condition many drugs and treatment modalities are developed. Dapagliflozin is an oral antidiabetic drug which acts by sodium-glucose cotransport-2 (SGLT-2) inhibition. Its effectiveness seen in type-2 diabetes mellitus makes it an option for Add-On therapy.
Methods: This study is a retrospective observational study conducted at tertiary care hospital, GGH, Kurnool. The study proposal has been reviewed and approved by institutional ethics committee. All adult diabetic patients who were prescribed Dapagliflozin during the period of January 2021 to February 2022, total 45 were included in the study. FBG, HbA1c collected through hospital records from General Medicine and Endocrinology. Patients who stopped drug before 3 months period were excluded.
Results: Administration of dapagliflozin as an add-on therapy was found 26.63% decrease in base line mean FBG 184 mg/dl to 135 mg/dl after 3mnoths which is significant (p=0.001). Mean HbA1c significantly reduced by 0.96 percentage point after 3 months (p=0.001). Dapagliflozin effectively reduced the FBG and HbA1c when used in combination with other OHAs or insulin within 3 months.
Conclusions: Dapagliflozin as an add-on therapy significantly reduced the HbA1c level and fasting blood glucose of Type-2DM patients, in a 3-month treatment period. Due to the frequency of Genitourinary tract infections, caution is indicated while treating the patients.

Keywords: Dapagliflozin, SGLT-2 Inhibitor, Type-2DM, FBG, HbA1c

INTRODUCTION

Diabetes mellitus (DM) is one of the prevalent morbid conditions all over world and India. Day by day, increase in its prevalence is attributed to lifestyle derangements.[1] Type 2 DM is a metabolic disorder that is characterized by high blood glucose due to insulin resistance and relative insulin deficiency. The classic symptoms are excess thirst, frequent urination, and constant hunger. To treat this condition many drugs and treatment modalities are developed. Dapagliflozin is an oral antidiabetic drug which acts by Sodium-Glucose cotransport-2 (SGLT-2) inhibition. Dapagliflozin, with its unique and complementary mechanism of action, appears to be an important addition to the therapeutic options for the management of type 2 diabetes, particularly when used as

an add-on therapy.[2] SGLT-2 localizes almost exclusively to the kidney proximal tubules, where it reabsorbs most of the ~180 g of glucose that is filtered through the glomeruli each day[3]. In DM patients, the SGLT-2 cotransporters are significantly upregulated, increasing glucose reabsorption and leading to glucose conservation and prolonged hyperglycaemia. Dapagliflozin is a highly selective and reversible inhibitor of SGLT-2 that acts by inhibiting tubular reabsorption of glucose in glomerular filtrate by SGLT-2 located at segments 1 and 2 in the proximal renal tubule. It results in a dose-dependent increase in urinary glucose excretion and ultimately, an improvement in glycaemic parameters.[4]

Dapagliflozin well absorbed orally but absorption decreases if given along with fatty food. Dapagliflozin is approximately 91% protein bound. The metabolism of dapagliflozin is primarily mediated by UGT1A9. Dapagliflozin is not appreciably cleared by renal excretion, but its metabolites are primarily eliminated via the renal pathway.[2,5] Current study aims to assess the effectiveness of Dapagliflozin as an add-on drug in combination with other hypoglycemic agents in reducing glycated hemoglobin (HbA1c) and fasting blood glucose (FBG) levels in T2-DM patients.

METHODS

Study design, location and duration

The study was done retrospectively at general medicine & endocrinology departments in Government general hospital, Kurnool. Inclusion criteria is adult diabetic patients who were prescribed Dapagliflozin as an Add-On therapy during the study period. Exclusion criteria is Patients who stopped drug before 3 months period. Current study was conducted from January 2021 to February 2022.

Data collection

Data of all adult diabetic patients who were prescribed Dapagliflozin as an Add-On therapy during the study period was obtained. Age, sex, duration of diabetes mellitus, fasting blood glucose, HbA1c values at the time of addition of dapagliflozin and after 3months period were collected through hospital and lab records from general medicine & endocrinology departments. Patients who stopped drug before 3 months period were excluded.

Data analysis

Collected data was entered into Microsoft excel and data was analyzed by IBM SPSS software version 29 using paired t test.

RESULTS

The mean age of patients is 55±6 years, in total 45 patients 69% (31) were male and 31% (14) were female. The mean fasting blood glucose and HbA1c levels at baseline were 9.2±0.99% and 184±31.91 respectively (Table 1). In this study, all patients received dapagliflozin as an add-on therapy in combination with ongoing diabetic treatment. In the follow-up period, Paired T test was used to evaluate the difference in HbA1c and FBG following treatment with dapagliflozin. P values for the changes in FBG and HbA1c from baseline were significant (p=0.001 & p=0.001, respectively) (Table 2). After 3 months of add-on therapy 49 mg/dl (26.63%) decrease in base line mean fasting blood glucose levels were observed (Figure 1). Mean HbA1c significantly reduced by 0.96 percentage point after 3 months (Figure 2). Out of 45 patients 4 (8.89%) were experienced urinary tract infections which was treated by oral antibiotic therapy.

Table 1: The demographic and clinical characteristics of patients at baseline.

Demographic	N (%)	Mean (SD)
Gender		
Male	31(68.9)	-
Female	14 (31.1)	-
Age	-	55.73 (6.17)
FBG	-	184 (31.91)
HbA1c	-	9.20 (0.99)

Table 2: HbA1c and FBG levels at baseline and 3 months post-treatment.

Outcome measures	Baseline mean (SD)	At 3 months mean (SD)	P value
FBG	184 (31.91)	135.6 (20.39)	0.001
HbA1c	9.20 (0.99)	8.23 (0.94)	0.001

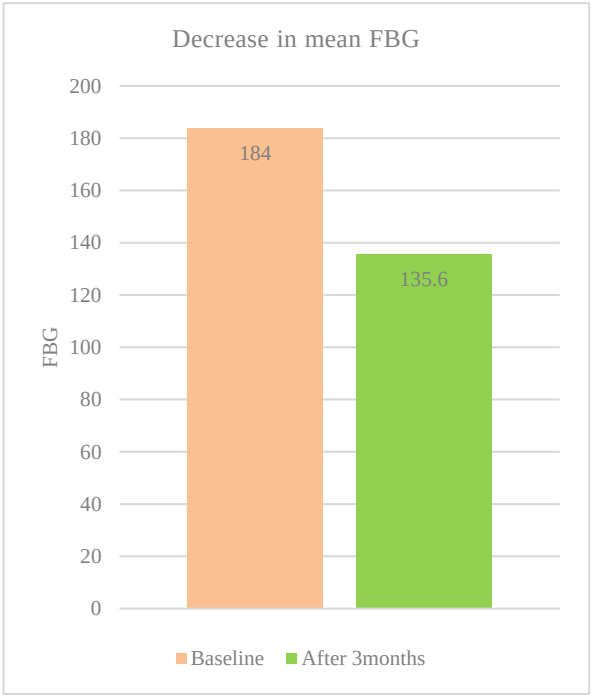

Figure 1: Decrease in mean FBG after addition of Dapagliflozin to existing regimen.

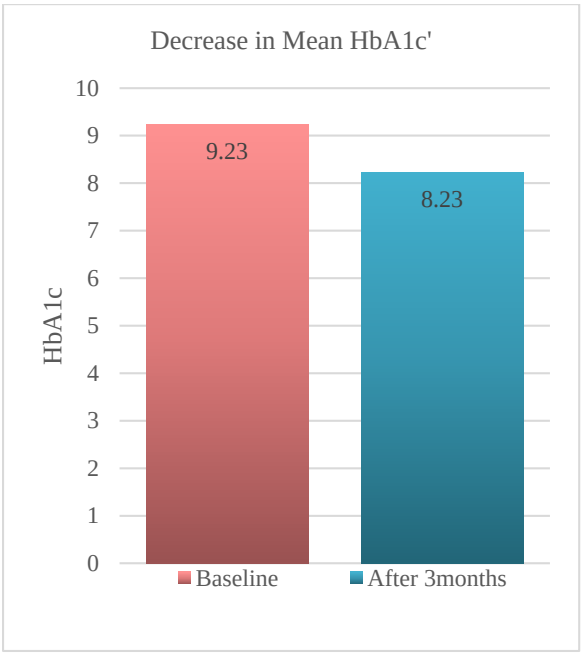

Figure 2: Decrease in mean HbA1c after addition of Dapagliflozin to existing regimen.

DISCUSSION

SGLT2 inhibitors are placed before DPP4 inhibitors in the hierarchical order of recommended use as monotherapy as well as an add-on therapy in 2020 American association of clinical endocrinologists (AACE)/American College of Endocrinology (ACE) comprehensive glycaemic control algorithm.[6] This study provides clinicians a research evidence on the use of dapagliflozin and its effectiveness in the management of T2-DM in combination with OHAs or insulin. Type2-DM is a progressive chronic disease, and over time, its treatment requires intensification.[7] Dapagliflozin has a different mechanism of action. By inhibiting SGLT2, dapagliflozin increases urine glucose excretion and lowers blood glucose levels by preventing the kidney's ability to reabsorb filtered glucose. Its mode of action is unrelated to insulin sensitivity and pancreatic cell activity.[4,8] Because of this Dapagliflozin is associated with low risk of hypoglycemia. For people who don't have better glycemic control, Dapagliflozin 'Add-On' therapy is a better and safe treatment option. According to Fioretto et al dapagliflozin is completely insulin-independent and efficacious as a single therapy or in combination with other agents.[9] In another study by Jeon et al significant improvement due to addition of dapagliflozin to an existing drug regimen was noted.[10] In a study by Moustafa et al Dapagliflozin significantly reduced the HbA1c level and FBG of type 2 diabetes patients as add-on therapy, regardless of the type of the co-administered OHA or insulin.[11] In a study by Strojek et al revealed that although incidents suggestive of genital infections were recorded more frequently in patients on dapagliflozin, it was usually well tolerated and dramatically improved HbA1c in patients with uncontrolled T2DM on sulphonyl urea monotherapy.[12] The results of current study also revealed that Dapagliflozin significantly improved the glycemic control of Type-2 diabetic patients when used in combination with standard therapy. SGLT-2 inhibitors also have multiple nonglycemic effects in patients with T2DM, including improvements in cardiovascular and renal outcomes and reductions in BP and body weight.[13] These pleiotropic effects are beneficial for the prevention or reduction of macro and microvascular complications and helps in prevention and improvement of cardiovascular diseases, heart failure and chronic kidney diseases.[14,15]

Limitations

Limitations of current study were; this is a retrospective study, other comorbidities and other antidiabetics using by patients were not taken into consideration. A prospective study including other comorbidities and comparison between groups of different existing regimens, Dapagliflozin as add-on therapy may be needed.

CONCLUSIONS

Dapagliflozin as an add-on therapy significantly reduced the HbA1c level and fasting blood glucose of Type-2DM patients, in a 3-month treatment period. Due to the frequency of Genitourinary tract infections, caution is indicated while treating the patients with Dapagliflozin.

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