Endocrinology & Metabolic Syndrome

OPEN ACCESS Freely available online

Research Article

Use of Dapagliflozin as the Drug in the Management of Type 2 Diabetes in India

Subhash Kumar*

Department of Endocrinology, Diabetes and Obesity Care Center, Patna, Bihar, India

ABSTRACT

Objective and aim: Uncontrolled diabetic patients were increasing day by day despite availability of multiple oral antidiabetic drugs. The main objective of the study was to evaluate the efficacy of dapagliflozin 10 mg on Indian subjects who were uncontrolled despite on multiple (≥ 4) oral antidiabetic drugs.

Methods: Patients treated with Dapagliflozin 10 mg as an add-on drug, on those patients who were poorly controlled despite optimum doses of more of equal to four OADs, metformin, sulfonylureas, pioglitazone, hydroxychloroquine, DPP-4 inhibitor and alpha-glycosidase inhibitors were included in this analysis. Total 245 patients with ≥ 3 regular follow-ups visiting a Diabetes Specialty Clinic were considered for this retrospective analysis.

Results: The mean Fasting Blood Glucose (FPG) was 168.4 ± 19.8 mg/dl and mean Post Prandial Glucose (PPG) was 238.3 ± 28.6 mg/dl. The mean baseline HbA1c was 8.4 ± 1.2 %. The mean duration required to control diabetes with dapagliflozin 10 mg was 7.9 weeks. 83.5% of the total cases responded to treatment with a DPP-4i ($P < 0.05$). The response in age group <55 years was 90.3%, whereas in ≥ 55 years group, it was 83.3%. Those with BMI <23.5 kg/m^2 had significantly higher response (94.6%) as compared to 82.3% in patients with BMI ≥ 23.5 kg/m^2. At the end of the monitoring period, there was significant reduction in mean FPG by-31.4 ± 18.3 mg/dL (P=0.001), mean PPG by -64.8 ± 21.3 mg/dL (P=0.001), mean HbA1c by -1.3 ± 0.8 (P=0.001), weight by -1.2 kg (P=0.001), mean SBP by -3.6 mmHg (p=0.01) and mean DBP by -2.0 mmHg (p=0.01). Common adverse events included hypoglycemia, pollakiuria, and thirst. But none required a medical assistance.

Conclusion: Dapagliflozin is effective in achieving the desired glycemic control. Early initiation of dapagliflozin is recommended for tighter glycemic control.

Keywords: T2DM; Glycemic control; Dapagliflozin

INTRODUCTION

Diabetes, an exemplary of a chronic disease, has reached epidemic proportions not only in India but also worldwide. It is estimated that the global burden of Type 2 Diabetes (T2DM) is expected to increase to 592 million by 2033 [1]. There were over 72.9 million cases of diabetes in India in 2017 [2]. Among the Southeast Asian region India is considered to have the greatest number of people affected with diabetes which is as much as 74 million within the age group of 18–99 years 9.8% age-adjusted comparative prevalence and in the age group of 20–79 years 50.7% premature mortality [3]. In a population-based cross-sectional study done by Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) where sample was taken across 15 Indian states, the overall prevalence of diabetes was 7.3% [4]. There is evidence of an epidemiological transition; with diabetes prevalence being higher in low socioeconomic groups of urban areas in more economically developed states. There is sufficient evidence of an "Asian phenotype" in diabetes [5]. Asians have a 2-4 times higher risk of T2DM than white Europeans, independent of weight, and develop diabetes 5-10 years earlier than them [6].

Correspondence to: Subhash Kumar, Department of Endocrinology, Diabetes and Obesity Care Center, Patna, Bihar, India, E-mail: drsubhash.patna@rediffmail.com

Received: 04-Jul-2022, Manuscript No. EMS-22-001-PreQc-22; **Editor assigned:** 07-Jul-2022, PreQC No. EMS-22-001-PreQc-22 (PQ); **Reviewed:** 26-Jul-2022, QC No. EMS-22-001-PreQc-22; **Revised:** 29-Jul-2022, Manuscript No. EMS-22-001-PreQc-22 (R); **Published:** 05-Aug-2022, DOI: 10.35248/2161-1017.22.11.360

Citation: Kumar S (2022) Use of Dapagliflozin as the Drug in the Management of Type 2 Diabetes in India. Endocrinol Metab Syndr. 11: 360.

For diabetes as a novel therapeutic strategy Sodium-Glucose Cotransporter-2 (SGLT-2) inhibitors are using by clinicians worldwide. By specifically inhibiting the activity of SGLT-2, renal glucose reabsorption in the proximal convoluted tubule can reduce by SGLT-2 inhibitors, leading to increased urinary glucose excretion [7-9]. There were several studies which confirm the efficacy of dapagliflozin as mono therapy or as add on in reducing HbA1c, FPG, and body weight [10-15].

At present, there are many clinical studies and meta-analysis on dapagliflozin whether in mono therapy or in combined with metformin, DPP4i, sulfonylureas, thiazolidinedione, and other hypoglycemic agents for the treatment of T2DM, but there are few data on dapagliflozin as 4^{th} or 5^{th} add on to type 2 diabetes patients who were initially uncontrolled on any 3 oral drug combination. The main objective of the study was to evaluate the efficacy of dapagliflozin 10 mg on Indian subjects who were uncontrolled despite on multiple (≥ 4) oral antidiabetic drugs.

MATERIALS AND METHODS

This was a retrospective observational trial conducted at private diabetic clinic at Patna, India. A predesigned study pro forma was used to retrieve the clinical data from electronically stored patient's profile. Patients treated with Dapagliflozin 10 mg as an add-on drug, on those patients who were poorly controlled despite optimum doses of more of equal to four OADs, metformin, sulfonylurea, pioglitazone, hydroxychloroquine, DPP-4 inhibitor and alpha-glucosidase inhibitors were included in this analysis. Any patents who had documented micro or macro vascular complications, any previous renal and retina abnormalities, with thyroid dysfunction, pregnant and lactating women were excluded from this study. Total 245 patients with ≥ 3 regular follow-ups visiting a Diabetes Specialty Clinic were considered for this retrospective analysis. The study was conducted in accordance with the design and specific provisions of this protocol, in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice (GCP) and the applicable regulatory requirements. The primary endpoint of the current study was the change in glycemic profile including HbA1c from baseline to week 24 with addition of dapagliflozin 10 mg. Secondary endpoints of the current study includes changes in Fasting Plasma Glucose (FPG), Post Prandial Plasma Glucose (PPG) and weight from baseline. Safety assessment was measured with confirmed hypoglycemia event (plasma glucose ≤ 70 mg/dl and requiring assistance) and incidence of Urinary Tract Infection (UTI). SPSS software was used to analyze the clinical data. Descriptive statistics were used to analyze statistical variables (i.e. frequencies were used for categorical variables and mean, standard deviation was used for continuous variables). A P value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 demonstrated the demographic clinical details of 245 participants. The mean Fasting Blood Glucose (FPG) was 168.4 ± 19.8 mg/dl and mean Post Prandial Glucose (PPG) was 238.3 ± 28.6 mg/dl. The mean baseline HbA1c was 8.4 ± 1.2%.

Concomitant antidiabetic drugs which were used were illustrated in Figure 1. Apart of metformin (93%), DPP4i (63%) and sulfonylurea (70%) were the commonest oral OHAs used followed by thiazolidinedione (58%) and α-GI (16%).

At the end of the monitoring period, there was significant reduction in mean FPG by-31.4 ± 18.3 mg/dL (P=0.001), mean PPG by -64.8 ± 21.3 mg/dL (P=0.001), mean HbA1c by -1.3 ± 0.8 (P=0.001), weight by -1.2 kg (P=0.001), mean SBP by -3.6 mmHg (P=0.01) and mean DBP by -2.0 mmHg (P=0.01) (Table 2).

Table 1: Principal clinical parameters for study participants at baseline.

Characteristics	N=245
Age (Years)	53.4 ± 11.2
Male (N%)	160 (65%)
Weight (Kg)	81.2 ± 16.3
BMI (Kg/m^2)	25.1 ± 3.7
Duration of Diabetes (Years)	7.2 ± 3.8
SBP (mmHg)	131.7 ± 15.6
DBP (mmHg)	84.5 ± 3.7
FPG (mg/dl)	168.4 ± 19.8
T-chol (mg/dL)	204.5 ± 22.8
LDL-C (mg/dL)	110.7 ± 19.8
HDL-C (mg/dL)	54.3 ± 2.6
TG (mg/dL)	130.6 ± 50.8

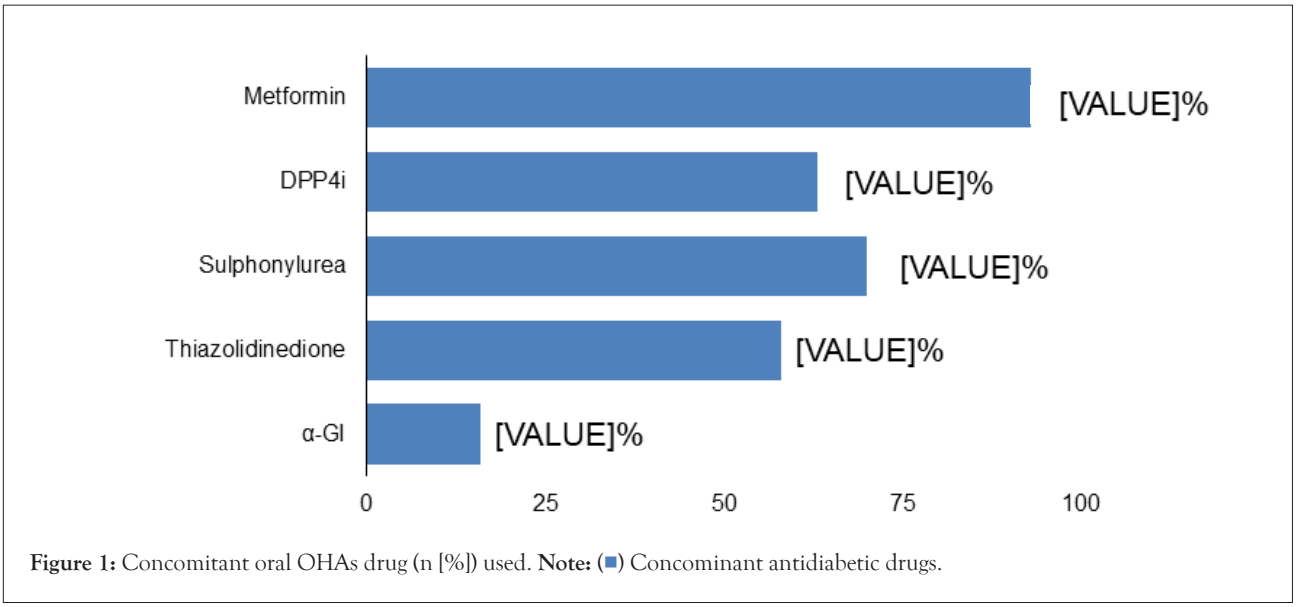

Figure 1: Concomitant oral OHAs drug (n [%]) used. **Note:** (■) Concominant antidiabetic drugs.

Table 2: Change in clinical parameters for study participants from baseline to 24 weeks.

Parameters	Baseline	After 24 Weeks	Δ Differences	P Value
Weight (Kg)	81.2 ± 16.3	80 ± 14.5	-1.2 ±0.7	0.001
SBP (mmHg)	131.7 ± 15.6	128.1 ± 16.3	-3.6 ± 1.6	0.01
DBP (mmHg)	84.5 ± 3.7	82.5 ± 2.5	-2.0 ± 1.2	0.01
FPG (mg/dl)	168.4 ± 19.8	133.4 ± 14.7	-31.4 ± 18.3	0.001
PPG (mg/dl)	238.3 ± 28.6	173.5 ± 18.2	-64.8 ± 21.3	0.001
HbA1c (%)	8.4 ± 1.2	7.1 ± 1.1	-1.3 ± 0.8	0.001

The mean duration required to control diabetes with dapagliflozin 10 mg was 7.9 weeks. 83.5% of the total cases responded to treatment with a DPP-4i (P<0.05). The response in age group <55 years was 90.3%, whereas in ≥ 55 years group, it was 83.3%. Those with BMI <23.5 kg/m^2 had significantly higher response (94.6%) as compared to 82.3% in patients with BMI ≥ 23.5 kg/m^2. Common adverse events included hypoglycemia, pollakiuria, and thirst. But none required a medical assistance.

DISCUSSION

There were numerous clinical trials were event after desperate use of several oral hypoglycemic drugs very few uncontrolled type 2 diabetes patients has achieved their glycemic control and weight gain and multiple hypoglycemic event were supposed to be the greatest concern [16,17]. With multiple subtypes including SGLT1 to SGLT6 the Sodium-Glucose Co-Transporter (SGLT) is a glucose transporter, which offers a strong efficacy to achieve target glycemic control and dapagliflozin is one of them which offers a reduction in blood glucose levels along with it also reduces renal glucose reabsorption, leading to urinary glucose excretion [18-21].

In current trial despite use of various OHAs when dapagliflozin 10 mg was added here was significant reduction in mean FPG by -31.4 ± 18.3 mg/dL (P=0.001), mean PPG by -64.8 ± 21.3 mg/dL(P=0.001), mean HbA1c by -1.3 ± 0.8 (P=0.001), weight by -1.2 kg (P=0.001), mean SBP by -3.6 mmHg (P=0.01) and mean DBP by -2.0 mmHg (P=0.01). In line with current observation, several studies reported with dapagliflozin in combination with glimepiride, exenatide, metformin slow extended release, saxagliptin, sitagliptin and pioglitazone a significant reduction in HbA1c [22-28].

Due to the mechanism of dapagliflozin and its Pharmacodynamic (PD) properties along with subsequent PK, in clinical trials some adverse effects of dapagliflozin have been evaluated like hypoglycemia, Urinary Tract Infections (UTIs) etc [29-31]. In current studies despite there was an initiation if such AE but it was managed and none required a medical assistance. In our current study we have demonstrated that age and BMI is a fact for the response rate to treatment with dapagliflozin. In current study, the response in age group <55 years was 90.3%, whereas in ≥ 55 years group, it was 83.3%. This finding was in line with the observation few older studies [32,33].

CONCLUSION

Current retrospective has some limitations despite it indicated several significant findings about dapagliflozin. Lifestyle behaviors, diet and patient's adherence to medication regimen cannot be measured or followed and also the sample size was smaller. Despite of the limitations dapagliflozin undoubtedly established the superior efficacy of dapagliflozin to achieve target blood glucose level and provides an additional benefit to the reduction in body weight. A longitudinal follow-up studies with larger sample sizes should focus on future research. Dapagliflozin is effective in achieving the desired glycemic control. Early initiation of dapagliflozin is recommended for tighter glycemic control.

REFERENCES

1. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271-81.
2. Banerjee J, Dhas Y, Mishra N. Middle-aged Indians with type 2 diabetes are at higher risk of biological ageing with special reference to serum CDKN2A. J Diabetes Res. 2020.
3. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas. Diabetes Res Clin Pract. 2019;157:107843.
4. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR–INDIAB population-based cross-sectional study. Lancet Diabetes Endo. 2017;5(8):585-96.
5. Rajadhyaksha V. Managing diabetes patients in India: Is the future more bitter or less sweet? Perspect Clin Res. 2018;9(1):1.
6. Gujral UP, Pradeepa R, Weber MB, Narayan KV, Mohan V. Type 2 diabetes in South Asians: Similarities and differences with white Caucasian and other populations. Ann N Y Acad Sci. 2013;1281(1):51-63.
7. DeFronzo RA, Hompesch M, Kasichayanula S, Liu X, Hong Y, Pfister M, et al. Characterization of renal glucose reabsorption in response to dapagliflozin in healthy subjects and subjects with type 2 diabetes. Diabetes care. 2013;36(10):3169-76.
8. Gerich JE. Role of the kidney in normal glucose homeostasis and in the hyperglycaemia of diabetes mellitus: Therapeutic implications. Diabet Med. 2010;27(2):136-42.
9. Vallon V, Platt KA, Cunard R, Schroth J, Whaley J, Thomson SC, et al. SGLT2 mediates glucose reabsorption in the early proximal tubule. J Am Soc Nephrol. 2011;22(1):104-12.
10. Bailey CJ, Iqbal N, Tjoen C, List JF. Dapagliflozin monotherapy in drug-naive patients with diabetes: A randomized-controlled trial of low-dose range. Diabetes Obes Metab. 2012;14(10):951-9.
11. Kaku K, Kiyosue A, Inoue S, Ueda N, Tokudome T, Yang J, et al. Efficacy and safety of dapagliflozin monotherapy in Japanese patients with type 2 diabetes inadequately controlled by diet and exercise. Diabetes Obes Metab. 2014;16(11):1102-10.
12. Ji L, Ma J, Li H, Mansfield TA, Tjoen CL, Iqbal N, et al. Dapagliflozin as monotherapy in drug-naive Asian patients with type 2 diabetes mellitus: A randomized, blinded, prospective phase III study. Clin Ther. 2014;36(1):84-100.
13. Ferrannini E, Ramos SJ, Salsali A, Tang W, List JF. Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: A randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes care. 2010;33(10):2217-24.
14. Kaku K, Inoue S, Matsuoka O, Kiyosue A, Azuma H, Hayashi N, et al. Efficacy and safety of dapagliflozin as a monotherapy for type 2 diabetes mellitus in Japanese patients with inadequate glycaemic control: A phase II multicentre, randomized, double-blind, placebo-controlled trial. Diabetes Obes Metab. 2013;15(5):432-40.
15. List JF, Woo V, Morales E, Tang W, Fiedorek FT. Sodium-glucose co-transport inhibition with dapagliflozin in type 2 diabetes. Diabetes care. 2009;32(4):650-7.
16. Lipska KJ, Yao X, Herrin J, McCoy RG, Ross JS, Steinman MA, et al. Trends in drug utilization, glycemic control, and rates of severe hypoglycemia, 2006–2013. Diabetes care. 2017;40(4):468-75.
17. Hayward RA, Reaven PD, Wiitala WL, Bahn GD, Reda DJ, Ge L, et al. Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2015;372(23):2197-206.
18. Wood IS, Trayhurn P. Glucose transporters (GLUT and SGLT): Expanded families of sugar transport proteins. Br J Nutr. 2003;89(1):3-9.
19. Gallo LA, Wright EM, Vallon V. Probing SGLT2 as a therapeutic target for diabetes: Basic physiology and consequences. Diab Vasc Dis Res. 2015;12(2):78-89.
20. Rieg T, Masuda T, Gerasimova M, Mayoux E, Platt K, Powell DR, et al. Increase in SGLT1-mediated transport explains renal glucose reabsorption during genetic and pharmacological SGLT2 inhibition in euglycemia. Am J Physiol Renal Physiol. 2014;306(2):F188-93.
21. Vallon V. Molecular determinants of renal glucose reabsorption. Focus on "Glucose transport by human renal Na+/D-glucose co-transporters SGLT1 and SGLT2". Am J Physiol Cell Physiol. 2011;300(1):C6-8.
22. Christos PJ, Chemaitelly H, Abu-Raddad LJ, Zirie MA, Deleu D, Mushlin AI. Prevention of type II diabetes mellitus in Qatar: Who is at risk? Qatar Med J. 2015;2014(2):13.
23. Strojek K, Yoon KH, Hruba V, Sugg J, Langkilde AM, Parikh S. Dapagliflozin added to glimepiride in patients with type 2 diabetes mellitus sustains glycemic control and weight loss over 48 weeks: A randomized, double-blind, parallel-group, placebo-controlled trial. Diabetes Ther. 2014;5(1):267-83.
24. Tatarkiewicz K, Polizzi C, Villescaz C, D'Souza LJ, Wang Y, Janssen S, et al. Combined antidiabetic benefits of exenatide and dapagliflozin in diabetic mice. Diabetes Obes Metab. 2014;16(4):376-80.
25. Strojek K, Yoon KH, Hruba V, Elze M, Langkilde AM, Parikh S. Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with glimepiride: A randomized, 24-week, double-blind, placebo-controlled trial. Diabetes Obes Metab. 2011;13(10):928-38.
26. Rosenstock J, Mathieu C, Chen H, Garcia-Sanchez R, Saraiva GL. Dapagliflozin versus saxagliptin as add-on therapy in patients with type 2 diabetes inadequately controlled with metformin. Arch Endocrinol Metab. 2018;62:424-30.
27. Jabbour SA, Hardy E, Sugg J, Parikh S. Dapagliflozin is effective as add-on therapy to sitagliptin with or without metformin: a 24-week, multicenter, randomized, double-blind, placebo-controlled study. Diabetes Care. 2014 Mar 1;37(3):740-50.

28. Rosenstock J, Vico M, Wei LI, Salsali A, List JF. Effects of dapagliflozin, an SGLT2 inhibitor, on HbA1c, body weight, and hypoglycemia risk in patients with type 2 diabetes inadequately controlled on pioglitazone monotherapy. Diabetes care. 2012;35(7):1473-8.

29. Strojek K, Yoon KH, Hruba V, Elze M, Langkilde AM, Parikh S. Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with glimepiride: A randomized, 24-week, double-blind, placebo-controlled trial. Diabetes Obes Metab. 2011;13(10):928-38.

30. Wilding JP, Norwood P, T'joen C, Bastien A, List JF, Fiedorek FT. A study of dapagliflozin in patients with type 2 diabetes receiving high doses of insulin plus insulin sensitizers: Applicability of a novel insulin-independent treatment. Diabetes care. 2009;32(9):1656-62.

31. Anderson SL. Dapagliflozin efficacy and safety: A perspective review. Ther Adv Drug Saf. 2014;5(6):242-54.

32. Wilding J, Bailey C, Rigney U, Blak B, Kok M, Emmas C. Dapagliflozin therapy for type 2 diabetes in primary care: Changes in HbA1c, weight and blood pressure over 2 years follow-up. Prim Care Diabetes. 2017;11(5):437-44.

33. Viswanathan V, Singh KP. Use of Dapagliflozin in the management of type 2 diabetes mellitus: A real-world evidence study in Indian patients. Diabetes Technol Ther. 2019;21(8):415-22.