Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024

Original Research Article

EFFECTIVENESS OF DAPAGLIFLOZIN IN THE MANAGEMENT OF TYPE-2 DIABETES MELLITUS IN COMBINATION WITH OTHER OHA'S &/OR INSULIN

Dr. Jai Prakash[1], Dr. Vikas Babu[2]

[1]Assistant Professor, Department of General Medicine, Varun Arjun Medical College, Shahjahanpur, Uttar Pradesh, India.
[2]Assistant Professor, Department of General Medicine, Autonomous medical College (ASMC), Hardoi, Uttar Pradesh, India.

Corresponding Author
Dr. Jai Prakash, Assistant Professor, Department of General Medicine, Varun Arjun Medical College, Shahjahanpur, Uttar Pradesh, India.

Received: 08-01-2024 / Revised: 12-01-2024 / Accepted: 13-02-2024

ABSTRACT

Background
To investigate the efficacy of "dapagliflozin" in the treatment of type 2 diabetes mellitus when combined with insulin &/or other OHAs

Methods
At this investigation, 130 subjetcs with uncontrolled T-2 DM combined with various OHAs &/or insulin were studied at the department of medicine. Pre-made questionnaires were used to record specifics regarding each patient's family history, medical history, clinical examination, & course of therapy. In this study, dapagliflozin was administered as an adjuvant medication to all patients who have received standard treatment for their diabetes. After three months of Dapagliflozin medication, differences in HbA1c & FBS levels were assessed.

Results
At baseline, the study subjects' mean HbA1C was 8.31%, mean FBS was 184.7 mg/dl, & mean PPBS was 279.25 mg/dl. These were the diabetic values. Following the intervention, the study participants' mean HbA1C was 7.05%, mean FBS was 131.73 mg/dl, & mean PPBS was 204.98 mg/dl. These were the diabetic parameters. Therefore, both FBS & PPBS significantly decreased.

Conclusion
In ordinary clinical practice, this research offers compelling real-world proof supporting the untimely use of "dapagliflozin" in Indian subjects with type 2 diabetes to improve glucose control & gain additional benefits including weight loss.

Keywords: Insulin , Dapagliflozin, OHA , Type-2 Diabetes Mellitus

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024

Introduction: Globally, diabetes mellitus (DM) affects about 400 million people & is a serious public health concern. Life-threatening chronic microvascular, macrovascular, & neuropathic consequences are gradually brought on by this metabolic condition. Nephropathy, neuropathy, cardiovascular & renal difficulties, retinopathy, food-related disorders, & other issues are among the numerous complications linked to diabetic mellitus. There are two varieties of DM: type 1 & type 2. Type 2 diabetes is by injury of pancreatic beta cells, which inhibits the person's ability to use insulin. Type 1 diabetes is an autoimmune disease that affects pancreatic cells, reducing the production of insulin.[1-5]

As of right now, the majority of guidelines advise pharmacologic therapy for diabetic management based on an assessment of glycated haemoglobin (HbA1c) levels. Given the patient's characteristics & drug profiles, a second agent may be started if lifestyle modifications plus metformin are unable to attain the desired glycemic target.[6]

Metformin, sulfonylureas, nonsulfonyl urea secretagogues, glucagon-like peptide-1 analogues are among the main anti-diabetic medications whose effectiveness is dependent on insulin. Their effectiveness decreases as type 2 diabetes mellitus (T2DM) progresses & pancreatic islet β-cell activity deteriorates. Insulin resistance is exacerbated by thiazolidinediones & sulphonylureas, which lead to weight gain. Not surprisingly, over two thirds of diabetes patients in the USA & Europe receiving standard care were unable to achieve glycaemic control. On the other hand, dapagliflozin, an extremely specific inhibitor of SGLT2, stands out for its “insulin-independent” action on decreasing glucose reabsorption, especially by the kidney's end tubule, which allows the body to excrete more glucose from plasma into urine.[7-10]

Dapagliflozin is the second sodium-glucose cotransporter 2 (SGLT2) inhibitor to be licensed by the US Food & Drug Administration (FDA). SGLT2 inhibitors are a novel family of oral antihyperglycemic medications with an inventive mode of action. Effective & palatable oral medications for the management of T2-DM can eventually reduce the catastrophic outcomes linked to uncontrolled T2-DM & enhance superiority of life. When a novel class of medications using glucose urea was created in 1990 to treat T2-DM, it was hampered by its low bioavailability, which resulted from both quick breakdown & poor absorption. This finding made SGLT2 inhibitors, a potential class of medications for the treatment of T2-DM, possible. Among these medications is canagliflozin, which rose to prominence as the.[11-13]

The effectiveness of dapagliflozin has been thoroughly demonstrated in clinical trials including a variety of populations, primarily those in the West. Nevertheless, the usefulness of this class of drugs in the Indian populace—which has distinct demographic & cultural traits—has not been extensively studied in the real world until recently.

MATERIALS & METHODS

130 individuals with Type-2 Diabetes Mellitus who presented to the OPD/IPD of Medicine & other departments during the research period participated in this prospective study conducted at the department of medicine. Every patient gave their verbal & written informed consent for the purpose of the clinical evaluation & laboratory research. The study was approved by the Research & Ethical committees, & it began twelve months later.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024

Inclusion Criteria

a. Every patient who is older than 18 but younger than 75 years of age.
b. Every case of Type 2 Diabetes Mellitus previously diagnosed & treated with OHAs &/or insulin for more than three months.
c. T2-DM (HbA1c greater than 7.0% & less than 11.0%) that is not well controlled.

Exclusion Criteria

a. Individuals with recently diagnosed Type 2 Diabetes Mellitus.
b. Individuals whose eGFR is less than 45 mL/min per 1.73 m^2 of body surface.
c. Individuals using loop diuretics.

Study Plan

Pre-made questionnaires were used to record specifics regarding each patient's family history, medical history, clinical examination, & course of therapy. In this study, dapagliflozin was administered as an adjuvant medication to all patients who have received standard treatment for their diabetes. After three months of Dapagliflozin medication, differences in HbA1c & FBS levels were assessed. After data was gathered, statistical analysis was performed.

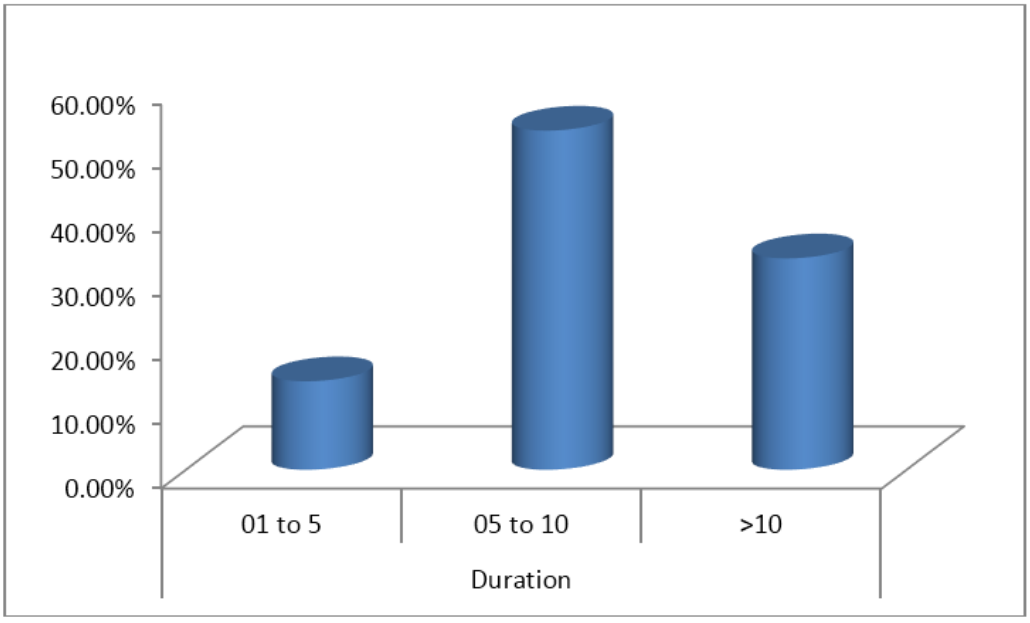
Statistical analysis

The data collected was tabulated in an Excel spreadsheet with the assistance of a statistician. Statistical analysis was conducted using the means and standard deviations of measures for each group using SPSS 22.00. The researchers employed the t-test to determine the disparity between the two groups, using a significance level of $p < 0.05$.

RESULTS

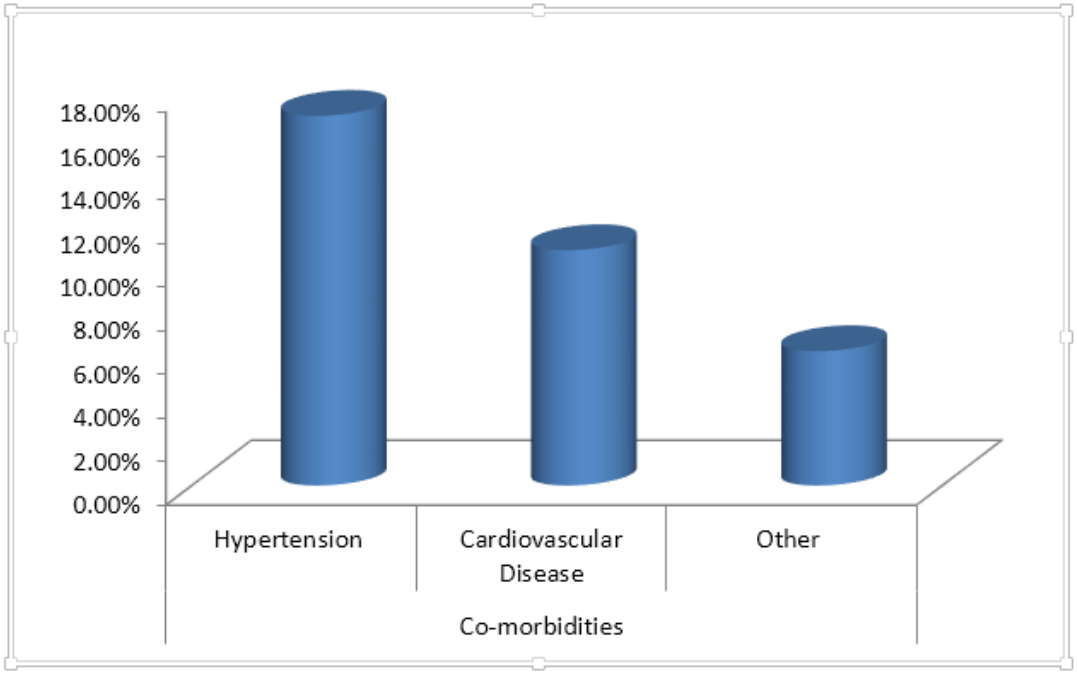
According to the current study, 58.46% of the individuals were men & 41.54% were women. The age group of 50 to 59 years was the largest, followed by 60 years & under, with just 6.92% of individuals falling into the under 40 years age group. The subjects' average age was 53.87±10.95 years. Of all the subjects, 30% had a history of type 2 DM, while 78% had no family history of the condition. 53.07 percent of the participants had type 2 diabetes mellitus between the ages of 5 & 10 years, whereas 33.1 percent had the condition from older than 10 years. Among those aged 1 to 5, only 13.9% had type 2 DM. (graph 1).

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024



Graph 1: Duration of diabetes among the study subjects

Among all the participants, hypertension affected 17.69%, cardiovascular disease affected 10.8%, & other co-morbidities affected 6.92%. (graph 2).



Graph 2: Co-morbidities among the study subjects

The weight of the research participants before & after the intervention was significantly different, as Table 1 demonstrated.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024

Table 1: Body weight comparison of research participants before & after the intervention

Weight (kg)	Mean	SD
Before the Intervention	71.73	5.59
After the Intervention	68.82	4.58
t test	3.79	
p value	0.041*	

*: statistically significant

Table 2 presented a statistically significant contrast between the study individuals' pre- & post-intervention diabetes measures.

Table 2: Pre- & post-intervention comparison of the research participants' diabetes parameters

Variables	Before Intervention		After Intervention		t test	p value
	Mean	SD	Mean	SD		
HbA1c	8.35	0.60	7.09	0.51	5.12	0.007*
FBS	184.74	5.3	131.77	6.24	14.07	0.001*
PPBS	279.29	10.87	205.02	9.46	9.62	0.004*

*: statistically significant

DISCUSSION

One of the SGLT2 inhibitor classes, dapagliflozin, is authorized for use in treating type 2 diabetes globally in individuals whose glycemic control is not sufficiently controlled with traditional medications. Based on international trials including a small number of Indian patients, "dapagliflozin" is currently approved in India. After six months of therapy, a substantial reduction in HbA1c readings was shown when compared to a placebo.[14, 15] It is unclear, nevertheless, if dapagliflozin data from real-world research will yield results that are comparable to those from clinical trials. We carried out this real-world trial in Indian T2DM patients to ascertain the efficacy & safety of dapagliflozin in order to comprehend its usage in standard clinical practice.

According to the current study, 58.46% of the individuals were men & 41.54% were women. Male predominance (57.5%) was observed among the patients in a study conducted by Viswanathan V et al[16], which produced similar results. The results of a study conducted by Moustafa Al AdAwi et al.[17] were comparable as well. This contrasts with the current findings, which indicate a female predominance among the respondents according to Joaqui et al. (2018).

The age group of 50 to 59 years was the largest, followed by 60 years & under, with just 6.92% of individuals falling into the under 40 years age group. The subjects' average age was 53.87±10.95 years. The average age of the participants in a research by Joaquiet al [18] was 55.05 years. In a study conducted by Moustafa Al AdAwi et al[17], the subjects' mean age was 57 years. The average age of the patients in a research by Viswanathan V et al [16] was 52.31 years.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024

Of all the subjects, 30% had a history of type 2 DM, while 78% had no family history of the condition. In patients without a personal history of diabetes or who have not yet developed the disease, the existence of a family history of the disease may have clinical ramifications for risk stratification. 53.08 percent of the participants had T-2 DM within the last 10 years, whereas 33.1 percent had the condition longer than that. Among those aged 1 to 5, only 13.9% had type 2 DM. The average duration of diabetes was 5.7 years in a research by Jabbour SA et al[19]. The average duration of type 2 DM was 5.93 years in a research by Joaquiet al[18]. 16.92% of the individuals had high blood pressure, 10.77% had heart problems, & 6.15% had additional co-morbidities. In a research by Viswanathan V et al. (2016), 47.5% of the participants had hypertension as a comorbidity.

At baseline, the patients' mean body weight was 71.873±5.59 kg & their mean height was 162.05± 4.84 cm. Following the intervention, the individuals' mean body weight was 68.82± 4.58 kg. The weight of the research participants before & after the intervention was significantly different, as this table demonstrated. In our investigation, following months of dapagliflozin medication, there was a significant 2.88 kg reduction in mean (SD) body weight. Greater decreases in body weight were observed in patients with higher baseline BMIs than in those with lower baseline BMIs. Studies have showed that dapagliflozin can result in *200–300 daily calorie loss[15]. The group that added dapagliflozin to metformin plus exenatide saw the biggest weight loss (between 2.2 & 3.8 kg), with a consistent downward linear trend. The “DURATION-8” research, which revealed decreases of 1 to 2.6 kg at week 28 [22] & 0.7 to 2.8 kg at week 52, is comparable to the data shown here. Although its pattern was nonlinear, it did settle between weeks 28 & 52. The effect of GLP1 analogs on weight, which resulted in subjects losing up to 4.2 kg among diabetics[24], & up to 8 kg among non-diabetics[14,15], can explain this.

At baseline, the study individuals with diabetes had an average HbA1c of 8.35±0.6, an FBS of 184.74±5.3, & PPBS of 279.3± 10.9. Following the intervention, the study participants' mean HbA1c was 7.09±0.51, their FBS was 131.77±6.24, & their PPBS was 205.02± 9.5. Dapagliflozin lowered HbA1c in a manner that was largely similar across randomized, controlled clinical studies involving patients who had never received therapy. After six months of treatment, dapagliflozin's effect on blood glucose was comparable to that of metformin-XR monotherapy, & in individuals whose metformin monotherapy was not well managed after a year of treatment, it was comparable to glipizide.In our investigation, this cohort also exhibited a marginally greater decline in HbA1c & FPG in contrast to the information gathered by Jabbour & cols[19]. They did, however, note that, contrary to our findings, the proportion of subjects with a HbA1c <7% increased to 53.9% at 28 weeks & 44% at 52 weeks. After six months of dapagliflozin medication, the mean (SD) HbA1c level was 7.62% (1.04%) in our study group; this is near the goal HbA1c level (<7.0%) advised by the ADA.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024

LIMITATIONS

Among the research drawbacks is the lack of an active comparator arm, which precluded comparison with other oral antidiabetics such as dipeptidyl peptidase 4 inhibitors (DPP4i) or GLP-1. Nonetheless, the sizeable patient base guaranteed the production of trustworthy data to precisely evaluate the average deviation from the baseline in the efficient metrics. Yet, the sample size was insufficient to characterize uncommon adverse events. Inherent limitations of real-world evidence researches, such as bias, confounding, & poor data quality, further restrict this study.

CONCLUSION

In this prospective clinical interventional study, dapagliflozin significantly reduced body weight & HbA1c levels after the intervention compared to baseline, & it was well tolerated by T2DM patients. There were no fresh safety findings discovered in the trial, suggesting that dapaglifozin has a tolerable tolerability profile. In ordinary clinical practice, this research offers compelling real-world confirmation supporting the untimely use of “dapagliflozin” in Indian subjects with type 2 diabetes to improve glucose control & gain additional benefits including weight loss.

REFERENCES

1. Khursheed SR. Singh S, Kapoor WB, M. Kumar GR. Treatment strategies against diabetes: Success so far & challenges ahead, Eur. J. Pharmacol. 2019: 862.
2. Roglic SWG, Green A, Sicree HR. King, Global Prevalence of Diabetes: Estimates for the year 2000 & projections for 2030, Diabetes. Care 27 2004: 1047–1053.
3. Wong C, Salami H, Dass C. Potential of insulin nanoparticle formulations for oral delivery & diabetes treatment, J. Control. Release 2017; 264: 247–275.
4. Ripsin CM, Kang H, Urban RJ. Management of blood glucose in type 2 diabetes mellitus. AmFam Physician 2009; 79: 29–36.
5. Pretki M, Nolan CJ. Islet beta cell failure in type 2 diabetes. J Clin Invest 2006; 116: 1802–12.
6. Clar C, Gill JA, Court R, et al. Systematic review of SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes. BMJ Open 2012; 2: e001007.
7. Chao EC, Henry RR. SGLT2 inhibition—a novel strategy for diabetes treatment. Nat Rev Drug Discov 2010; 9: 551–9.
8. Hu L, Zhou ZY. Research progress of sodium-glucose co-transporter-2 inhibitor drugs. Med Recapitulate 2011; 12: 3782–5.
9. Care D, Suppl SS. Comprehensive Medical Evaluation & Assessment of Comorbidities: Standards of Medical Care in Diabetes – 2020. Diabetes Care. 2020; 43(1): S37-S47.
10. Care D, Suppl SS. Glycemic Targets: Standards of Medical Care in Diabetes – 2020. Diabetes Care. 2020; 43(1): S66-S76.
11. Care D, Suppl SS. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes – 2020. Diabetes Care. 2020; 43(1): S98-S110.
12. Defronzo RA, Norton L, Abdul-Ghani M. Renal, metabolic & cardiovascular considerations of SGLT2 inhibition. Nat Rev Nephrol. 2017; 13(1): 11-26.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 03 ,2024

13. Ehrenkranz RRL, Lewis NG, Kah CR, Roth J. Phlorizin: a review. Diabetes Metab Res Rev. **2015;** 21: 31–38.
14. Meng W. Discovery of dapagliflozin: a potent, selective renal sodium-dependent glucose cotransporter2 (SGLT2) inhibitor forthe treatment of type 2 diabetes. Journal of Medicinal Chemistry. 2008; **51**(5): 1145–49.
15. Han S. Dapagliflozin, a selective SGLT2 inhibitor, improves glucose homeostasis in normal & diabetic rats. Diabetes. 2008; **57**(6): 1723–29.
16. Viswanathan V, Singh KP. Use of Dapagliflozin in the management of type 2 diabetes mellitus: a real-world evidence study in Indian patients (FOREFRONT). Diabetes technology & therapeutics. 2019; 21(8): 415-22.
17. AdAwi RMA, Jassim Z, Elgaily D, Abdelaziz H, Sree B, Ibrahim MIM. Assessment of Dapagliflozin Effectiveness as Add-on Therapy for the Treatment of Type 2 Diabetes Mellitus in a Qatari Population. Scientific Reports:2019: 9:6864:43052-43056.
18. Joaqui VB, Gómez NB, Ortiz RC, Toro LM, Lombo JP, Cifuentes CA, García MA, Lomba AA. Effectiveness of triple therapy with dapagliflozin add-on to dual therapy over 52 weeks in patients with uncontrolled type 2 diabetes mellitus in a centre of high complexity, Cali-Colombia. Archives of Endocrinology & Metabolism. 2021; 65: 49-59.
19. Jabbour S.A, Hardy E, Sugg J, Parilh 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; 37: 740–750.