Original Article

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Assessment of Dapagliflozin Effectiveness as Add-on Therapy for the Treatment of Type 2 Diabetes Mellitus

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Abstract

Background: To assess effectiveness of Dapagliflozin as add-on therapy for the treatment of Type 2 Diabetes Mellitus. **Method:** Dapaglifozin was added as add on treatment in all the patients after the initial standard management. They were divided into groups based on the initial combinations with comparable baseline readings for HbA1c and fasting blood glucose (FBG). Differences in the values of HbA1c and FBG following treatment with Dapagliflozin was evaluated at 3 months. **Result:** Among all 130 subjects, the 56.92% were males and 43.08% were females. Maximum subjects belonged to the age group of 50-59 years. The mean age of the subjects was 54.02 years. Out of 130 subjects, 29.23% had a history of T2DM. Most of the subjects had T2DM from last 8-10 years (53.08%), Out of 130 subjects, 16.92% had hypertension, 10.77% had cardiovascular disease and 6.15% had other co-morbidities. The mean body weight and height among the subjects after the intervention was 68.96Kg and 162.09 respectively. Glycemic parameters among the study subjects after the intervention showed a mean HbA1c value of 7.05%, mean FBG value of 131.73mg/dl and mean PPBG value of 204.98mg/dl. Mean HbA1c level achieved after 6 months of Dapagliflozin treatment was 7.62% in our patient population. **Conclusion:** Dapagliflozin was well tolerated in patients with T2DM and it lowered HbA1c levels and body weight after the intervention compared to baseline. The study found no adverse effect, implying that Dapaglifozin has a tolerable tolerability profile.

Keywords: Dapagliflozin, Oral hypoglycemic drug, Diabetes Mellitus

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Introduction

Diabetes mellitus (DM) is a serious public health concern that affects approximately 400 million people worldwide.[1]

In many nations, it has reached epidemic proportions, with Asian countries in particular seeing a dramatic increase.

This metabolic disorder has chronic micro-vascular, macro-vascular and neuropathic life-threatening complications. D.M is characterized by a lack of insulin secretion, pancreatic cell damage or insulin resistance. A propensity for sedentary lives could explain continuous increase in diabetic patients globally, which is expected to reach three hundred sixty six million in 2030.[2]

Currently, most guidelines prescribe pharmacologic therapy for diabetic management based on glycated hemoglobin or glycohemoglobin (HbA1c) values. When lifestyle management and metformin fail to meet the glycemic target, a second agent may be used, taking into account drug profiles and patient-related factors.

Metformin, sulfonylureas, thiazolidinediones, glucagon-like-peptide-1 analogues, and dipeptidyl peptidase-4 inhibitors are all insulin-dependent antidiabetic medications.

Weight increase is a side effect of sulphonylureas & thiazolidinediones, which exacerbates insulin resistance.[3] Dapagliflozin, on the other hand, as a highly selective inhibitor of sodium glucose co-transporter-2 (SGLT-2), is unique in its insulin-independent action on reducing glucose reabsorption, particularly by the proximal tubule in the kidney, allowing more glucose from plasma to be eliminated into urine.[4,5]

The SGLT-2 cotransporters are highly elevated in diabetic individuals, resulting in increased glucose reabsorption and extended hyperglycemia. Dapagliflozin is a highly potent and reversible SGLT-2 that works by blocking tubular reabsorption of up to half of the glucose filtered by SGLT-2 in

segments one and two of the proximal renal tubule, resulting in a dose-dependent increase in urinary glucose excretion and, as a result, an improvement in glycemic control.[6–8]

It can be used alone in newly diagnosed individuals or with other Oral hypoglycemic agents or Injectables in patients who have had diabetes for a long time.

Treatment with dapagliflozin reduce the Body Weight, decrease in systolic BP and it has a low intrinsic propensity to cause hypoglycemia.[9] The mean half-life of Dapagliflozin is approximately 14 hours which makes it suitable for once-daily dosing.[10]

Dapagliflozin has a variety of effects on HbA1c, fasting blood glucose, body weight (B.W), systolic BP and weight loss, as well as a low proclivity for hypo-glycaemia and a lower risk of cardiovascular events.

There are only a few real-world studies that have looked at the usefulness of Dapagliflozin in Indian population, particularly among Western Uttar Pradesh, which has its own demographic, culture, and way of life.

Subjects and Methods

Study Design and Place

Carried out at Teerthanker Mahaveer Medical College & Research Centre as an Interventional hospital based study.

Oral & Written Informed consent were obtained from every patient for clinical examination & lab investigations.

Study Population

Patients presenting with T2DM in OPD/IPD of Medicine and other departments during the study period were evaluated.

Study Period

The period of study was 12 months after the approval of The Research Committee and The Ethical committee.

Sample Size

130 patients of T2DM with uncontrolled D.M status with same treatment since more than 3 months.

Inclusion Criteria

- All the patient with age more than 18 years and less than 75 years of age.
- All previously diagnosed cases of T2DM on O.H. As and/or Insulin for more than 3 months.
- Inadequately controlled T2DM (HbA1c greater than 7.0% and less than 11.0%).

Exclusion Criteria

- Patients who are newly diagnosed cases of T2DM
- Patients with e.G.F.R less than 45mL/min/1.73m2 of body surface.
- Patients taking loop diuretics.

Study Plan

All participants in this trial received Dapagliflozin as an add-on medicine in addition to their regular diabetic care. They were separated into groups based on the most prevalent combinations with similar HbA1c and FBG baseline levels.

HbA1c and F.B.S levels at the follow up.

Differences in the values of HbA1c and FBG following treatment with Dapagliflozin was evaluated at 3 months.

Ethical approval was obtained from the TMU Ethical Committee prior to the data collection.

Details about each patient's medical history, family history, clinical examination and treatment was recorded by preformed questionnaires.

Statistical analysis

It was done using S.P.S.S. software version 24 and the test used to analyzed significant difference was t test with level of significance set at <0.05.

Result

Table 1: Gender distribution among the study subjects

Gender	N	%
Male	74	56.92
Female	56	43.08
Total	130	100

The current study showed that among all the subjects 56.92% were males and 43.08% were females.

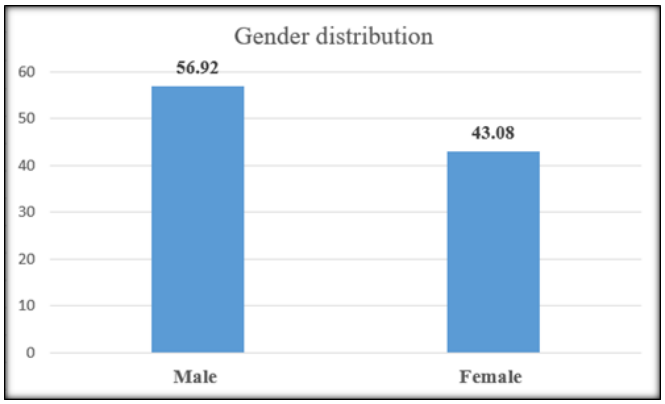

Figure 1: Gender distribution

Table 2: Age distribution among the study subjects

Age Group (in years)	N	%
<40	9	6.92
40-49	28	21.54
50-59	54	41.54
>60	39	30.00
Total	130	100
Mean±SD	54.02±11.05	

Maximum subjects belonged to the age group of 50-59 years followed by > 60 years and only 6.92% subjects belonged to <40 years age group. The mean age of the subjects was 54.02±11.05y years.

Table 3: Family history among the study subjects

Family History	N	%
Yes	38	29.23
No	92	77.77
Total	130	100

Among all the subjects 77.77% had no family history of type 2 Diabetes Mellitus whereas 29.23% had a history of T2DM.

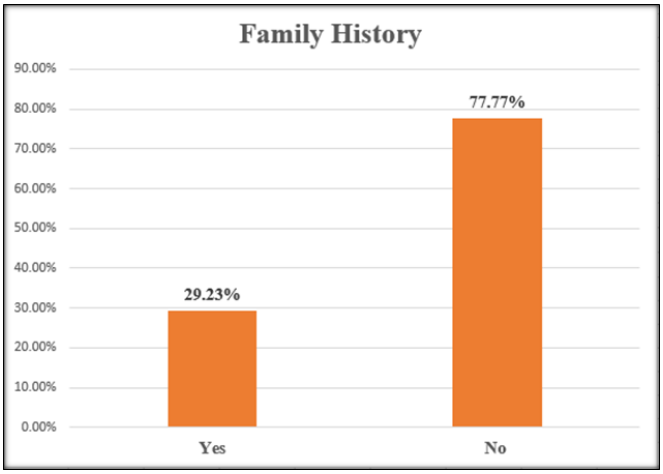

Figure 2: Family history

Table 4: Duration of diabetes among the study subjects

Duration	N	%
1-5	18	13.85
5-10	69	53.08
>10	43	33.08
Total	130	100

Most of the subjects had T2DM from 5-10 years (53.08%), whereas 33.08% had T2DM from >10 years. Only 13.85% had T2DM from 1-5 years.

Table 5: Co-morbidities

Co-morbidities	N	%
Hypertension	22	16.92
Cardiovascular Disease	14	10.77
Other	8	6.15

Out of all the subjects, 16.92% had hypertension, 10.77% had cardiovascular disease, and 6.15% had other co-morbidites.

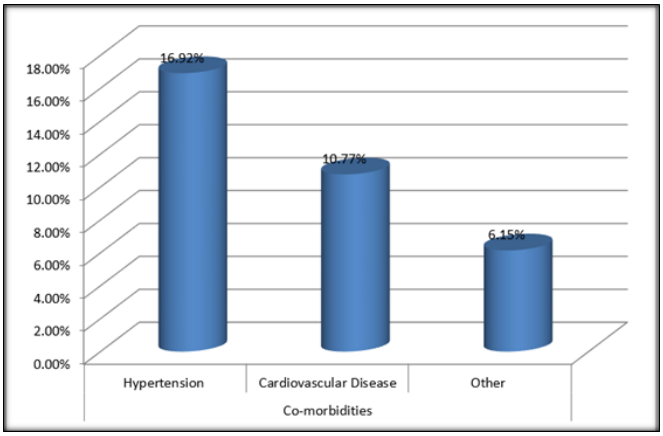

Figure 3: Co-morbidities among the study subjects

Table 6: Comparison of body weight before and after the intervention among the study subjects

Weight (kg)	Mean	SD
Before the Intervention	71.84	5.76
After the Intervention	68.96	4.51
t test	3.62	
p value	0.042*	

*: statistically significant

This table showed a significant comparison between the weight of study subjects before and after the intervention.

This table showed a significant comparison between the diabetic parameters of study subjects before and after the intervention.

Discussion

This study was carried out at Teerthanker Mahaveer Medical College & Research Centre as an Interventional hospital based

Table 7: Comparison of diabetic parameters among the study subjects before and after the intervention

Variables	Before Intervention		After Intervention		t test	p value
	Mean	SD	Mean	SD		
HbA1c	8.31	0.56	7.05	0.47	5.08	0.009*
FBG	184.7	5.2	131.73	6.2	14.03	<0.01*
PPBG	279.25	10.83	204.98	9.42	9.58	0.005*

*: statistically significant

study among 130 patients presenting with uncontrolled T2DM combination with other O.H.A.'s and/or insulin.

The current study showed that among all the subjects 56.92% were males and 43.08% were females.[11] Maximum subjects belonged to the age group of 50-59 years followed by > 60 years and only 6.92% subjects belonged to < 40 years age group. The mean age of the subjects was 54.02 years. Among all the subjects 77.77% had no family history of T2DM whereas 29.23% had a history of T2DM Most of the subjects had T2DM from 5-10 years (53.08%), whereas rest (33.08%) had T2DM from > 10 years. Only few (13.85%) had T2DM from 1-5 years.[12] Out of all the subjects, 16.92% had hypertension, 10.77% had cardiovascular disease, and 6.15% had other co-morbidites. In a study done by Joaquiet al,[13] the mean duration of T2DM was 5.93 years. Out of all the subjects, 16.92% had hypertension, 10.77% had cardiovascular disease, and 6.15% had other co-morbidites. In a study done by Viswanathan V et al, hypertension as a comorbidity was observed in 47.5% subjects.[14] The mean body weight and height among the subjects at baseline was 71.84Kg and 162.09cm respectively. The mean body weight and height among the subjects after the intervention was 68.96Kg and 162.09 respectively. After months of Dapagliflozin medication, a substantial reduction in mean (S.D) body weight of 2.88 kg was seen in our study. Patients with a higher B.M.I at the start of the study lost more weight than those with a lower B.M.I. Dapagliflozin has been proven to cause a daily calorie decrease of 200–300 calories.[14] Diabetic parameters among the study subjects at baseline showed a mean HbA1c value of 8.31%, mean FBG value of 184.7mg/dl, and mean PPBG value of 279.25mg/dl.[15] Diabetic parameters among the study subjects after the intervention showed a mean HbA1c value of 7.05%, mean FBG value of 131.73mg/dl, and mean PPBG value of 204.98mg/dl. When compared Jabbour and colleagues, this group likewise experienced a somewhat larger reduction in HbA1c and FBG in our study. Mean (SD) HbA1c level achieved after 6 months of Dapagliflozin treatment was 7.62% (1.04%) in our patient population; this is close to the target HbA1c level (<7.0%) recommended by the American Diabetes Association.[14]

Limitations

The limitations of our study include absence of an active comparator arm, which did not allow comparison with other oral antidiabetics namely G.L.P.-1 or D.P.P.4.i. However, the large patient population ensured the generation of reliable data to accurately assess the mean change from baseline in the efficacy parameters. Still, the sample size was not large enough to describe rare AEs. This study is also limited by issues that are inherent to the real-world evidence studies, such as presence of confounders, data quality, and bias.

Conclusion

Dapagliflozin was well tolerated in this first Moradabad (U.P) based prospective clinical interventional study in patients with T2DM, and it lowered HbA1c levels and body weight after the intervention compared to baseline. The study found no adverse effect, implying that Dapaglifozin has a tolerable tolerability profile. This trial provides excellent real-world evidence for the early uses of Dapagliflozin among Indian with T2DM in routine clinical practice to achieve better glycemic control with other advantages such as weight loss.

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