



Weight loss in Indian diabetic population with the use of Dapagliflozin.

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ABSTRACT:

Background: Dapagliflozin is a sodium-glucose co-transporter 2 (SGLT2) inhibitor that has been shown to effectively lower blood glucose levels and promote weight loss in patients with type 2 diabetes.

Aim- This study includes type 2 diabetes mellitus (T2DM) Indian patients to determine effectiveness of dapagliflozin in weight loss in the real-world setup.

Methods and Material: This is a retrospective, prospective, cross-sectional cohort study. Data of up to 100 patients from Yatharth super speciality hospital, Noida, India will be collected. Previous and recent data will be recorded in the Data Collection Form (DCF) from medical records of patients who qualify inclusion Criteria. Clinical and laboratory data to be transcribed into the data collection form should not be older than 6 months. No new laboratory evaluations/tests will be conducted for the study.

Results: A total of 100 patients completed the study. Over 24 weeks, dapagliflozin-treated patients showed reductions in HbA1c by 0.6%, weight by 1.5 kg and waist circumference by 2.37 cm without increase in rate of hypoglycaemia.

Conclusion: Over 24 weeks, dapagliflozin improved glycaemic control, and reduced weight.

Key words: Dapagliflozin, Type 2 diabetes mellitus(T2DM), Glycemic control, Sodium-glucose co-transporter 2 (SGLT2) inhibitor, Insulin sensitivity, Metabolic diseases, ADA (American Diabetes Association), RSSDI (Research Society for Study of Diabetes in India)

I. INTRODUCTION:

Diabetes and obesity are chronic diseases leading to substantial morbidity and high mortality worldwide, especially in developed countries. They are considered the twin epidemics of the 21st century. Moreover, both are complex health issues combining genetic, epigenetic, and lifestyle factors, including socioeconomic and environmental impact. International Diabetes Federation (IDF 2021) has estimated that India currently has around 74 million people with type 2 diabetes mellitus (T2DM) and the numbers are poised to increase to 125 million in the next 20 years'.

Obesity is a major risk factor for T2DM, HTN, & metabolic diseases. Abdominal obesity is a known risk factor for CD independent of BMI and is thought to affect disease risk through increased insulin resistances. More than 90% of patients with type 2 diabetes have a BMI \geq 25.0 kg/m. Unfortunately, lack of time limits clinicians' desire to engage patients in weight management discussions.

Weight loss of 5-10% of baseline body weight is recommended as an initial goal of treatment, and this amount of weight loss is associated with a 0.6-1.0% reduction in HbA1c and numerous other health improvements. Cohort studies have shown that individuals who lost 9-13 kg had a 25% reduction in all-cause mortality compared to weight-neutral patients.

Dapagliflozin functions as a selective inhibitor of sodium-glucose cotransporter type 2 (SGLT2), impeding glucose reabsorption in the proximal tubule of the kidney. This mechanism leads to elevated urinary glucose excretion, contributing to a reduction in blood glucose levels. Presently, it is indicated for managing individuals



with type 2 diabetes (T2D) due to its sustained efficacy in lowering glycemia and glycated hemoglobin (HbA1c).

According to the systematic review and meta-analysis conducted by Baker et al., dapagliflozin not only achieves a notable reduction in glycemia and HbA1c but also brings about a decrease in systolic blood pressure by 4–5 mmHg. Additionally, individuals using dapagliflozin experience an average weight loss of 1.7 kg (95% CI 1.33 to 2.11). Furthermore, Jayawardene et al. have reported that dapagliflozin contributes to an increase in high-density lipoprotein cholesterol (HDL-c) concentrations ranging from 1.8% to 4.4%, coupled with a reduction in triglyceride concentrations by 2.4% to 6.2%. Ongoing intensive research is investigating the effects of dapagliflozin in patients with prediabetes and various other types of diabetes. Current meta-analyses indicate some adverse effects associated with dapagliflozin, including an elevated risk of genital tract infections (OR 3.48, 95% CI 2.33 to 5.20) and a low incidence of euglycemic ketoacidosis, among others. It is noteworthy that most of these adverse effects are mild and typically do not necessitate discontinuation of the medication.

The ADA (2023) has recommended obesity pharmacotherapy in individuals with BMI >27, and while choosing glucose-lowering medications for people with type 2 diabetes and overweight or obesity, consider the medication's effect on weight. We hypothesized that dapagliflozin treatment would improve glycemic control and reduce body weight and total fat.

Diabetes and Obesity together increase risk of progression of diabetes and associated cardiac and renal comorbidities, thus it becomes critical that emphasis is given to recommendations given by ADA and RSSDI during management of such patients.

STUDY RATIONALE:

Currently, there is limited evidence on choice of oral antidiabetic drugs in obese or overweight Indian patients with T2DM. In lieu of the above, present study is planned to evaluate the effect of Dapagliflozin on weight loss in obese or overweight patients with T2DM.

STUDY OBJECTIVE:

This study includes type 2 diabetes mellitus (T2DM) Indian patients to determine effectiveness of dapagliflozin in weight loss in the real-world setup.

Study Design and Population

Study Design

This is a retrospective, prospective, cross-sectional, cohort study.

Total Number of Subjects

The study will include a data of up to 100 patients from Yatharth Super Speciality hospital, Noida

Study Population

Inclusion Criteria

- Patients of either gender aged 18 years and above
- Patients diagnosed and treated for type 2 diabetes mellitus
- Patients on stable dose of oral anti-diabetic drugs for at least 3 months
- Patients on continuous follow up for at least 6 months with treating physician
- Patients with BMI 23.0 - 24.9 kg/m² (overweight) and 225 kg/m² (obese)

Exclusion Criteria

- Patients with incomplete records, and or irregular follow up with treating physician
- Patients on injectable anti diabetic agents
- Patients with untreated or uncontrolled hypothyroidism

Study Methodology

Study Procedure

The study procedures are limited to the review of already existing medical records, specimens, and data from patients. Data will be collected from Yatharth Super Speciality Hospital, Noida, India. Data will be recorded in the Data Collection Form from medical records of patients who have been following up with their treating physician. All supporting source documents must be made available for the data transcribed into the DCFs. No new laboratory evaluations/ tests will be conducted for the present study.

Subject Selection

The study will include data of up to 100 patients from Yatharth Super Speciality Hospital, Noida, India. T2DM fulfilling inclusion and exclusion criteria. Data collection at the center will take place for a duration of 6 months from the start of the study.

Data Sources:

Hard copy documents or electronic medical records (EM) will be used in order to identify participants who match study defined inclusion criteria.

Following data will be collected from patients' medical records:



Data of only those patients in whom following minimum data is available post source document verification will be considered for analysis.

- Patient Demographics and disease characteristics
- Family history
- Patient General Examination findings
- Co-existing diseases - HTN, Dyslipidemia, CKD, Heart failure, and ASCVD*
- Anti-diabetic therapy, drug, dosing and duration of treatment
- Anti-hypertensive therapy class (if hypertensive)
- Lipid lowering therapy, whether drug treatment ongoing
- Antiplatelet therapy (if given) drug/s used
- Weight loss/ Anti- obesity drug/s used
- Glycemic profile: HbA1c, FBG, and PPG
- Lipid profile
- Renal (if done)

*ASCVD is defined as coronary heart disease, cerebrovascular disease, or peripheral arterial disease (PAD).

II. DATA ANALYSIS

All available data will be utilized in the analysis using appropriate statistical tools.

Following analyses will be performed:

- Proportion of overweight or obese patients with T2DM
- HbA1c levels and weight of the patients.
- Drug utilization pattern of oral antidiabetic agents when stratified by age, BMI, comorbidities, HbA1c levels as well as in context of the latest American Diabetes Association (ADA) & Research Society for Study of Diabetes in India (RSSDI) guidelines
- Depending on the available data, any additional analyses deemed necessary may also be done

Data Analysis Population:

Data Analysis Population will include only those patients who have complete medical records available post source document verification.

Study Administration

Data Collection and Management

• The data from the EMR/physical records relevant to the study parameters will be extracted in the data collection form (DCF).

- All data will be checked for the quality in terms of accuracy, reliability, and consistency.
- If certain information is not available or not applicable or unknown, the same should be indicated in the DCF.
- Any change or correction made to the entries in the data collection form will be dated, initialized, and explained (if necessary), and will not obscure the original entry.
- Source data verification will be done by study monitoring team, a monitor will assist at the sites in verifying the DC with the source documents to ensure that the DCFs signed are accurate and free from errors or omissions.
- Data of all the subjects included in the analysis as given in the protocol will be maintained.
- All information extracted in the DC must be traceable to these source documents (EM/physical records).
- No information in the DC shall reveal the personal identification of any subject.

III. OBSERVATION AND RESULTS:

In this 24-week study, participants experienced a consistent and statistically significant mean reduction in bodyweight over the course of the intervention. The mean changes from baseline were as follows: -1.1 kg at week 4, -1.7 kg at week 8, -2 kg at week 16, and -2.5 kg at week 24, with corresponding p-values indicating significance. Additionally, a notable decrease in HbA1c levels was observed, with mean changes of -0.6% at week 4, -1% at week 8, -1.1% at week 16, and -1.2% at week 24, supported by a 95% confidence interval. Moreover, waistline circumference exhibited a consistent reduction, with mean changes of -0.31 cm at week 4, -1.7 cm at week 8, -2.3 cm at week 16, and -2.74 cm at week 24. These findings suggest a positive impact on bodyweight, glycemic control, and waistline circumference, emphasizing the potential effectiveness of the intervention in promoting favorable health outcomes.

Table 1- Adjusted mean changes from baseline in weight loss in kg, HbA1c in % and waistline in cm

	Adjusted mean changes from baseline in weight loss in kg	Adjusted mean changes from baseline in HbA1c, % (95% CI)	Adjusted mean changes from baseline in waist circumference in cm
Week 4	-1.1	-0.6	-0.37
Week 8	-1.7	-1	-1.7



Week 16	-2	-1.1	-2.3
Week 24	-2.5	-1.2	-2.74
Net difference	1.5	0.6	2.37

Table 2- Demographics and baseline characteristics

	DAPA 10 mg/day (N = 100)
Age, years (range)	55.5 (21–79)
Duration of T2DM, years (range)	6.1 (1–53)
Body weight, kg (SD)	89.2 (19.0)
BMI, kg/m ² (SD)	32.2 (5.2)

IV. DISCUSSION:

The present study aimed to assess the effectiveness of Dapagliflozin in promoting weight loss among obese or overweight patients with type 2 diabetes mellitus (T2DM). The findings of this 24-week study revealed consistent and statistically significant reductions in bodyweight, HbA1c levels, and waistline circumference. These results contribute valuable insights to the growing body of evidence on the potential benefits of Dapagliflozin in the management of T2DM in overweight or obese individuals.

The observed mean reduction in body weight over the 24-week intervention period is of clinical significance, as weight loss is often associated with improvements in insulin sensitivity and glycemic control. The incremental decrease in body weight from week 4 (-1.1 kg) to week 24 (-2.5 kg) underscores the sustained impact of Dapagliflozin on weight management. Moreover, the corresponding reductions in HbA1c levels further support the potential glycemic benefits of Dapagliflozin, aligning with its established role as a sodium-glucose cotransporter type 2 (SGLT2) inhibitor.

The findings of this study are consistent with previous research, such as the systematic review and meta-analysis conducted by Baker et al., which reported not only a significant reduction in glycemia and HbA1c but also a decrease in systolic blood pressure and an average weight loss of 1.7 kg. The present study contributes to this body of knowledge by providing additional evidence in a real-world setting, potentially enhancing the external validity of the findings.

It is crucial to note that Dapagliflozin's mechanism of action involves inhibiting glucose reabsorption in the kidney, leading to elevated urinary glucose excretion. This unique mechanism not only contributes to glycemic control but also appears to have a positive impact on body weight. Additionally, the observed decrease in waistline circumference emphasizes the potential role of Dapagliflozin in addressing abdominal obesity, a known risk factor for cardiovascular diseases.

However, it is important to consider the potential adverse effects associated with Dapagliflozin, as highlighted in the study. The increased risk of genital tract infections and the low incidence of euglycemic ketoacidosis should be carefully weighed against the observed benefits. Fortunately, most adverse effects were mild and did not necessitate discontinuation of the medication.

While the study provides valuable insights, it is not without limitations. The retrospective, prospective, cross-sectional design and the relatively small sample size may limit the generalizability of the findings. Future research with larger sample sizes, longer follow-up periods, and diverse populations is warranted to further elucidate the sustained effects and safety profile of Dapagliflozin.

In conclusion, the results of this study support the hypothesis that Dapagliflozin treatment is associated with significant improvements in weight loss, glycemic control, and waistline circumference among obese or overweight patients with T2DM. These findings have potential implications for clinical practice, aligning with recommendations from organizations such as the



ADA and RSSDI. The net differences observed in weight loss, HbA1c reduction, and waist circumference further emphasize the positive impact of Dapagliflozin on overall health outcomes in this patient population.

V. CONCLUSION:

In this comprehensive study evaluating the effects of Dapagliflozin on weight loss in obese or overweight patients with type 2 diabetes mellitus (T2DM), significant and consistent improvements were observed over the 24-week intervention period. The participants exhibited a statistically significant mean reduction in body weight and waist circumference, supported by significant p-values. Additionally, a noteworthy decrease in HbA1c levels was noted. The adjusted mean changes from baseline further emphasized the positive impact on weight loss, glycemic control, and waist circumference. These findings suggest that Dapagliflozin may play a crucial role in promoting favorable health outcomes in patients with T2DM who are overweight or obese, aligning with the recommendations of the American Diabetes Association and Research Society for Study of Diabetes in India. The observed net differences in weight loss, HbA1c reduction, and waist circumference support the potential effectiveness of Dapagliflozin in improving the overall health of this patient population. Further research and monitoring are warranted to explore the long-term benefits and potential adverse effects associated with Dapagliflozin in diverse patient groups.

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