

Role of Dapagliflozin in the Management of Body Mass Index (BMI) and Glycated Hemoglobin (Hba1c) in Obese Type 2 Diabetic Patients

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ABSTRACT

Objective: To evaluate the effect of Dapagliflozin on BMI and HbA1C in Type 2 Diabetic Patients

Study Design: Retrospective / observational study.

Place and Duration of Study: This study was conducted at the internal department of Medicine, Khyber Teaching Hospital Peshawar from August 2020 to July 2021.

Materials and Methods: Total 333 diabetic patients, with mean age of 45.66 years, were enrolled in the study. Average BMI was 32.8 while average HbA1C was 9.94% at the time of enrollment. After taking prior informed consent and documentation of the demographic profile of the patients, SGLT2 inhibitors (Dapa) 10 mg was given for the treatment of T2DM. The main aim was reduction in HbA1C and BMI. Both BMI and HbA1C level was recorded at 0 months and 6 months. The statistical analysis was done using SPSS version 22.0 and graph were constructed using GraphPad prism software

Results: In total 333 diabetic patients, 39.9% (133) were females and 60.1% (200) were males. The mean age was 45.66 ± 8.3 years. The mean HbA1c at initial enrollment was 9.94 ± 0.53% and at follow-up, it was 8.42 ± 0.74%. Similarly, the mean BMI was 23.8 ± 1.1 at the time of enrollment, which was reduced to 31.4 ± 1.2 after follow-up. Statistically significant difference was recorded between initial and follow-up HbA1c values with p-value and 95% CI <0.001, -1.5-1.5. Similarly, the mean BMI reduction was significant from 32.8 ± 1.1 to 31.4 ± 1.2 with a p-value, 95% CI <0.001, -1.4-1.2.

Conclusion: SGLT-2 inhibitor, dapagliflozin is a very good anti-diabetic drug with additional benefits of BMI reduction.

Key Words: Diabetes Mellitus, Glycated hemoglobin (HbA1c), SGLT-2 inhibitors, Body Mass Index (BMI), Dapagliflozin.

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INTRODUCTION

Diabetes is common metabolic disorder where Type-2 diabetes mellitus contribute more than 90% of all cases through the world¹. Some of the recent figures taken from International Diabetic Federation (IDF) report, the

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situation is alarming, which the global prevalence of 10.5%, affecting more than 536.6 million people throughout the world. In 2045, it is expected to be 12.5%, with a total number of 783.2 million people². In Pakistan, the prevalence is 30% affecting every third person with a total number of approximately 33 million adults³. Insulin deficiency due to any reason or insulin resistance or both usually lead into T2DM⁴.

Obesity is another hug metabolic disorder, which is closely linked with T2DM. According to WHO, more than 1 billion people worldwide are obese, where 650 million are adults, 340 million are adolescents and 39 million are children and this number is still increasing very rapidly⁵. In Pakistan, the prevalence of obesity is more than 27.85%^{6,7}.

The target in the treatment of T2DM is to decrease HbA1C level, treat the comorbidities and prevent complications and the drugs which are commonly used for this purpose either increase the secretion of insulin or decrease the resistance to insulin. Some drugs uses

both aforementioned mechanisms and some of the drugs decrease the absorption of glucose from GI tract⁸.

The sodium-glucose transport 2 (SGLT-2) inhibitors, also known as gliflozin, and include Dapagliflozin (Dapa), Empagliflozin (Empa) and Canagliflozin (Cana) and Ertugliflozin (Ertu)⁹. They remove about 80 to 100 grams of glucose per day from the body by blocking its reabsorption through inhibition of SGLT2 receptors in the kidneys, thus decrease blood glucose level and as well as remove 320 to 400 kcal from the body leading to weight loss. We have used Dapagliflozin in our patients for the treatment of diabetes and observation of its impact on obesity^{10,11}.

Though SGLT-2 inhibitors have significant effects on weight reduction, but little is known about it especially at national level. To fill this gap, this study was conducted on these drugs to explore its effect on diabetes and obesity in Pakistani population.

MATERIALS AND METHODS

The study was carried out in the internal medicine department, Khyber teaching hospital Peshawar. The duration of study was 12 months (August 2020 to July 2021). Total 333 type 2 diabetic patients, who were overweight or obese, were selected. HbA1C level was recorded at 0 and 6 months. BMI was recorded at 0 and 6 months. BMI was calculated using weight and height as follows: BMI= weight (kilograms)/height (meters squared). BMIs were classified according WHO BMI classification¹⁰ and Asia-Pacific BMI Classification.

The group age were 31 to 60 years and out of all 333 patients, 39.9% (133) were females and 60.1% (200) were males. To avoid any confounders, all patients with some other major comorbidities like congestive cardiac failure, ascites, chronic renal failure and cirrhosis were excluded from the study as these conditions can affect weight due to fluid retention. The study design was descriptive prospective.

Data Collection: The project was approved by the Medical Research department KMC/KTH. Total 333 obese diabetic patients were enrolled in the study. After proper consent, demographic data including BMI was recorded using purposefully designed proforma and 5cc blood was withdrawn using 5cc disposable syringe and forward to KTH laboratory for HbA1c analysis. Dapagliflozin 10mg was prescribed to all the patients and were followed for 6 months. After 6 months, all the patients were re-interviewed, the demographics were recorded and HbA1c was repeated.

Table No.2: Gender based differences between study variables

Variable	Gender	N	Mean	SD	t-value	p-value	95% CI
Age	Female	133	45.59	9.03	0.124	0.90	1.9-1.7
	Male	200	45.71	7.8			
Initial HbA1C	Female	133	9.9	0.53	0.29	0.76	0.1-0.13
	Male	200	9.9	0.53			
HbA1C	Female	133	8.4	0.74	1.09	0.27	0.07-0.25

Data Analysis: The numerical values were expressed in mean \pm SD while categorical variables were expressed in frequency and percentages. Independent sample t test was applied to determine gender based differences. t-test was applied to find the mean differences between initial HbA1c, initial BMI and HbA1c and BMI after follow-up. p-value <0.05 was considered significant. Data was analyzed using SPSS version 22.0.

RESULTS

This study enrolls 333 diabetic patients in which 39.9% (133) were females and 60.1% (200) were males. The mean age was 45.66 ± 8.3 years. Similarly, the mean HbA1c at initial enrollment and follow-up was $9.94 \pm 0.53\%$ and $8.42 \pm 0.74\%$ respectively. Similarly, the mean BMI at the time of enrollment was 23.8 ± 1.1 which was reduced to 31.4 ± 1.2 after follow-up. All the values are summarized in table 1 for detail overview.

Table No.1: Demographic Data of Enrolled Patients

Variable	Minimum value/No	Maximum value/%	Mean	SD
Female	133	39.9	-	-
Male	200	60.1	-	-
Age	31	60	45.66	8.32
Initial HbA1C	9.1	10.7	9.94	0.53
HbA1C after follow-up	7.1	9.9	8.42	0.74
Initial BMI	31.3	34.6	32.8	1.1
BMI after follow-up	28.8	33.8	31.4	1.2

To determine whether gender imparts any significant importance on study variables, independent sample t-test was applied. The result reveals that there were no statistical differences between age, initial HbA1c and BMI and values of HbA1c and BMI after follow-up in both genders. All the values were non-significant with p-values >0.05. Table 2 summarizes the details of all difference between variables based on gender.

after follow-up	Male	200	8.3	0.73			
Initial BMI	Female	133	32.8	1.1	0.34	0.83	0.22-0.27
	Male	200	32.8	1.14			
BMI after follow-up	Female	133	31.41	1.18	0.75	0.77	0.30-0.22
	Male	200	31.45	1.21			

The mean differences were recorded between initial HbA1c and HbA1c after follow-up and initial BMI and BMI after follow-up. The mean HbA1c at the time of enrollment of patients were $9.94 \pm 0.53\%$ while it was reduced to $8.4 \pm 0.74\%$. Statistically significant difference was recorded between initial and follow-up HbA1c values with p-value and 95%CI <0.001, -1.5-1.5. Similarly, the mean BMI at time of patient enrollment was 32.8 ± 1.1 while after follow-up it was reduced to 31.4 ± 1.2 . The results were found statistically significant with p-value, 95%CI <0.001, -1.4-1.2. All the values are given in table 3 and graphically shown in figure 1.

Table No.3: Mean differences between initial variables and after follow-up

Variable	Mean	SD	t-value	P-value	95% CI
Initial HbA1C	9.94	0.53	36.2	<0.001	-1.5-1.3
HbA1C after follow-up	8.4	0.74			
Initial BMI	32.8	1.1	20.6	<0.001	-1.4-1.2
BMI after follow-up	31.4	1.2			

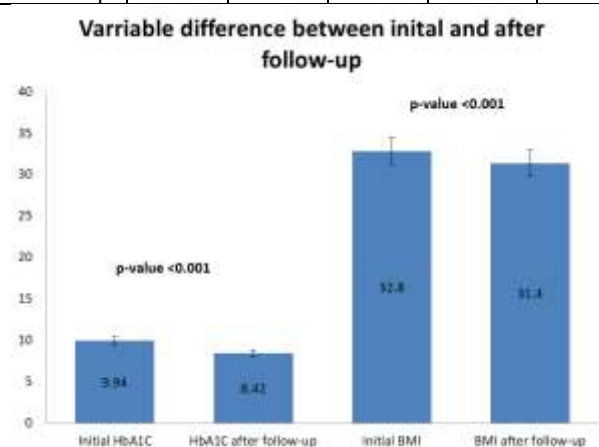


Figure No.1: Differences between HbA1c and BMI values at initial and after follow-up

DISCUSSION

In last decade, the treatment of Diabetes Mellitus is revolutionized and multidisciplinary approach is used to address the diabetes and prevent its complications. At the same time, treatment of co-morbidities like obesity,

hypertension etc is also very important to prevent the grave complications, morbidity and mortality due to coexistence of these disease. So far, many drugs have been used, but SGLT-2 inhibitors may be considered as a magic bullet, as these drugs not only treat diabetes, but also can be used to treat the comorbidities and complications of diabetes. SGLT-2 inhibitors remove glucose from the body and thus reduce diabetes and decrease weight. These effects of one the most important drug in this class, named Dapagliflozin is evaluated in this study.

Our finding regarding the efficacy of Dapa on HbA1C is closed to the finding of a multi-center study conducted by Morieri ML et all, in Italy, where they have targeted the effect of Dapa on HbA1C and hypertension in diabetic patients. They have noted an average decrease of 1.20% in HbA1C level, which is close to our observed value of 1.52¹².

In another study conducted by Kudo T et all, in Japan, where .66% reduction in HbA1C was observed in diabetic patients with Standard dose of dapagliflozin, using it for good 12 months. This effect was comparatively less than the effect observed in our study, but was equally significant¹³.

The effects of SGLT-2 inhibitors are also observed on the reduction of weight and BMI and now these drugs are the main weapon in the therapeutic armamentarium against obesity. In a study conducted by Iacobellis G and Gra-Menendez S, on the effects of dapagliflozin on epicardial fat thickness in patients with type 2 diabetes and obesity in, it was observed that there was a reduction of 3.5kg in weight and a reduction of 01 in BMI of T2DM patients¹⁴. These finding are closed to the finding of BMI reduction of 1.4% in these patients.

In another clinical trials, conducted by Oyama K et all, on the effects of dapagliflozin on Obesity, heart failure and renal dysfunction in type 2 diabetes mellitus patients, an average significant reduction of 1.8 in BMI was noted in these patients which is very closed to our finding of 1.4 in such patients. These finding in their clinical trials were different for different groups in term of BMI, where significant changes were observed in a group with very severely obsess patients¹⁵.

CONCLUSION

The new drugs SGLT-2 inhibitors are safe and effective choice to treat and manage not only hyperglycemia but also delaying micro and macro vascular complications. These drugs also have positive impacts to reduce BMI.

Our findings need to be replicated in multicenter studies to endorse our findings.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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