Effect of SGLT2 inhibitor (Empagliflozin) on HbA1c in most Prevalent Age Group of Type 2 Diabetic Patients

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ABSTRACT
Background: The new anti-diabetic drugs, which are known as sodium-glucose transport 2 (SGLT-2) inhibitors, remove about 80 to 100 grams of glucose per day from the body
Objective: Our objective is to evaluate the effect of SGLT2 inhibitor (Empagliflozin) on HbA1C in T2DM patients.
Method: The study was conducted in department of Medicine, Khyber teaching hospital Peshawar from October 2020 to September 2021. Total 400 newly diagnosed diabetic patients in accordance with American diabetes association (ADA) guidelines, with age group 45 to 55 years were enrolled in the study. All the patients were counsel verbally and after willingness, proper consent was singed from each patient. All the demographics were recorded on purposefully design proforma and SGLT2 inhibitors empagliflozin 10mg once daily was prescribed to the patients. All the patients were followed for 6 months with two follow-up intervals at 3 and 6 months.
Results: In total 400 patients, 123 (30.8%) were female and 277(69.3%) were male. The mean age was 50.13 ± 3.3 years. The mean starting HbA1C was 9.12 ± 0.46% while the mean HbA1C at subsequent follow-ups was 8.7 ± 0.46 and 8.4 ± 0.4% respectively. Gender does not affect the study variables significantly with p-value >0.05. Statistical strong significant differences were observed in HbA1C values at time of enrollment of patients (9.12 ± 0.46%) and after follow-up1 (8.7 ± 0.46) and follow-up 2 (8.4 ± 0.4%) with p-value <0.001.
Conclusion: Empagliflozin was found to improve diabetic profile of the patients. Our results need replication with a larger data from multiple centers to further validate our findings.
Key words: Type-2 Diabetes Mellitus, HbA1C, SGLT 2 inhibitors, Empagliflozin

Introduction

Type-2 diabetes mellitus is the most common metabolic disorder, contributing more than 90% of all diabetes cases worldwide. According to International Diabetic Federation (IDF) report, the global prevalence of diabetes in 2021 is 10.5%, affecting more than 536.6 million people. This figure can rise to 12.5% in 2045, where it will affect almost 783.2 million people[1]. According to the same report, the prevalence in Pakistan is 30% affecting approximately 33 million adults[1,2]. Pakistan stands third in the list of diabetes with higher number of total cases after China and India, but actually in the list of global prevalence, the position of Pakistan is first keeping in mind the size of population[3,4].

To treat T2DM, the target is to decrease HbA1C level, treat the comorbidities and prevent complications.

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Most of these drugs used so far are either increasing the secretion of insulin or increasing its sensitivity. Some of the drug utilizing both mechanisms. Ideals are those drugs which have cardiovascular safety and have negative or neutral effects on the weight[4, 6].

The new anti-diabetic drugs, which are known as sodium-glucose transport 2 (SGLT-2) inhibitors 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[7]. SGLT-2 inhibitors are also called gliflozin, and include Dapagliflozin (Dapa), Empagliflozin (Empa) and Canagliflozin (Cana) and Ertugliflozin (Ertu)[8, 9]. We have used Empa in our patients for the treatment of diabetes and observation of its effects by measuring HbA1C level. These drugs basically inhibit the reabsorption of glucose in the glomeruli, thus decrease HbA1C level[10, 11, 12].

In spite of these magic and important effects of SGLT-2 inhibitors, very little is known about these drugs at both national and international level. To fill this gap, this study was conducted on these drugs to know its effect on diabetes in Pakistani population.

Materials and methods

This study was conducted in the department of internal medicine in collaboration with department of Pharmacology, Khyber Medical College and Teaching Hospital (KMC/KTH) Peshawar. After getting ethical approval from the ethical board KMC/KTH, the project was started by enrolling patients. The duration of study was 12 months, starting from October 2020 to September 2021. Newly diagnosed and treatment naïve patients were enrolled in the study. The diagnosis was made according to the ADA guidelines. All the patients were verbally guided in their local language and after assuring willingness, proper consent was signed from each patient. The demographics include name, age, gender and HbA1C values were recorded on purposefully design proforma and Empagliflozin 10mg once daily was prescribed. All the 400 patients were followed for 9 months with two follow-up intervals (3 months and 6 months). Patients unwilling to participate and/or with major comorbidity like heart failure, ascites, chronic kidney disease and chronic liver diseases were excluded from the study.

Descriptive statistics were applied to present mean ± SD, frequency and percentages of the variables. Independent sample t test was applied to find out any possible differences in study variables based on gender. Student's t test was applied to determine the mean difference in HbA1C values at different follow-up. All the recorded values were 2 tailed and p-value <0.05 was considered statistically significant.

Results

Total participantsincluded were 400. Females were 123 (30.8%) while 277 (69.3%) were males. The mean age was 50.13 ± 3.30 years with minimum and maximum age in years was 45 and 55 respectively. Similarly, the mean HbA1c at the time of enrollment was 9.12mg/dl. All further details are summarized in table 1.

Table 1: Demographics of the patients

Variable	Minimum value/ No	Maximum value/ %	Mean	SD
Female	123	30.8	-	-
Male	277	69.3	-	-
Age	45	55	50.13	3.330
Initial HbA1C	8.40	10.00	9.1275	.46630
1st follow-up HbA1C	7.90	9.60	8.7743	.46026
2nd follow-up HbA1c	7.50	9.20	8.4060	.46975

The gender-based differences in the study variables which are shown in table 2. There were minimal differences in mean age, initial HbA1c and HbA1c at subsequent follow-ups. The mean age in female group was 50.39 ±0.3 years while that of male group was 50.01 ± 0.19 years. Similarly, the HbA1c at start between female and male group was 9.12 ± 0.04 and 9.12 ±0.02 mg/dl respectively. The mean differences were not statistically significant with p-value >0.05 which indicates that gender does not affect the study variables.

Table 2: Gender based differences

Variable	Gender	N	Mean	SD	t-value	p-value	95% CI
Age	Female	123	50.39	.304	1.05	0.29	0.3-1.08
	Male	277	50.01	.199			
Initial HbA1C	Female	123	9.1293	.04394	0.05	0.96	0.9-0.10
	Male	277	9.1267	.02749			
1st follow-up HbA1C	Female	123	8.7927	.04196	0.53	0.59	0.07-0.12
	Male	277	8.7661	.02755			
2nd follow-up HbA1c	Female	123	8.4472	.04173	1.13	0.24	0.04-0.15
	Male	277	8.3877	.02839			

There were statistical strong differences between HbA1c values at initial and subsequent follow-ups (p-value <0.001). The mean HbA1c at the start was 9.12 ± 0.46 which was reduced to 8.77 ± 0.46 at 1st follow-up and further decreased in 2nd follow-up which was 8.40 ± 0.46. See table 3 for detailed information. The graphical presentation is shown in figure 1.

Table 3: Mean difference between HbA1C at different follow-up intervals

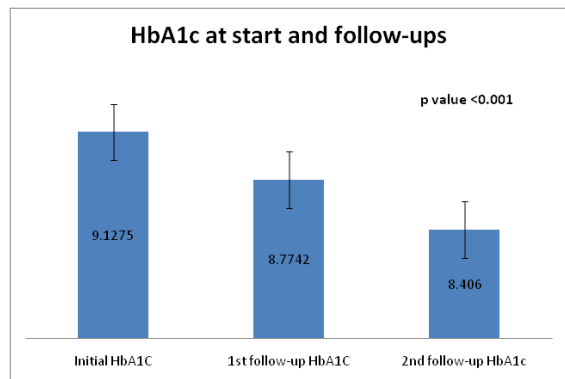| Variable	Mean	SD	t-value	P-value	95% CI
Initial HbA1C	9.1275	.46630	391.485	<0.001	9.08-9.7
1st follow-up HbA1C	8.7742	.46026	381.272	<0.001	8.7-8.8
2nd follow-up HbA1c	8.4060	.46975	357.892	<0.001	8.3-8.4

Figure 1: differences in HbA1c at start and follow-ups

Discussion

Diabetes mellitus is a common metabolic disorder which is usually considered as the most fascinating field for research and new drug development. Due to rising number of patients and complication, early diagnosis and early intervention with an appropriate drug in the therapeutic armamentarium against diabetes is the main goal of treatment. SGLT-2 inhibitors are rapidly gaining its popularity as they are good anti-diabetic drugs and can be used to prevent and treat other complications at the same time.

In our study, the mean HbA1C was 9.12 ± 0.46 which is reduced to 8.77 ± 0.46 on first visit at 3-months and 8.40 ± 0.46 at 6-months.

Empagliflozin is tested in a number of national and international trials. The finding of our study is close to the finding of international study conducted by Fang HS, Gao Q et all, titled as "the effect of oral diabetes medications on glycated hemoglobin (HbA1c) in Asians in primary care" in Singapore, where the HbA1C level reduction with Empa was close to 0.8 to 1% with different duration and dosages[13].

Apart from HbA1C reduction, Empa and other SGLT2 inhibitors are used for a number of additional benefits in T2DM patients. In study which was conducted in Japan by Tanaka A, Shimabukuro M, et all, titled as "Comparison of the clinical effect of empagliflozin on glycemic and non-glycemic parameters in Japanese patients with type 2 diabetes and cardiovascular disease treated with or without baseline metformin", to evaluate the effect of Empa on HbA1C reduction and additional non-glycemic parameters. It was found that HbA1C reduction was in the range of 0.6 to 0.9%, which is close to the value of our study[14].

Empa and other SGLT2 inhibitors have cardiac and renal protective qualities as well. These effects of Empa were evaluated along with HbA1C reduction in a local study conducted by Shafiq A, Mahboob E, et all, titled as "The dual role of empagliflozin: Cardio renal protection in T2DM patients". HbA1C reduction was 0.78% which is closed to the finding of our study[15].

HbA1C reduction in T2DM patients may be different with different doses of Empa. This effect was evaluated by another study conducted by Ozcelik S, Celik M, et all, titled as "the effect of low and high dose empagliflozin on HbA1C and lipid profile in type 2 diabetes mellitus" in Istanbul, where the HbA1C reduction was 1.18 to 1.54%, which is close to the value of our study[16].

Conclusion

SGLT-2 inhibitors, Empagliflozin is a very good drug. Apart from multiple other metabolic and cardiovascular effects, it is one of the best antidiabetic drugs for the reduction of HbA1C and tight control of diabetes in different patients. Large multicenter studies are needed to validate our findings with proper information of diet to explore the best sides of these drugs.

Conflict of Interest: Authors declare no conflict of interest.

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KEY FOR CONTRIBUTION OF AUTHORS:
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