



Original Article

Effect of Dapagliflozin on HbA1c in Type 2 Diabetics: A Descriptive Prospective Uncontrolled Before and After Study

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Abstract

Objective: To determine the efficacy of Dapagliflozin and its effect on HbA1c in Type 2 Diabetic patients.

Methods: We had conducted our descriptive study in the outdoor patient department of Holy Family Hospital, Rawalpindi. Hundred, Type 2 diabetic patients of both genders were enrolled through consecutive sampling to assess the efficacy of Dapagliflozin, an SGLT2 inhibitor in a Pakistani population. Those patients with HbA1c of $\geq 7\%$ who had fulfilled our inclusion criteria were given Dapagliflozin 10mg as either monotherapy or add-on therapy. HbA1c, BP, and body weight were noted at the start of drug therapy and after 12 weeks of drug use. The primary endpoint was $\geq 10\%$ relative percentage reduction of HbA1c after 12 weeks.

Results: Out of 100 subjects there were 40 males and 60 females in our sample. The average age of the patients was 49.37 ± 11.38 years. Dapagliflozin was given as a monotherapy to only two patients and others as an add on the drug. The average relative percent reduction after 12 weeks of treatment in HbA1c was 11.68 ± 6.20 . The sample results showed that the drug Dapagliflozin is effective for 62% of patients hence based on the sample results we conclude that the Dapagliflozin is effective against type 2 diabetics in our population for at least 53% of patients with a p-value of 0.034.

Conclusion: Over the period of 12 weeks, Dapagliflozin has shown a significant reduction in HbA1c and body weight of Type 2 diabetics in the Pakistani population. Once-daily dosing and a low rate of hypoglycemia make it a cost-effective and safe drug as well.

Keywords: HbA1c, SGLT-2 inhibitors, Dapagliflozin.

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Introduction

Sodium-glucose co-transporter 2 (SGLT2) is an activated protein channel located in the proximal renal tubule. The function of this protein is to reabsorb filtered glucose. SGLT2 accounts for more than 90% of glucose reabsorption from glomerular ultrafiltrate.¹ SGLT2 inhibitors belong to the new class of antidiabetic agents. The function of these agents is to block the SGLT2 which prevents glucose reabsorption and induces glycosuria, in this way they reduce plasma blood glucose levels.² In addition to reducing blood glucose level, these agents have other useful effects including weight reduction,

improvement in cardiovascular disease-related mortality, hepatic steatosis, and visceral fat mass.³

One of the SGLT2 inhibitors is Dapagliflozin. According to a study by Ferrannini E, et al monotherapy with Dapagliflozin was associated with an average of .9% reduction in HbA1c and 3 kg reduction in body weight in type 2 diabetics and lower risk of hypoglycemia.⁴ Combination therapy of SGLT2 including Dapagliflozin with other anti-hyperglycemic agents shows a synergistic effect and resulted in a clinically significant reduction in HbA1c.⁵

Dapagliflozin is being used worldwide and many

clinical trials have shown its beneficial effects. In Pakistan Dapagliflozin is recently launched so its effectiveness in the local population is still unknown. Thus, this study aims to evaluate its effectiveness in improving glycemic control in the Pakistani population.

Methods

Setting and Sampling: This descriptive study was conducted at Diabetic Clinic OPD, Holy Family Hospital (HFH) Rawalpindi from Nov 2018 to May 2019 through consecutive sampling from the type 2 diabetic population of Pakistan came to OPD in the hospital. The study was initiated after approval from the ethical committee. The patient's informed consent was also taken from the patients who agree to participate in the study.

Sample size: In a recent Japanese study conducted in 2020, a 70% reduction in HbA1c from the baseline was observed in 49.4% of patients by Dapagliflozin against type 2 diabetes. With the help of the above result keeping a 5% level of significance and absolute prevalence 10% the minimum required sample size is 97 so we take 100 patients for this study.

Inclusion and Exclusion criteria: 100 confirmed type 2 diabetic patients were included having aged 18 to 60 years, both male and female in our study. The patients who had type 1 diabetes, with renal impairment, those who were on dialysis, having a history of an allergic reaction to dapagliflozin, with lactose intolerance, glucose, and galactose malabsorption were not included in the study. Pregnant patients were also excluded from the study. A detailed history and clinical examination were noted down on a self-designed Performa.

Data Collection: Dapagliflozin 10 mg was started as a monotherapy or an add-on therapy. Age, gender, weight, blood pressure, Hb, creatinine, Duration of diabetes, and mode of Dapagliflozin were noted. At the end of the 12th week of treatment, BMI and HbA1c were noted again to assess the efficacy of the treatment. The efficacy of the drug was assessed through a relative reduction in post-treatment HbA1c relative to the baseline HbA1c greater than equal to 10%.

Data Analysis: The data was entered on SPSS 20. Descriptive analysis means \pm standard deviation and frequency and the percentage was performed for quantitative and qualitative variables. A paired t-test

was used to compare the BMI before and at the end of treatment. An Independent sample t-test was used to compare the patient's age, creatinine, Systolic, and diastolic blood pressure, and Hb. Duration of the diabetes was categorized into 5 different groups' i.e. new-onset patients, up to 5 years, between 6-10 years, between 11-15 years, and more than 15 years. Chi-square test was used to test the association of qualitative confounders with the efficacy of dapagliflozin. P-value ≤ 0.05 was assumed as significant.

Results

Out of 100 subjects there were 40 males and 60 females in our sample. The average age of the patients was 49.37 ± 11.38 years. The Dapagliflozin was prescribed alone only for 2 patients while for 98 patients' physicians prescribed the drug Dapagliflozin with the combination of other drugs i.e. Metformin, DPP IV Inhibitors, Insulin Glargine, Sulfonylureas, and Pioglitazone.

The average BMI, serum creatinine, Hb, systolic and diastolic blood pressure was 28.39 ± 5.26 , 0.85 ± 0.2 , 13.75 ± 1.43 , 131.41 ± 16.59 , 83.12 ± 11.84 , and 9.93 ± 2.13 respectively. The average relative percent reduction after 12 weeks of treatment in HbA1c was 11.68 ± 6.20 .

The efficacy of the treatment was decided if the relative percent reduction of HbA1c was greater or equal to 10. The sample results showed that the drug Dapagliflozin is effective for 62% of patients hence based on the sample results we conclude that the Dapagliflozin is effective against type 2 diabetics in our population for at least 53% of patients with a p-value of 0.034. Similarly, the average weight of the patients at baseline was 74.64 ± 14.91 kg which was reduced after 12 weeks of treatment by 74.03 ± 14.69 kg which was significantly low with a p-value of 0.000.

The proportion of efficacy between “the ways we use to take the drug”, duration of diabetes, age groups, and gender is mentioned in table 1. We observed that the proportion of efficacy of the treatment was the same between the categories of patient's characteristics. However, the results showed that the drug is more effective for females, as compared to males as the efficacy percent in females, was 71.7% whereas the efficacy of the treatment in male patients was just 47.5%. There were no adverse effects noted in our subjects during a period of 12 weeks.

Table 1: Comparison of the efficiency of Dapagliflozin with patient's characteristics

Variables	Categories	Dapagliflozin efficiency		P-value
		Insufficient reduction in HbA1c	Sufficient reduction in HbA1c	
Gender	Male	21	19	0.015
	Female	17	43	
Duration of diabetes	New-onset patient	6	13	0.76
	Up to 5 years	2	7	
	6 to 10 years	11	14	
	11 to 15 years	12	18	
Method of drug intake	Add-on	34	51	0.327
	Monotherapy	4	11	
Patients age in groups	Less or equal to 45	11	27	0.33
	Between 46 to 55	16	22	
	More than 55	11	13	

Discussion

The major findings which we deduced from our study is that Dapagliflozin is effective in reducing HbA1c in type 2 diabetics and effective in weight reduction. In our study, we had measured the relative percentage reduction of HbA1c after 12 weeks of Dapagliflozin use and according to our results, 62% of the study population had shown 10% or more of HbA1c reduction from the baseline value. Other clinical trials had also depicted the effectiveness of Dapagliflozin in reducing HbA1c like a retrospective cohort analysis done by Ruth E Brown and his colleagues had shown $0.9\% \pm 1.3\%$ reduction in HbA1c from the baseline value after 3 to 6 month of follow up with the p-value of 0.001.⁶

A study by Seigo Sugiyama and et al had concluded that Dapagliflozin caused body fat mass reduction by causing glucosuria and negative energy balance.⁷ Another study done by L. Zang, the colleagues demonstrated that Dapagliflozin caused weight reduction in patients with type 2 diabetes both in the early and late stage of the disorder.⁸ Similarly, in the study done by Bolinder, J, and et al, dapagliflozin-treated patients showed reductions in HbA1c by -0.3%, weight by -4.54 kg, waist circumference by -5.0 cm and fat mass by -2.80 kg without an increase in the rate of hypoglycemia.⁹ Like the above-mentioned studies, Dapagliflozin had shown positive results of bodyweight reduction along with a reduction in HbA1c. The average weight of 74.69 ± 16.91 kg was reduced to 74.03 ± 14.69 with a p-value of 0.000.

A review article by Anderson S L, suggests that

Dapagliflozin had shown to decrease HbA1c from 0.5% to 0.7% from the baseline value.¹⁰ According to this review article greater reduction in HbA1c was seen in patients with high HbA1c at baseline and higher reductions were seen when dapagliflozin was used as a multidrug therapy with other diabetic agents like Metformin, Sulfonylureas, and Pioglitazone.¹⁰ Other clinical trials also had demonstrated a better reduction in HbA1c when Dapagliflozin was used with other antidiabetic medications. A randomized control trial was done by Henry R, and colleagues have shown that combination therapy of metformin and dapagliflozin was superior in HbA1c reduction than metformin alone.¹¹ Two different studies one by K. Strojek and et al, and another study by Rosenstock J, and et al had demonstrated a greater reduction in HbA1c when Dapagliflozin was add on to glimepiride and pioglitazone respectively.^{12,13} In our study majority of the patients were on one or two antidiabetic medications before starting Dapagliflozin, out of 100, 54 patients had sufficient reduction in HbA1c with the p-value of 0.327. An insignificant p-value in our study could be because we had followed up with the patients only for 12 weeks. In the above-mentioned studies, patients were followed up for a minimum of 6 months to get the results.

In this study, 34 patients were on insulin either basal or mixed insulin regimen with other antidiabetic medications before starting Dapagliflozin, after the start of Dapagliflozin 17 patients showed a relative reduction of more than equal to 10% HbA1c with not a single patient had reported hypoglycemic episodes.

Studies in the past had revealed similar results. A randomized controlled trial by J P H Wilding and et al had shown that add on therapy of Dapagliflozin in a dose of 10mg in type 2 diabetics having high insulin requirement with or without using other oral anti glycemc agents had a mean reduction of HbA1c from 0.6% to 0.8% with bodyweight neutrality and fewer episodes of hypoglycemia.¹⁴

Another significant finding was the better response of Dapagliflozin in female patients with a p-value of 0.015, the reason could be the higher number of female subjects as compared to males in this study. Unlike the study done by Ruth E Brown and et al, we Were unable to detect a greater reduction of HbA1c in patients with shorter duration diabetes, and male gender.⁶ Likewise, no significant relationship was seen with specific age groups who were given Dapagliflozin and HbA1c. In our opinion, a larger sample size, and longer follow-up were required to discover the above-mentioned effects of Dapagliflozin on the Pakistani population.

Conclusion

Over the period of 12 weeks, Dapagliflozin has shown a significant reduction in HbA1c and body weight of Type 2 diabetics in the Pakistani population. Once-daily dosing and a low rate of hypoglycemia make it a cost-effective and safe drug as well. However, more studies are required to find out the extent of other beneficial effects of Dapagliflozin on the Pakistani population.

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Ethical Approval: The IRB/EC approved this study via letter no R41-RMU dated October 27, 2018.

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Authors' Contribution

NA, MN: Conception

SAK, IS: Design of the work

SA, FH: Data acquisition, analysis, or interpretation

SA, FH, SAK, IS: Draft the work

NA, MN: Review critically for important intellectual content

All authors approve the version to be published

All authors agree to be accountable for all aspects of the work

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