The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 5, 2025

EFFECT OF SODIUM GLUCOSE CO-TRANSPORTER-2 (SGLT-2) INHIBITORS ON BODY MASS INDEX AFTER 3 MONTHS OF USE IN DIABETIC PATIENTS

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DOI: https://doi.org/10.5281/zenodo.18798947

Keywords
sodium glucose co-transporter-2 inhibitors, body mass index, type II diabetes mellitus, glycemic index.

Article History
Received: 02 April 2025
Accepted: 25 April 2025
Published: 05 May 2025

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Abstract

Objective: *To compare the mean change in body mass index after using sodium glucose co-transporter-2 (SGLT-2) inhibitors versus placebo in patients with diabetes mellitus.*

Study design: *Quasi-experimental study.*

Place and duration of study: *Department of Medicine, Combined Military Hospital Multan for 6 months i.e. from 01 October 2024 till 31 March 2025.*

Methodology: *Sample size of 360 diabetic individuals were enrolled and divided in two groups. In group A, individuals were prescribed oral 100 gram Empagliflozin tablet along with diet plan and exercise. In group B, diet plan and exercise were prescribed. All patients were followed-up for about three months. BMI was measured before and after three months and mean change was calculated. All this information was recorded on Proforma and analysed in SPSS v.25.*

Results: *The mean age of individuals in SGLT-2 group was 50.30 ± 12.29 years, while in control group was 49.71 ± 110.99 years. In SGLT-2 group, there were 97 (53.9%) males while 83 (46.1%) females. In control group, there were 92 (51.1%) males while 88 (48.9%) females. The mean change in weight was observed as 5.69 ± 1.39 kg vs. 2.42 ± 1.20 kg in both groups, respectively, showing more change with SGLT-2 as compared to control group ($p<0.0001$). The mean change in BMI was observed as 2.00 ± 0.50 kg/m^{2}vs. 0.85 ± 0.42 kg/m^2 in both groups, respectively, showing more change with SGLT-2 as compared to control group ($p<0.0001$).*

Conclusion: *Thus, SGTL-2 inhibitors are effective in reducing BMI of diabetic patients as well as maintain glycemic index.*

INTRODUCTION

It is accredited that type 2 diabetes is a major public health issue that significantly affects both human life expectancy and medical costs. In many regions of the world, the prevalence of diabetes is on the rise due to rapid economic development and urbanisation.[1, 2] Diabetes significantly increases morbidity and premature mortality by affecting a person's functional abilities and quality of life.[3] It has recently come to light that those under 60 account for over one-third of diabetes-related fatalities. These changes have been attributed to an increase in the consumption of poor foods and sedentary lifestyles, which have been linked to higher fasting plasma glucose and Body Mass Index

(BMI).[4] For many individuals, blood pressure, blood glucose, and other objectives are still not optimally controlled. This has been partially ascribed to the absence of health promotion and awareness that are necessary for the management of diabetes.[5, 6]

The first-line treatment for diabetics is metformin. Weight loss is the main goal for obese diabetic patients. Many other treatments, including oral sulfonylureas and dipeptidyl peptidase-4 inhibitors, are used after metformin. Available medications include insulin, alpha-glucosidase inhibitors, pioglitazone, sodium-glucose co-transporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 receptor agonists, and pioglitazone, particularly in patients with fatty liver disease. According to recent research, SGLT2 inhibitors significantly lower cardiovascular events and mortality. Therefore, SGLT-2 should be taken into consideration next in patients with cardiovascular disease. SGLT-2 inhibitors have the benefit of lowering blood pressure, albuminuria, and body weight.[7, 8] The FDA has approved four medications—canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin—to help adults with type 2 diabetes mellitus improve blood sugar management in addition to diet and exercise, particularly in the elderly population.[9, 10]

Rationale of study was to compare the mean change in body mass index after using SGLT-2 inhibitors versus placebo in patients with diabetes mellitus. Literature showed that SGLT-2 inhibitors is more appropriate and effective in reducing weight as well as has good control over glycemic level of diabetic patients. But limited work has been done before as no evidence exist in local literature. Therefore, we conducted this trial to obtain the evidence and current extent of knowledge about effectiveness of SGLT-2 inhibitors for diabetic patients, especially with obesity.

METHODOLOGY

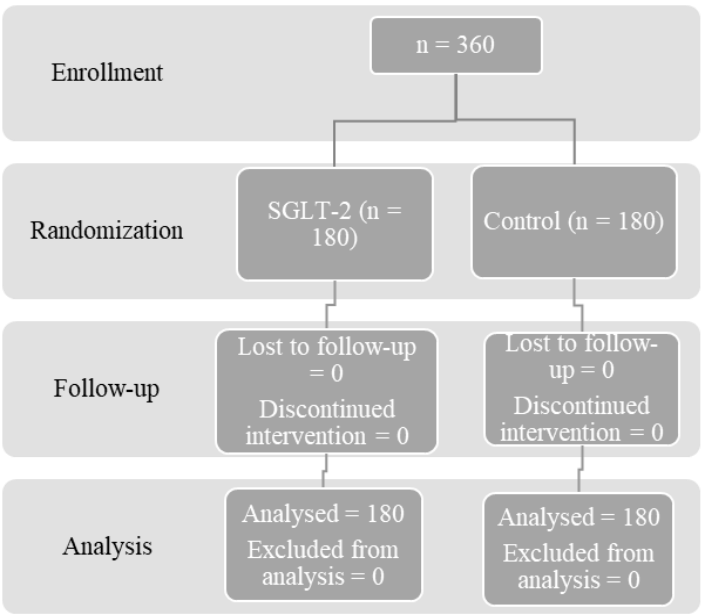
After approval from Ethical Review Committee of the hospital this Quasi-experimental study was conducted at the Department of Medicine, Combined Military Hospital Multan for 6 months i.e. *01 October 2024 till 31 March 2025*. Sample size of 360 cases; 180 in each group is calculated with 95% confidence level, 80% power of study and mean reduction in BMI i.e. 0.86±2.01 kg/m^2 with SGLT2 inhibitor and 0.4±0.9 kg/m^2 with control.[11] All the individuals were enrolled by applying Non-Probability, consecutive sampling technique after filtering the children for following criteria:

Inclusion: Individuals of age 30-70 years, both genders, diagnosed with type II diabetes mellitus. Diabetes was diagnosed when blood sugar level (random) at presentation was above 186 mg/dl and HbA1c was more than 6.5% on laboratory investigations.

Exclusion: Individuals already taking trail drug or any other anti-glycemic drug or insulin for >6 months were excluded from the trial.

Informed consent was obtained after explaining them the pros and cons of treatment. Demographics (name, age, sex, duration of diabetes, occupation, lifestyle, socioeconomic status and residence) were noted. At presentation, height, weight, and BMI, will be calculated. Then individuals were divided in two groups depends on agreement of taking oral medication for study purpose. Individuals who agreed to take oral 100 gram Empagliflozin tablet along with diet plan and exercise were categorized as group A. Individuals who did not want to take medication instead agreed to follow a diet plan and exercise were categorized as group B. All individuals were followed-up in OPD for 3 months. After 3 months, individuals were assessed again for height, weight, and BMI, and change in weight and BMI were calculated. All this information was recorded on Proforma.

Figure-1: Patient Flow Diagram (n= 360)



Data was entered & analysed by using SPSS version 25. Normality was checked by Shapiro-Wilk test. Both groups were compared for mean reduction in weight and BMI by using independent samples t-test. P-value ≤0.05 was taken as significant.

RESULTS

In this trial, we enrolled total 360 individuals. The mean age of individuals in SGLT-2 group was 50.30 ± 12.29 years, while in control group was 49.71 ± 110.99 years. In SGLT-2 group, there were 97 (53.9%) males while 83 (46.1%) females. In control group, there were 92 (51.1%) males while 88 (48.9%) females. Job details are given in table below. Mostly individual belonged to middle class. More than 180 individuals had sedentary lifestyle and this is associated with high risk of diabetes. Residential details are given in table below. In SGLT-2 group, there were 49 (27.2%) smoker and in control group, 49 (27.2%) smokers. In SGLT-2 group, there were 126 (70.0%) individuals who had hypertension and in control group, there were 122 (67.8%) individuals who had hypertension. Table-I

In SGLT-2 inhibitor group, the mean height of individuals was 1.69 ± 0.11 meters, while in control group was 1.69 ± 0.11 meters. At baseline, the mean weight of individuals was 103.18 ± 14.86 kg versus 102.91 ± 14.14 kg in control group. The mean weight was reduced to 97.48 ± 14.65 kg in SGLT-2 group and to 100.49 ± 13.78 kg in control group at end of study. The mean change in weight was observed as 5.69 ± 1.39 kg vs. 2.42 ± 1.20 kg in both groups, respectively, showing more change with SGLT-2 as compared to control group ($p<0.0001$). At baseline, the mean BMI of individuals was 36.24 ± 5.22 kg/m^2 versus 36.25 ± 5.96 kg/m^2 in control group. The mean BMI was reduced to 34.24 ± 5.11 kg/m^{2}in SGLT-2 group and to 35.41 ± 5.83 kg/m^{2}in control group at end of study. The mean change in BMI was observed as 2.00 ± 0.50 kg/m^{2}vs. 0.85 ± 0.42 kg/m^2 in both groups, respectively, showing more change with SGLT-2 as compared to control group ($p<0.0001$). At baseline, the mean BSR of individuals was 348.01 ± 68.46 mg/dl versus 358.81 ± 69.97 mg/dl in control group. The mean BSR was reduced to 200.27 ± 27.09 mg/dl in SGLT-2 group and to 214.49 ± 31.15 g/dl in control group at end of study, showing more change with SGLT-2 as compared to control group ($p<0.0001$). Table-II

Table-I: baseline information of individuals enrolled in the trial (n = 360)

	Trial groups	
	SGLT-2 inhibitor	Control
n	180	180
Age, in years	50.30 ± 12.29	49.71 ± 110.99
Sex of individuals		
Male	97 (53.9%)	92 (51.1%)
Female	83 (46.1%)	88 (48.9%)
Occupation		
Job	58 (32.2%)	48 (26.7%)
Business	49 (27.2%)	55 (30.6%)
Housewife	62 (34.4%)	67 (37.2%)
Retired	11 (6.1%)	10 (5.6%)
Socioeconomic status		
Low	21 (11.7%)	21 (11.7%)
Middle	129 (71.7%)	127 (70.6%)
High	30 (16.7%)	32 (17.8%)
Lifestyle		
Sedentary	91 (50.6%)	93 (51.7%)
Active	46 (25.6%)	22 (12.2%)
Routine work	43 (23.9%)	65 (36.1%)
Residence		
Rural	47 (26.1%)	52 (28.9%)
Urban	90 (50.0%)	83 (46.1%)
Industrial area	43 (23.9%)	45 (25.0%)
History of		
Smoking	49 (27.2%)	49 (27.2%)
Hypertension	126 (70.0%)	122 (67.8%)

Table-II: Comparison of anthropometric measurements of individuals (n = 360)

	Trial groups		p-value
	SGLT-2 inhibitor	Control	
n	180	180	
Height, in meters	1.69 ± 0.11	1.69 ± 0.11	0.970
Weight at baseline	103.18 ± 14.86	102.91 ± 14.14	0.859
Weight at end of trial	97.48 ± 14.65	100.49 ± 13.78	0.046
Change in weight	5.69 ± 1.39	2.42 ± 1.20	<0.0001
BMI at baseline	36.24 ± 5.22	36.25 ± 5.96	0.893
BMI at end of trial	34.24 ± 5.11	35.41 ± 5.83	0.044
Change in BMI	2.00 ± 0.50	0.85 ± 0.42	<0.0001
Blood sugar level at baseline	348.01 ± 68.46	358.81 ± 69.97	0.140
Blood sugar level at end of trial	200.27 ± 27.09	214.49 ± 31.15	<0.0001

DISCUSSION

In this trial, we observed that the mean weight was reduced to 97.48 ± 14.65 kg in SGLT-2 group and to 100.49 ± 13.78 kg in control group. The mean change in weight was observed as 5.69 ± 1.39 kg vs. 2.42 ± 1.20 kg in both groups, respectively, showing more change with SGLT-2 as compared to control group (p<0.0001). Furthermore, we observed that the mean BMI was reduced to 34.24 ± 5.11 kg/m^2in SGLT-2 group and to 35.41 ± 5.83 kg/m^2in control group at end of study. The mean change

in BMI was observed as 2.00 ± 0.50 kg/m^{2}vs. 0.85 ± 0.42 kg/m^2 in both groups, respectively, showing more change with SGLT-2 as compared to control group (p<0.0001).

Das et al., conducted a similar trial on 100 diabetic patients in Karachi and observed that HbA1c was reduced from 8.7 ± 1.5 % to 7.5 ± 1.1 % after 3 months, while up to 7.9 ± 1.2 % after 6 months and this reduction was observe to be significant (p <0.001). Similarly, mean BMI was reduced from 32.4 ± 5.9 kg/m^2 to 31.4 ± 5.8 kg/m^2 after 3 months and up to 31.8 ± 5.8 kg/m^2 after 6 months (p <0.01). They concluded that SGLT-2 inhibitor significantly improved glycemic control, and BMI among diabetics.[12]

Numerous studies show that empagliflozin causes a slight decrease in weight (< 3.2%), and that longer-term use is necessary to get a larger reduction in weight.[13, 14] The results of this trial, however, are consistent with other research that has demonstrated more noticeable weight loss during shorter time periods.[15-17] Like, in a research by Hussain et al., on diabetic patients belong to Pakistani population, following 12 weeks of treatment had a significant decrease of -2.9 ± 6.4 kg of whole body weight.[18]

Sanjari et al., conducted a quasi-experimental trial and observed that the mean reduction in weight was observed as 2.96 ± 1.96 kg (about 3.8% reduction) (P <0.001). The mean reduction in BMI was observed as -1.10 ± 0.71 kg/m^2 (about 3.72% reduction) (P <0.001). Similarly, the HbA1c was reduced from 6.52% to 6.38% (P < 0.001).[15]

Research involving individuals treated with canagliflozin, dapagliflozin, and empagliflozin who had mean HbA1c levels higher than 8% showed that 64% (compared to 32% placebo), 41% (compared to 26% placebo), and 32% (compared to 9% placebo) of the instances had their levels reduced to < 7%.[19] In a 12-week study, ipragliflozin at 50 mg daily reduced HbA1c levels by 0.66% and weight by 0.66 kg in comparison to the placebo.[20] In addition to a reduction of 12–32% in HbA1c levels, other trials with dapagliflozin and canagliflozin also indicated a drop of up to 5 mmHg in resting blood pressure. These results point to a potential advantage for people with diabetes and hypertension, as the two illnesses are frequently linked.[21, 22]

Findings of a meta-analysis, done by Naeem et al., in Pakistan, it was concluded that SGLT2 inhibitors improve glycemic control and facilitate effective weight management, underscoring their potential role in comprehensive diabetes care.[23] In another meta-analysis, done by Cho et al., on 5 randomized trials, it was reported that the mean weight loss with SGLT2 inhibitor was −1.62 kg as compared to placebo. Treatment with SGLT2 inhibitors was also associated with a greater reduction in BMI than placebo (mean difference = -0.47 kg/m^2; 95%CI; -0.62 to -0.31). But this meta-analysis was done for trial conducted on non-diabetic individual, receiving SGLT-2 inhibitor for weight reduction.[24]

In this trial, due to limited time period, we only observed two factors (weight and BMI), however more factors could be taken into considerations. Furthermore, prevalence of diabetes is increasing in local population, so multi-centric trials would be done in order to check effectiveness of SGLT-2 inhibitors among diabetics.

CONCLUSION

Thus, SGTL-2 inhibitors are effective in reducing BMI of diabetic patients as well as maintain glycemic index. Now in future, we will prescribe SGLT-2 inhibitors to achieve significant reduction in body weight and BMI of diabetics along with better control of glycemic level, instead of other less effective drugs. This would help in the improvement of our knowledge and to update guidelines in future for better treatment protocol.

CONFLICT OF INTEREST

None.

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