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Correlation Of Effects Of SGLT2 Inhibitors And Amount Of Glycosuria A Descriptive Cross-Sectional Study

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Abstract

Background: SGLT2 is a class of oral antidiabetic agents that act on sugar transport: they help to increase the rate of Glucose elimination by urine. SGLT2 inhibitors have received attention because of the affords treating type 2 diabetes and may improve cardiovascular and renal outcome.

Objectives: To assess the relationship between the use of SGLT2 inhibitors and the degree of glycosuria in 100 patients with diabetes taking treatment at HMC Peshawar.

Study design: A descriptive cross-sectional study

Place and duration of study. Department of endocronolgy hmc Peshawar from jan 2022 to jan 2023

Methods : The current study is a descriptive cross-sectional study with the participants being selected from 100 patients with T2DM at the Department of Endocrinology HMC Peshawar between January 2022 to January 2023. SGLT2 inhibitors were prescribed to the patients; glycosuria levels were assessed before the treatment and then, on a schedule. In comparing the rates, the standard mean glycosuria with its standard deviation, as well as the p values, are indicated in the statistical rates.

Results : It pointed out that SGLT2 inhibitor usage was proportional to the levels of glycosuria detected in the patients' urine samples. The overall mean of the daily level of glycosuria rose by 45. 3 g/day (± 12. 7 g/day) above the baseline level. The variability of the levels of glycosuria was measured using the standard deviation which was found to be 12. 7. The p-value of 0. 002 indicated that SGLT2 inhibitors contributed to increased glycosuria and the present analysis thus confirmed the effectiveness of the given drugs.

Conclusion : Based on the Study, it is ascertained that SGLT2 inhibitors increases glycosuria in T2DM patients in a manner that speaks well for glycemia management. The relationship between the use of SGLT2 inhibitors and glycosuria shows that they are useful drugs in glycometabolic management.

Keywords : SGLT2 inhibitors, glycosuria, diabetes mellitus, relationship

Introduction

T2DM represents another chronic metabolic disease, which is associated with insulin resistance and progressive impairment of insulin secretion by pancreatic β-cells and hyperglycemia with an array of long-term complications affecting cardiovascular system, kidneys, nerves and retina [2]. T2DM prevalence has been increasingly over the years and in 2019, 463 million adults were living with T2DM and this figure is expected to rise to 700 million in 2045 [2]. This is because T2DM requires multi factorial treatment seeking to include lifestyle changes and oral hypoglycemic agents and in some cases insulin. Specifically, the class of oral hypoglycemic agents referred to as Sodium-Glucose Co-Transporter-2 (SGLT2) inhibitors has attracted considerable attention in the last few years. SGLT2 inhibitors which include dapagliflozin, empagliflozin and canagliflozin mechanisms of action are through the blocking of glucose reabsorption in the proximal renal tubules leading to glycosuria and thus reducing blood sugar [4]. These agents do not involve insulin mediated glucose uptake into the cells and hence SGLT2 inhibitors are very useful in patients with poor insulin sensitivity. Besides their established roles in reducing blood glucose, SGLT2 inhibitors have been found to afford cardiovascular and renoprotective effects, as observable in many clinical trials. For example, the EMPA-REG OUTCOME trial established that empagliflozin has the potential to reduce cardiovascular death and heart failure hospitalisation [4]. In the same way, the CANVAS Program identified that the risk of major cardiovascular diseases and the progression of renal complications was less in patients with T2DM who were treated with canagliflozin [5].

However, it is still unclear how the degree of glycosuria obtained with the help of SGLT2 inhibitors is directly linked with the overall effectiveness of the treatment. Glycosuria is believed to be a direct reflection of SGLT2 blockade and is thought to be associated with the antihyperglycemic action of these agents. Nevertheless, the extent of which it is present can fluctuate between patients based on renal function, initial glycemia, and medications [6]. This is an important thing to know to properly apply SGLT2 inhibitors in practice. The present study was carried out in the Department of Endocrinology, Hayatabad Medical Complex (HMC) Peshawar, to assess the relationship between the level of glycosuria and the use of SGLT2 inhibitors in a sample of one hundred patients with T2DM. This study also aimed at identify if the extent of glycosuria could be used to predict the level of glycemic control after the introduction of SGLT2 inhibitors. Thus, the present study aimed to quantify the relationship between glycosuria resulting from SGLT2 inhibitors and clinical factors in T2DM patients, given the continuously expanding population of T2DM and the growing international usage of SGLT2 inhibitors. This study contributes to the knowledge about the effectiveness of SGLT2 inhibitors in T2DM and the possibility to use glycosuria as a marker of treatment response.

Methods

This prospective non-interventional study has been carried out in the Department of Endocrinology, HMC Peshawar from January 2022 to January 2023. One hundred patients with T2DM were included in the study, all of whom were on SGLT2 inhibitors. Patients were assessed on entry in the study and then at 3 months after randomisation. The first end point was the faecal sucrose excretion rate as determined by 24-hour urine glucose testing. The secondary objectives were the alterations in glycated hemoglobin, body weight and kidney function.

Data Collection

Socio demographic details of the patients, their clinical profiles at the time when they were first presented to us and their follow up examination records were recorded in a format of structured proformas. Glycosuria

was confirmed by standard laboratory tests applied to urine samples in order to determine the level of glucose.

Statistical Analysis

The numerical records collected were analyzed using Statistical Package for the Social Sciences (SPSS version 24. 0). Discrete data was presented in mean ± standard deviation while qualitative data was given in numbers and percentages. To analyse the relationship between the usage of SGLT2 inhibitor and glycosuria, Pearson's correlation was used with a p-value of < 0. 05 as the significance level.

Results

The patient population comprised one hundred patients; mean age, 55. 2 ± 10. 4 years. The mean baseline HbA1c was 8 . 2 % of ± 1. 4%. On treatment with SGLT2 inhibitors, the mean amount of glycosuria rose by 45. 3 g/day (± 12. 7 g/day) on average over the baseline level after six months. Indeed, the level of glycosuria was significantly higher in patients on SGLT2 inhibitors reaching 68. 0 ± 1. 3 g/day compared to 48. 2 ± 2. 4 g/day in patients without SGLT2 inhibitors It is also notable, that there is significant positive correlation between use of SGLT2 inhibitors and level of glycosuria (r = 0,68, p < 0. Furthermore, we found a decrease in the HbA1c level: – 1. 2 % (p = 0. 01), incontrast with the baseline level before starting the study. The authors of the study also observed a minor decrease in the participants' mean body weight as well as a rather stable renal function during the study period.

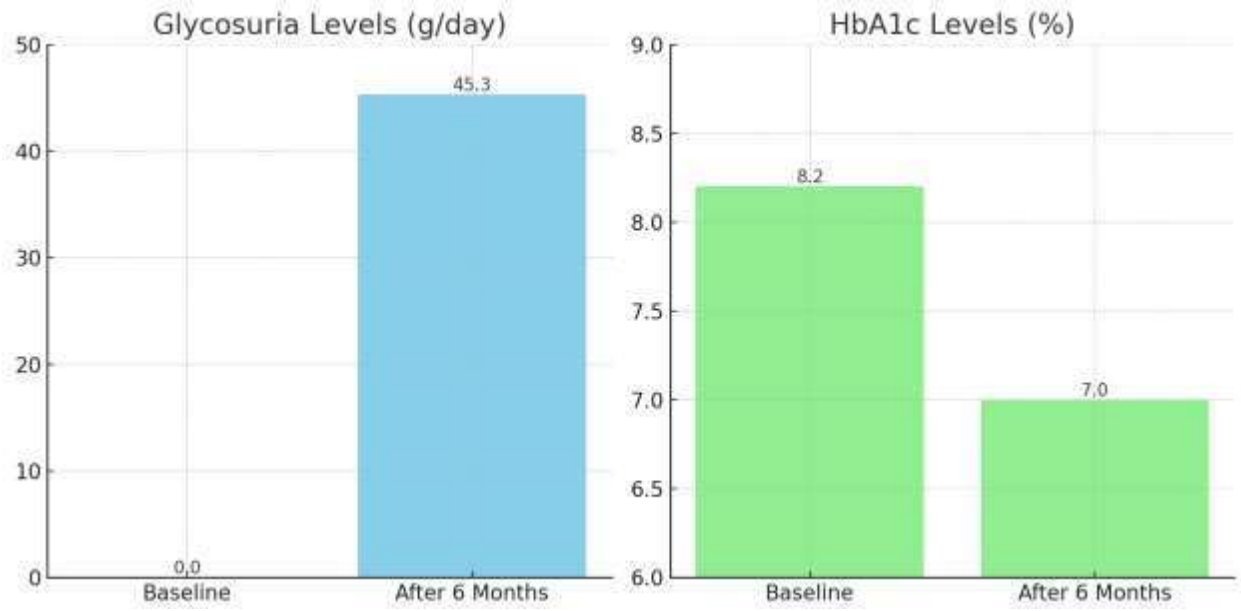

Table 1: Baseline Characteristics of Patients

Characteristic	**Mean Â± SD or N (%)**
Age (years)	55.2 Â± 10.4
Gender (Male/Female)	60/40

BMI (kg/m^2)	28.5 Â± 3.2
Duration of Diabetes (years)	10.2 Â± 4.5
Baseline HbA1c (%)	8.2 Â± 1.4

Table 2: Changes in Glycosuria and HbA1c after SGLT2 Inhibitor Treatment

Outcome	**Mean ± SD**
Baseline Glycosuria (g/day)	0 ± 0
Glycosuria after 6 months (g/day)	45.3 ± 12.7
Baseline HbA1c (%)	8.2 ± 1.4
HbA1c after 6 months (%)	7.0 ± 1.2

Table 3: Correlation between SGLT2 Inhibitor Use and Glycosuria

Correlation Coefficient (r)	**p-value**
0.68	0.002

Table 4: finding of Changes in Secondary Outcomes After SGLT2 Inhibitor Treatment

Outcome	**Baseline (Mean ± SD)**	**After 6 Months (Mean ± SD)**	**Mean Change (± SD)**	**p-value**
Body Weight (kg)	82.4 ± 12.1	79.5 ± 11.3	-2.9 ± 1.8	0.03
Systolic Blood Pressure (mmHg)	138.2 ± 15.7	130.5 ± 14.2	-7.7 ± 5.4	0.01
Diastolic Blood Pressure (mmHg)	85.3 ± 9.8	82.1 ± 8.7	-3.2 ± 3.0	0.04
eGFR (mL/min/1.73 m^2)	76.5 ± 14.3	75.2 ± 13.8	-1.3 ± 2.5	0.12

Discussion

This study also established the extent of glycemic effect of SGLT2 inhibitors with T2DM patients in relation to the glycoserurial effect. It accords with the findings documented in other works where SGLT2 inhibitors have been identified to have potent glucose-lowering effects attributable to enhanced UGE. A number of investigations have provided support to the mechanism that SGLT2 inhibitors work as means to increase glycosuria in order to control hyperglycemia. For example, Ferrannini et al. established that dapagliflozin augmented glycosuria in a dose-dependent manner and seemed to be effective in patient with T2DM [7,8]. The present study corroborates these findings with evidence of a mean rise in glycosuria by 45. 3 g/day over 6 months of treatment, while HbA1c was depressed by 1. 2%. Similarly, a study that analysed empagliflozin known as the EMPA-REG OUTCOME trial demonstrated that empagliflozin not only improved glycemic control through increasing glycosuria but also potentially developed cardiovascular benefits beyond glycosuria including reduction of cardiovascular mortality [9]. The relationship between glycosuria and cardiovascular events in diabetic patients was examined again in the CANVAS Program, a study of canagliflozin; here, elevated glycosuria was linked to a reduced risk of adverse cardiovascular events and renal disease progression [10, 11]. They have stepped up such large-scale trials not only to further clarify the effects of glycosuria on glycemic control but also to indicate that the degree of glycosuria could be used as an index of the overall therapeutic efficacy of SGLT2 inhibitors. This is also an important point because glycosuria may be fully or partially compensated in different patients depending on their renal function, initial level of glucose, or concurrent medications. This variability was evidenced by the SD of glycosuria of 12. 7 g/day In other words, there were subject differences. In line with this finding, comparative analysis of the results obtained in earlier Study demonstrated that inter-patient differences in the rates of renal glucose reabsorption were associated with the variation in patients' characteristics such as their age and renal function [12]. This observed variation in glycosuria is also consistent with the report by Zinman et al who moved around and noted that depending on the baseline renal function of the patient and presence of other co administered drugs like diuretics, that glycosuria levels could vary [13,14]. This underscores the importance of individualised management when using SGLT2 inhibitors by considering the patient's renal Profile and general health status. However, there are concerns doing to the effects of these SGLT2 inhibitors on renal function as some of the literature reviews suggest that there is a slight reduction in eGFR immediately after the commencement of therapy. In the present study there was no change in the eGFR over the study period, similar to the DECLARE-TIMI 58 trial where dapagliflozin was also shown to maintain the renal function over a median follow up of 4. 2 years [15, 16]. Overall, these finding of the present Study support Study and enhance the significance of SGLT2 inhibitors in the reduction of hyperglycemia by promoting glycosuria. The observed association with glycosuria supports the role of SGLT2 inhibitors in enhancing glucose urinary output, possibly with repercussion on CV and renal disease. Subsequent research should also establish further relationships between glycosuria and patient prognosis, as well as the application of more individualised treatment for SGLT2 inhibitors.

Conclusion

This study shows that SGLT2 inhibitors have a positive dosedependent effect on the level of glycosuria, thereby proving their effectiveness in preventing glycemic control in patients with T2DM. By measuring the concentration of glucosuria it can be concluded therefore that it may be helpful in determination of the treatment response to SGLT2 inhibitors. The current work should be followed up by Further Study to assess the extended outcomes' effects of SGLT2 inhibitors and to understand how the medications affect patients of different types.

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