Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

Evaluation of Cardiovascular and Renal Outcomes of Dapagliflozin in Patients of Type-2 Diabetes Mellitus with Chronic Kidney Disease

Sushanta Shekhar Panda[1], Nirmal Kumar Mohanty[2], Lorika Sahu[3], Vedvyas Mishra[4], Trupti Rekha Swain[5], Jayanta Kumar Panda[6] and Trupti Rekha Swain[7]

[1]Senior resident, Department of Pharmacology, S.C.B Medical College and Hospital, Cuttack
[2]Associate Professor, Department of Cardiology, S.C.B Medical College and Hospital, Cuttack
[3]Senior resident, Department of Pharmacology Bhima Bhoi Medical College and Hospital, Balangir
[4]Assistant Professor, Department of Pharmacology, S.C.B Medical College and Hospital, Cuttack
[5]Professor and Head, Department of Pharmacology, S.C.B Medical College and Hospital, Cuttack
[6]Professor and Head, Department of Medicine, S.C.B Medical College and Hospital, Cuttack
[7]Professor and Head, Department of Pharmacology, S.C.B Medical College and Hospital, Cuttack

Corresponding author:
Dr. Trupti Rekha Swain
Professor and Head, Department of Pharmacology
S.C.B Medical College and Hospital, Cuttack
Email: drtruptiswain@gmail.com

Abstract

Background and objective: Diabetic nephropathy, often known as DN, is the condition that is responsible for the majority of diabetes-related cases of chronic kidney disease. Since the 1990s, we have been employing RAAS blocking, which encompasses aldosterone antagonists such as spironolactone and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, in order to delay the progression of diabetic nephropathy. After the advent of novel anti-hyperglycemic drugs, such as SGLT2 (sodium-glucose-linked transporter type 2) inhibitors, the focus of therapy has switched from controlling difficulties to avoiding micro- and macrovascular consequences. This shift in focus has occurred because of the introduction of these therapies. It has been since the introduction of these medications that this shift in strategy has taken place. This modification came about as a consequence of the introduction of these innovative drugs. When it comes to the treatment of type 2 diabetes mellitus (T2DM), chronic kidney disease (as proved by the DAPA-CKD study), and heart failure (as revealed by the DAPA-HF research), dapagliflozin, which is an SGLT2 inhibitor, has been shown to be successful. Due to the fact that, in the context of our setup, no previous study of a comparable kind had been conducted to determine the impact of dapagliflozin on diabetic patients who had been diagnosed with chronic kidney disease (CKD), this investigation was carried out.

Material and methods: This clinical inquiry lasted for a period of one and a half years, beginning in June 2021 and ending in November 2022. It was a prospective observational study from a clinical perspective. The research was carried out with the participation of sixty individuals who had a history of both type 2 diabetes and chronic kidney disease (CKD). Dapagliflozin, 10 milligrams once day, was administered to thirty individuals as part of their routine therapy for type 2 diabetes with chronic kidney disease (CKD). The standard treatment approach was utilized for the remaining thirty individuals who were diagnosed with type 2 diabetes. Within the scope of this analysis, the effects of dapagliflozin on modifiable variables were the primary consideration. A complete set of measurements was obtained, including those pertaining to safety, weight, estimated glomerular filtration rate, albumin-creatinine ratio in urine, systolic and diastolic blood pressure, and both. The first recording of the parameters was place at the beginning of the study, and further evaluations took place three, six, and twelve months after the initial recording session.

Results: At the end of the year, the research discovered that a number of factors, including blood pressure, urine albumin-creatinine ratio, body weight, glycated hemoglobin, fasting blood sugar, and mean estimated glomerular filtration rate, all experienced a significant decline (p=0.0001, p=0.0001, p=0.0001, p=0.0001, p=0.0001, p=0.0001, p=0.0001, p=0.0001, p=0.0004. When it comes to adverse drug reactions (ADRs), the most common ones were infections of the urinary system or vaginal tract, nausea, vomiting, and gastrointestinal discomfort. There was a statistically significant increase in the frequency of adverse drug reactions (ADRs) in the group that was given dapagliflozin (67.6% vs to 32.4% in the control arm; p=0.0006). However, the vast majority of the occurrences were found to be on the less serious side.

Conclusion: Dapagliflozin was well accepted by individuals with type 2 diabetes and chronic renal illness, and it was able to considerably enhance the parameters of glucose management, kidney function, and heart function when it was added to the usual treatment. In addition to this, there was a significant improvement in the management of blood sugar. According to the findings of this study, those who have type 2 diabetes mellitus are at a greater risk of developing genitourinary infections.

Key-words: India, T2DM, SGLT-2 inhibitors, diabetic nephropathy, CKD

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

INTRODUCTION

In the proximal convoluted tubule of the kidneys, the sodium-glucose-linked transporter type-2 (SGLT-2) is responsible for mediating approximately 90 percent of the active glucose reabsorption that takes place in that region. Both as monotherapy and as add-on therapy in conjunction with current anti-hyperglycemic drugs, such as insulin, dapagliflozin, a selective and reversible SGLT-2 inhibitor, has been authorized by the Food and Drug Administration (FDA) for the treatment of type 2 diabetes mellitus (T2DM) [1]. For this particular treatment plan, the dosage that is indicated is one dose one time per day. In order to halt the progression of diabetic nephropathy, medications such as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and aldosterone antagonists, such as spironolactone, have been utilized since the 1990s. As a result of the development of novel anti-hyperglycemic medications, such as SGLT2 inhibitors, the focus of attention in the treatment of type 2 diabetes has shifted from merely managing the consequences of the disease to focusing on avoiding complications. Nephropathy induced by diabetes is the most common cause of chronic kidney disease (CKD) at the present time [3,4]. This is due to the fact that one in every three diabetics who have the condition see a reduction in their renal function. The SGLT2 inhibitor dapagliflozin has proven to be effective in treating a variety of conditions, including type 2 diabetes mellitus, chronic kidney disease (the DAPA-CKD trial is scheduled to begin in 2020), and heart failure (the DAPA-HF study is scheduled to begin in 2019).

There is a significant proportion of the population in Odisha that is affected by type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD), which places a significant burden on the healthcare system of the state. Our establishment is a tertiary care hospital located in eastern India, and it offers medical treatment to a wide variety of patients throughout the region. There is no study that has been carried out there. These studies have focused mostly on the positive effects that dapagliflozin has on the cardiovascular system, including the kidneys and the heart. Even while earlier research has demonstrated that it is possible to get favorable results for the kidneys and the heart, this study is one of a kind since it focused on a distinct set of participants. As a result of this, the purpose of this study was to investigate the effects of dapagliflozin at a standard dose of 10 mg once daily on the cardiovascular system and kidneys in patients who had been diagnosed with chronic kidney disease and diabetes at the conclusion of the third, sixth, and twelve months spent receiving treatment. Changes in systolic blood pressure, diastolic blood pressure, and body weight were the cardiovascular data that were assessed. The renal parameters that were studied were the glomerular filtration rate and the urine albumin-creatinine ratio. The body weight was also analyzed.

MATERIALS AND METHODS

The current research was carried out in the pharmacy department of S.C.B. Medical College and Hospital in Cuttack, Odisha, over the course of a period of one and a half years, beginning in June 2021 and ending in November 2022. The research was an observational study using a prospective cohort. The study was carried out in conjunction with the Department of General Medicine and Cardiology from the University of Michigan. The permission of the Institutional Ethics Committee (IEC Regd No. ECR/84/Inst/OR/2013/ No.1045) was acquired prior to the beginning of the study in order to ensure that it is in accordance with the ethical criteria that have been established. An informed consent form was submitted by each and every participant prior to their inclusion in the research, and the confidentiality of any patient information that was pertinent to the investigation was maintained during the whole investigation. Both the Declaration of Helsinki and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use-Good Clinical Practice (ICH-GCP) were adhered to throughout the course of this research project.

In terms of modifiable cardiovascular and renal outcomes, the major objective of the current study was to determine how dapagliflozin affected both those who were given the medicine and those who were not given the drug. A number of metrics were utilized in order to evaluate these effects. These measurements included body weight, estimated glomerular filtration rate, urine albumin-to-creatinine ratio, systolic and diastolic blood pressure, and estimated glomerular filtration rate. The secondary objective of the current experiment was to evaluate the effectiveness and safety of the medicine that was being investigated with regard to glycemic control. The levels of glycosylated hemoglobin and fasting blood sugar were compared between the two groups in order to determine whether or not dapagliflozin is effective in lowering blood sugar levels. As part of the process of evaluating the safety profile, the adverse drug responses that occurred in the group that was treated with medicine were documented. For the purpose of this particular experiment, advanced hemodynamic markers such as cardiac output and stroke volume, in addition as renal parameters such as blood urea nitrogen (BUN) level and BUN/creatinine ratio, were not measured.

Patients who were being treated at the Department of General Medicine and Cardiology and who were suffering from both type 2 diabetes and chronic renal disease made up the research population. Participants in the study

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

were required to meet the following criteria: they were at least 18 years old, they had an estimated glomerular filtration rate (eGFR) that ranged from 45 to 59 ml/minute/1.73 square meters at the beginning of the investigation, they had a glycated hemoglobin (HbA1C) concentration that fell within the range of 7–11%, they had a urine albumin–creatinine ratio (UACR) of 30 mg/g or higher, and they were willing to adhere to the study protocol. When the HbA1C of a person is greater than 6.5, the individual is considered to have diabetes mellitus. The Indian context is one in which things are just as they are. As a consequence of this, patients who had glycated hemoglobin levels that ranged from 7 to 11% were qualified to take part in the investigation. Participants with baseline eGFRs ranging from 45 to 59 ml/minute/1.73 square meters were selected for our study because the emphasis of our investigation was on mild to moderate chronic renal illness. It was determined that the inclusion criterion for the study was a urinary album concentration (UACR) of 30 mg/g or above, which indicates chronic kidney disease (CKD). Patients with acute complications of diabetes mellitus, such as diabetic ketoacidosis and diabetic hyperosmolar coma, were not included in the study. Patients with non-diabetic kidney diseases, such as glomerulonephritis, urinary tract infections, stroke, or cardiac failure (New York Heart Association functional class III–IV), were also not included in the study. In addition, individuals who were pregnant, those who had type 1 diabetes mellitus, those who were taking dapagliflozin within the month before to the beginning of the trial, and those who had previously taken any other SGLT-2 inhibitors were not permitted to take part in the study.

For the purpose of determining the sample size, the formula n = Z2pq/d2 was utilized. Here, Z represents the 95% confidence interval, p represents the disease prevalence, q represent the difference between 1 and p, and d represents the loss to follow-up, which was established at 10%. As a consequence of this, there were thirty (n=30) participants in each research arm, which resulted in a total sample size of sixty (N=60) for the whole study. The effectiveness of the study was eighty percent. Each individual who took part in the study was assigned to one of the two groups. The individuals who were assigned to Group A were given dapagliflozin (10 mg) in addition to their regular medicine for chronic kidney disease (CKD) and type 2 diabetes, whereas the individuals who were assigned to Group B were given only the standard treatment. A pre-designed case record form was utilized in order to collect the following information: baseline glycated haemoglobin (HbA1C), fasting blood sugar (FBS), systolic blood pressure (SBP), diastolic blood pressure (DBP), body weight, urine albumin-to-creatinine ratio (UACR), and estimated glomerular filtration rate (eGFR). When the patients returned for follow-up appointments three, six, and twelve months following their initial visit, the same parameters were examined once more. This was done in order to keep track of their progress. A suspected adverse drug reaction reporting form was provided by the Pharmacovigilance Programme of India (PvPI). This form was intended to be used for the reporting of all adverse drug reactions (ADRs). A modified version of the WHO-UMC Causality Assessment Scale is shown here. For the purpose of determining the severity of adverse drug reactions (ADRs) and the factors that led to them, the Hartwig-Siegel Scale was utilized.

The following step was to import the information about the patient that was listed on the case record form into a spreadsheet that was created using Microsoft Excel. SPSS version 20.0 was utilized in order to carry out the analysis of the data. For the purpose of expressing categorical data, both frequencies (n) and percentages (%) were utilized. Two concepts, namely the mean and the standard deviation, were utilized in order to accurately depict the numerical data. The Student's unpaired t-test was utilized to compare the means of the two groups, and the chi-square test was utilized to compare the categories. It is necessary for the p-value of the distinctions to be lower than 0.05 in order for them to be considered statistically significant.

RESULTS

Table 1. Baseline characteristics of the study participants in the two groups

Parameters	Total (N=60)	Group A n (%)	Group B n (%)	p-value*
Gender distribution				
Male	35 (58.3)	17 (56.7)	18 (60%)	0.8
Female	25 (41.7)	13 (43.3)	12 (40%)	
Age distribution (in years)				
50-60	10 (16.7)	9 (30)	1 (3.3)	
61-70	46 (76.7)	18 (60)	28 (93.3)	0.008
>70	4 (6.7)	3 (10)	1 (3.3)	
Co-morbidities				
Hypertension alone	13 (21.7)	6 (20)	7 (23.3)	
Dyslipidemia alone	15 (25)	8 (26.7)	7 (23.3)	1.0

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Both	24 (40)	12 (40)	12 (40)	
None	8 (13.3)	4 (13.3)	4 (13.3)	

*Chi-square test; N=total sample size; n=frequency

The cardiovascular and renal outcomes of seventy people who were diagnosed with type 2 diabetes and chronic kidney disease were investigated to determine their outcomes. In Group A, patients with type 2 diabetes and chronic renal disease received their normal medicine in addition to dapagliflozin. On the other hand, patients in Group B, who also had type 2 diabetes and chronic renal illness, received just their usual therapy. Not only was the baseline recorded, but the parameters were also captured three times at the end of the third, sixth, and twelve months. The demographic information of the participants is presented in Table 1, which may be seen here. There was a shift in the proportion of males to females when one group transitioned into another. Group B individuals averaged 65.9±2.3 years old during the investigation, whereas Group A subjects averaged 63.2±8.1 years. Among the study's notable participants, a sizeable proportion were in their 70s (p = 0.008). Hypertension and dyslipidemia were the two most prevalent co-morbidities found in the study population.

The following table shows the many modifiable cardiovascular and renal adverse events that are different between those who are not receiving dapagliflozin and those who are. With respect to the mean standard deviation, the following measurements are provided: glycated hemoglobin (in percent), body weight (in kilograms), eGFR (in milliliters per minute per square meter), UACR (in milligrams per gram), and fasting blood sugar (in milligrams per deciliter). The average HbA1C levels in both groups decreased steadily throughout the research. The HbA1C levels of group A changed by 0.3% from the beginning of the study to the conclusion of the 12th month, whereas those of group B changed by just 0.12%. The difference between the two groups' mean HbA1C readings at the end of the year was 0.31%. This differentiation was applied to both categories. A statistically significant conclusion was reached, as demonstrated by the findings of the Student's t-test (P = 0.0001) according to the findings. The results of the investigation demonstrated that the levels of FBS significantly decreased over time for both of the groups. commencement with the commencement of the trial and continuing until the end of the inquiry, there was a substantial difference in the FBS levels of the two study groups. In group B, the mean change in FBS from the beginning of the trial to the end of the year was 9.33 mg/dl, but in group A, the change was 16.9 mg/dl. The mean FBS levels of the two groups at the end of the year were different by 2.3 mg/dl, which was the difference between them. Based on the results of the student's t-test, it was determined that this finding possessed a p-value of 0.004, indicating that it was statistically significant. A p-value that was larger than 0.05 was used as the starting point for our comparison of the average body weights of the two groups. The group that was given dapagliflozin saw a steady decrease in body weight, whereas the group that was not given dapagliflozin experienced an increase. After a year, it was discovered that group A had lost 2.3 kilograms of weight, which was much lower than the 1.2 kilograms that group B had gained. The students' t-test, which had a significance threshold of $p<0.05$, demonstrated that there was a highly significant difference in the average body weight between the two groups at each and every follow-up. Patients in group A had an estimated glomerular filtration rate (eGFR) of 2.9 ml/min/1.73 square meters at the end of the 12th month, whereas patients in group B had an eGFR of 2.65 ml/min/1.73 square meters. This difference was in comparison to the starting values of the patients in both groups. Despite this, the UACR finally decreased in the group that was given dapagliflozin whereas it increased in the group that was given the control. According to the findings of this study, the systolic component decreased as the duration of the dapagliflozin treatment period increased. Nevertheless, there was an increase in the number of individuals who were classified into the other groups. There were statistically significant variations between the two groups in terms of eGFR, UACR, and blood pressure levels at the beginning of the research and during the course of the study.

Table 2. Cardiovascular and renal outcomes in the two groups

Parameters	Group A	Group B	p-value*
HbA1C At baseline 3rd month 6th month 12th month	 7.9±0.25 7.9±0.26 7.6±0.28 7.6±0.25	8.03±0.2 8.0±0.2 7.84±0.21 7.91±0.21	0.151 0.026 0.001 0.0001
FBS At baseline 3rd month 6th month 12th month	163.7±2.73 159.6±2.84 154.5±2.87 146.8±3.49	153.8±2.66 154.73±2.84 156.63±3.66 144.47±2.77	0.0001 0.0001 0.015 0.004
Body weight At baseline 3rd month 6th month	89.5±2.8 88.8±2.75 87.9±2.65	89.78±1.34 90.08±1.35 90.45±1.21	0.49 0.006 0.0001

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12th month	87.2±2.65	91±1.26	0.0001
eGFR	56.6±6.04	52.35±7.54	0.0001
At baseline 3rd month 6th	55.8±5.78	52.16±7.44	0.001
month	54.8±5.72	51.97±7.46	0.007
12th month	53.7±5.74	49.7±7.58	0.0001
UACR	394.1±13.91	441.9±18.83	0.0001
At baseline 3rd month 6th	388.8±13.58	461.1±21.71	0.0001
month	385.3±13.54	484.4±14.46	0.0001
12th month	379.5±13.18	509.97±20.0	0.0001
Blood Pressure	134/76	131/74	0.001
At baseline 3rd month 6th	133/77	132/74	0.006
month	132/77	132/74	0.004
12th month	131/75	134/72	0.0001

*Student's unpaired T-test; HbA1C=glycated haemoglobin; FBS=fasting blood sugar; eGFR=estimated Glomerular filtration rate; UACR=Urinary albumin-creatinine ratio

During the experiment, the participants encountered adverse drug reactions such as nausea, vomiting, headache, gastrointestinal disturbance, urinary tract infection (UTI), vaginal infection, and nasopharyngitis (Table 3).
The trial's subjects reported 37 different adverse drug reactions in total. Of these, only 12 (32.4%) individuals in the control group had these incidents, whereas 25 (67.6%) occurred in patients taking dapagliflozin. According to the results of the chi-square test (p=0.0006), the dapagliflozin group saw an increase in the overall number of adverse drug reactions that was statistically significant. An examination was carried out by the pharmacovigilance team to ascertain the cause and intensity of each adverse drug response (ADR). They discovered that most adverse drug reactions (ADRs) seen during the study may have been caused by the suspected medicine, and the severity of these reactions was categorized as low. However, comparing individual adverse drug reactions (ADRs) between the two experimental arms revealed no statistically significant changes.

Table 3. Adverse drug reaction profile of the participants in the two groups

ADR	Total	Group A (n=30)			Group B (n=30)			
		n (%)	Causality Assessment	Severity Assessment	n (%)	Causality Assessment	Severity Assessment	p-value*
Nausea	7 (11.7)	4 (13.3)	Possible	Mild	3 (10)	Possible	Mild	0.7
Vomiting	7 (11.7)	4 (13.3)	Possible	Mild	3 (10)	Possible	Mild	0.7
Headache	4 (6.7)	3 (10)	Unlikely	Mild	1 (3.3)	Unlikely	Mild	0.3
GI upset	9 (15)	4 (13.3)	Possible	Mild	5 (16.7)	Possible	Mild	0.72
UTI	3 (5)	3 (10)	Possible	Mild	0	NA	NA	0.2
Genital infection	3 (5)	3 (10)	Possible	Mild	0	NA	NA	0.2
Nasopharyngitis	4 (6.7)	4 (13.3)	Unlikely	Mild	0	NA	NA	0.1
Total	37	25			12			0.0006

*Chi-square test; ADR=Adverse drug reaction; GI=gastrointestinal; UTI=urinary tract infection, n=frequency, NA=Not applicable

DISCUSSION

By the year 2035, it is anticipated that diabetes would have afflicted more than 350 million individuals around the globe in a variety of geographical regions [4]. There are approximately 34.4% of people in India who are affected by diabetic kidney disease (DKD) [5]. It is possible that the prognosis is fairly unpredictable due to the fact that established DKD is accompanied with a large number of micro- and macroangiopathies. It has been demonstrated that the SGLT-2 inhibitor dapagliflozin can decrease the course of chronic renal disease and reduce the risk of heart failure in those who have type 2 diabetes [6, 7]. Furthermore, it has been demonstrated that dapagliflozin has an anti-inflammatory impact on the kidneys that is independent of any other effects [8]. Glycated hemoglobin, fasting blood sugar, body weight, estimated glomerular filtration rate, urine albumin creatinine ratio, blood pressure, and the safety and efficacy of dapagliflozin were evaluated during the course of this trial in patients who were diagnosed with type 2 diabetes and chronic kidney disease (CKD).

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According to the current study, from the start of the trial to the conclusion of the 12th month, the mean levels of FBS and HbA1C dropped consistently. When compared to the control, the dapagliflozin-induced decline was seen to be substantially higher. In comparison to the control, dapagliflozin was demonstrated to improve the glycemic index and other short-term glycemic markers in additional studies [7,9], including fasting plasma glucose. These results aligned with those previously obtained results. The kidneys' proximal convoluted tubules, which have greater levels of sodium-glucose cotransporter-2 receptor activation, are in charge of facilitating the body's enhanced absorption of both glucose and salt in diabetics. Dapagliflozin is an SGLT-2 inhibitor that decreases excessive sodium and glucose reabsorption in addition to decreasing insulin resistance, raising the quantity of glucose expelled in urine, and improving the function of pancreatic beta cells [7]. For the same reason, dapagliflozin was effective in lowering the plasma glucose levels when the patient was fasting. However, dapagliflozin is not particularly good at controlling glucose variability, which is the fluctuation of blood glucose levels, even if it does a good job at controlling glucose levels [10].

It is possible for people with type 2 diabetes to have weight gain as a result of insulin resistance, which can further worsen insulin resistance. Because diabetes is an illness that lasts for a long time, it is essential to take drugs that assist with managing one's weight control. When compared to the control group, the groups who were given dapagliflozin consistently shown a reduction in their overall body weight, as demonstrated by our research. This study's findings corroborated those of another that discovered dapagliflozin decreased overall body weight. This was mostly achieved by reducing visceral and subcutaneous adipose tissues on the body in addition to body fat mass [11]. The study continued by stating that although the exact mechanism causing weight loss is unknown, it might be caused by either a drop in body fat from burning calories or a reduction in fluid from osmotic diuresis. The results of another trial conducted in Mexico [12] showed that patients with diabetes or prediabetes reacted better to a combination of dapagliflozin and metformin medication for weight loss than they did to metformin alone. Research has shown that SGLT-2 inhibitors are becoming more and more significant in the weight loss process [13, 14].

There are two key indicators of the gradual loss of renal function as well as early indicators of kidney injury. These include a higher urine albumin/creatinine ratio (urine albumin/Cr level anything above 30 mg/g) or an estimated glomerular filtration rate of less than 60 ml/min/1.73 square meters. It is believed that both of these signs point to renal injury. Throughout the current inquiry, there was a progressive decline in eGFR in both research arms (Figure 1). The rate of eGFR slope between the drug under study and the control group at the end of the year only differed by 0.25 ml/min/1.73 square meters; nonetheless, the discrepancies remained statistically significant for the whole experiment. In several studies, dapagliflozin was shown to slow down the rate at which eGFR declined [15,16], leading to a similar decline in eGFR. According to the findings of the DAPA-CKD research, the moderate impact that dapagliflozin had on the rate of change of eGFR, also known as the slope of eGFR, considerably delayed the beginning of long-term renal and cardiovascular difficulties in patients with chronic kidney disease when compared to the placebo [15,17]. According to the findings of another study, SGLT-2 inhibitors are to blame for an early drop in eGFR that occurs within the first few weeks of treatment. A partial reversal of this drop occurred over the course of the subsequent few weeks, which resulted in a reduction in the slope of the eGFR decline in comparison to the placebo. [18] It was called after the phenomena that is commonly referred to as the trajectory-and-hare pair.

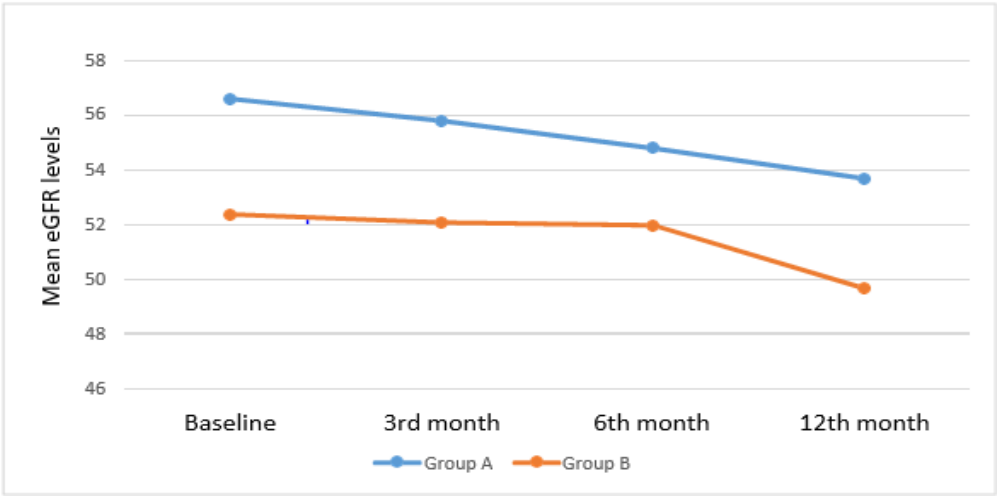

Figure 1: Comparison of the slope of eGFR between the two study arms; eGFR=estimated glomerular filtration rate

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

People with type 2 diabetes who had normal or very normal renal function saw a significant reduction in albuminuria when they were given dapagliflozin [19]. For the duration of the DAPA, the mean UACR was found to be 29.3% lower with dapagliflozin compared to placebo (95% confidence interval: -33.1% to -25.2%; $p<0.0001$ [20]). It is possible that those who were diagnosed with chronic kidney disease (CKD) or type 2 diabetes did not have the same reduction in albuminuria while taking the medication. It has been proven in a number of further trials, such as the CREDENCE research, that SGLT-2 inhibitors are beneficial in avoiding further damage to the kidneys in individuals who have type 2 diabetes and chronic renal impairment (17, 22). The results of these earlier studies provided support for our findings, which demonstrated that dapagliflozin significantly reduced UACR in contrast to the medication that was previously considered to be the standard.

In this particular trial, dapagliflozin was found to be effective in lowering systolic blood pressure. Consistent with other research, this found that dapagliflozin treatment reduced systolic blood pressure rapidly and maintained the reduction over time [23]. Possible explanations for the drop in systolic blood pressure include an increase in plasma vasodilators such cAMP, BNP, ANP, and angiotensin II, and a reduction in plasma vasoconstrictors like renin, endothelin-1, and angiotensinogen [23]. SGLT-2 inhibitors have been proven to reduce systolic blood pressure (SBP) through a variety of effects, including weight reduction, reduced arterial stiffness, osmotic diuresis, and renal remodelling, according to recent research. [24]. According to Reference [25], its blood pressure-lowering capabilities and those of β-blockers or calcium-channel blockers have synergistic effects.

Furthermore, despite the fact that dapagliflozin was linked with a greater number of side effects (25 in group A compared to 12 in group B, $p=0.0006$), the individuals who participated in our experiment had a positive reaction to it. The side effects that were reported the most frequently were nausea, vomiting, and discomfort in the gastrointestinal tract. The impact that dapagliflozin has on the amount of glucose that is produced in urine is thought to be the cause of an increase in the number of cases of genital and urinary tract infections [26]. Dapagliflozin patients had a significantly greater chance of getting urinary tract infections (UTIs) and vaginal infections when compared to the placebo group. This conclusion is in line with the findings of prior investigations [27] that discovered dapagliflozin to considerably increase the prevalence of these problems. Instances of hypoglycemia were not documented at any point. Previous studies [28, 29] have demonstrated that dapagliflozin has the ability to lower HbA1C and body weight without increasing the likelihood of hypoglycemia occurs. These results were consistent with those seen in other investigations.

According to the findings of the current study, the addition of dapagliflozin to the conventional treatment for diabetes and chronic kidney disease resulted in a significant reduction in glycemic parameters such as fasting blood sugar and hemoglobin A1C, as well as modifiable cardiovascular risk indicators such as blood pressure and body weight. There was a decrease in renal measurements, such as the estimated glomerular filtration rate, following the introduction of dapagliflozin into the investigation; however, these parameters subsequently restored to their initial values. As an additional point of interest, the ratio of urine albumin to creatinine was found to be considerably lower in the group that was administered dapagliflozin in comparison to the other groups. Dapagliflozin is associated with an increased risk of infections, particularly vaginal and urinary tract infections, among individuals who have type 2 diabetes mellitus, according to this study, which adds to the data that supports this hypothesis. Although there are a few limitations to this study, such as a restricted assessment time and a small sample size, it is noteworthy since it is the first study of its kind to be conducted in eastern India.

Conclusion

The patients who were given dapagliflozin experienced a significant reduction in their glycated hemoglobin ($p=0.0001$), fasting blood sugar ($p=0.004$), body weight ($p=0.0001$), mean estimated glomerular filtration rate ($p=0.0001$), urine albumin-creatinine ratio ($p=0.0001$), and blood pressure ($p=0.0001$) at the conclusion of a period of twelve months. Therefore, it is acceptable to draw the conclusion that the addition of dapagliflozin to the standard of treatment for those who have type 2 diabetes and chronic renal disease may result in improvements in the parameters of both the cardiovascular system and the kidneys.

Conflicts of interest: Nil
Funding: Nil
Acknowledgements: Nil

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