Frequency of Urinary Tract Infection in Diabetic Patients Using Dapaglifzlozin

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Abstract

Objective: To assess the frequency of urinary tract infection in diabetic patient using dapagliflozin

Material and Method: This descriptive case series conducted on180 patients, from 30-70 years with type 2 DM fulfilling selection criteria. Demographic information was also recorded. Then patients were prescribed 10 mg dapagliflozin for 24 weeks. Then patients were followed-up in OPD for 24 weeks. After 24 weeks, urine sample was taken and sent to the laboratory of the hospital. Reports were assessed and if bacterium detected in urine sample, then urinary tract infection was labeled. Patients with urinary tract infection were managed as per hospital protocol.

Results: In our study, of 180 cases, mean age was calculated as 49.95+5.35 years. Gender distribution shows that 110(61.1%) cases were male and 70(38.9%) cases were females. Frequency of urinary tract infection in diabetic patient using Dapagliflozin was recorded in 11(6.1%) of the patients. The data stratified for age, BMI, HbA1c, and smoking, to control effect modifiers came to be significant at $p < 0.05$

Conclusion: We concluded, that frequency of urinary tract infection is not higher in diabetic patient using dapagliflozin. Patients with increase age, prolonged duration of diabetes, family history of UTI, uncontrolled diabetes and female gender are at risk for developing UTI.

Keywords: Urinary tract infection, Diabetic, Dapagliflozin

Introduction

Metabolic disorder, known as type 2 diabetes affects millions worldwide.[1] Adults with diabetes currently number 463 million, but by 2030 and 2045, that number is expected to rise to 578 and 700 million, respectively. 90% of all forms of diabetes are Type 2.[2] Diabetes can result in life-threatening complications or even early death. Common complications of diabetes include cardiovascular disease, renal disease, retinopathy, diabetic foot, and neuropathy.[3,4]

Moreover, urinary tract infections (UTIs) are more common in diabetics. An estimated 150 million people are anticipated to get this infection annually. Bladder dysfunction, low immunity, and glycosuria all of which are thought to be risk factors. Diabetics are likely to get UTI, which have poorer consequences.[5,6] Moreover, resistant microorganisms are more frequently found. Pyelonephritis, consequence of urinary tract infections in diabetics that can lead to organ damage and even death.[7] SGLT2i, or sodium-glucose cotransporter-2 inhibitors, are drugs that treat type 2 diabetes by acting on kidneys. In kidneys, glucose is reabsorbed in the loop of Henle's proximal tubule. The SGLT2 protein, is in charge of this reabsorption. SGLT2i medications such as canagliflozin, dapagliflozin, and empagliflozin act at this site.[8] It was concluded in one meta-analysis that, dapagliflozin 5 mg raised the chance of overall adversities, whereas dapagliflozin 10 mg had lower risk of UTI than its 5 mg counterpart.[9] Patients with diabetes who get UTIs have trouble controlling their blood sugar,

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which makes blood sugar monitoring more necessary, lowers quality of life, and puts financial burden on the patient. Different research indicated that diabetes patients on 10 mg of dapagliflozin had 0.09% prevalence of urinary tract infections.[10] Prescriber information does not regard it as a precaution prior to prescribing. Further investigation is required to determine whether SGLT2 inhibitor use in these patients increases the risk of urinary tract infection beyond attributable risk to either of these risk factors in isolation.[11] So, we have conducted this study so that we can get local evidence and we can plan screening of diabetic patients using dapagliflozin on regular intervals for urinary tract infection during follow-up and routine examination in order to improve management protocols and prevent UTI and provide improved quality of life to patients.

Materials and Methods

This descriptive case series was conducted at Department of Medicine, Govt. Teaching Hospital Shahdra, Lahore over a period of six months. The study included 180 patients, selected using non-probability consecutive sampling, with 95% confidence level and 3% margin of error, considering an expected percentage of urinary tract infection of 4.3% in diabetic patients treated with dapagliflozin. Inclusion criteria involved patients aged 30-70 years of both genders diagnosed with diabetes, while exclusion criteria included patients currently positive for urinary tract infection, those with serum creatinine >1.2mg/dl, and pregnant females. Data collection involved enrolling eligible patients from the hospital's outpatient department, obtaining informed consent, and recording demographic and medical information. Patients were prescribed 10 mg dapagliflozin for 24 weeks and followed up in outpatient department. After 24 weeks, urine samples were collected, and if bacteria were detected, urinary tract infection was labeled, and patients were managed according to hospital protocol.

Data analysis was performed using SPSS version 26. Quantitative variables were presented as mean and standard deviation, while qualitative variables were presented as frequency and percentage. Data was stratified by various factors to control for effect modifiers, and chi-square tests were applied to compare urinary tract infection rates in stratified groups, with a p-value ≤0.05 considered significant.

Results

A total of 180 cases fulfilling the selection criteria were enrolled to assess the frequency of urinary tract infection in diabetic patient using dapagliflozin. Table 1 shown below is displaying qualitative variables of the study population. Age distribution shows that 87(48.3%) were between 30-50 years of age whereas 93(51.7%) cases were between 51-70 years of age. Gender distribution shows that 110(61.1%) cases were male and 70 (38.9%) were females. Frequency of smoking in the cases was recorded in 46(25.6%) whereas 134(74.4%) were nonsmokers. Frequency of family history of UTI was recorded in 35(19.4%) cases whereas 145(80.6%) had no history of UTI. Frequency of frequency of urinary tract infection in diabetic patient using Dapagliflozin was recorded in 11(6.1%) of the patients whereas 169 (93.9%) cases had no findings of the UTI. Table 2 is showing quantitative variables of study population, mean duration of diabetes mellitus was calculated as 8.28+ 3.54 years, mean BMI 30.67+2.37. and mean of HbA1c calculated was 9.7+2.37. frequency of UTI noted high among females (3.9%), age group 51-70 years (6.1%), prolonged duration of DM > 5year (6.1%), family history of UTI (6.1%), high BMI > 30mg/kg^2 (3.9%), smoking (4.4%) and uncontrolled DM HbA1c >7% (3.9%) as compared to their counterparts. The data stratified for age, BMI, HbA1c, and smoking, to control effect modifiers came to be significant at $p < 0.05$, as shown in table 3.

Table 1: *Analysis of Qualitative Variables*

PARAMETERS		Frequency (n=180)	Percentage
Age	30-50	87	48.3%
	51-70	93	51.7%
Gender	Male	110	61.1%
	Female	70	38.9%
Smoking	Yes	46	25.6%
	No	134	74.4%
Family history of UTI	Yes	35	19.4%
	No	145	80.6%
UTI	Yes	11	6.1%
	No	169	93.9%

Table 2: *Analysis of Quantitative variables*

PARAMETERS	MEAN (n=180)	SD
Duration of DM (years)	8.28	3.54
BMI Kg/m^2	30.67	2.37
HbA1c (%)	9.7	2.37

Table 3: *Data stratification using chi square*

CHARECTERISTICS		UTI		P value
		YES	NO	
Age (years)	18-50	0	87(48.4%)	0.001
	51-70	11 (6.1%)	82 (45.5%)	
Gender	Male	4 (2.2%)	106 (58.9%)	0.08
	Female	7 (3.9%)	63 (35%)	
Duration Of DM (Years)	Upto 5	0	35 (19.4%)	0.086
	>5 Y	11 (6.1%)	134(74.5%)	
HbA1C (%)	Upto 7	4 (2.2%)	114 (63.3%)	0.000
	>7	7 (3.9%)	55 (30.6)	
BMI (kg/m^2)	Upto 30	4 (2.2%)	75 (41.7%)	0.000
	>30	7 (3.9%)	94 (52.2%)	
Smoking	Yes	8 (4.4%)	46 (25.6%)	0.035
	No	3 (1.6%)	123 (68.4%)	
Family History	Yes	11 (6.1%)	35 (19.4%)	0.086
	No	0	134 (74.5%)	

Discussion

SGLT2 inhibitor, dapagliflozin has demonstrated encouraging outcomes in treatment of diabetes; yet, questions have been raised about its possible link to urinary tract infections. Clinical decision-making and patient care require an understanding of the prevalence and contributing variables to UTTIs in diabetes patients using dapagliflozin. Our study has observed the incidence of UTIs in our research group, taking into account a range of clinical and demographic variables.

In our study of 180 cases, mean age and BMI was calculated as 49.95+5.35 years and BMI 30.67+2.37. Gender distribution shows that more male patients 61.1% versus 38.9% females. Similar demographics were seen previously, one study found mean age of type 2DM was 45.1 years in males and 45.0 years in females and there were more male patients 52.5% as compared to females 47.5%.[12] Previous study discovered that BMI of 20–21 kg/m^2 was associated with increased chance of developing DM.[13]

Frequency of urinary tract infection in diabetic patient using Dapagliflozin was recorded in 11(6.1%) of the patients. And occurrence is high among those with prolonged duration of DM, females, uncontrolled DM, increase age, and family history of UTI. Similar, results were documented in one previous review that 5.3% of diabetic individuals using dapagliflozin at doses of 5 or 10 mg had UTIs. Compared to males, women were more impacted (76.2%; p < 0.05) and patients over 50 years old (85.7%) had the highest prevalence of UTIs.[14]

Higher doses increase the amount of glucose excreted in urine, which might possibly raise the risk of UTIs by creating ideal habitat for bacterial growth. The findings of one recent review confirmed this rise in risk. Since there was no statistically significant correlation between UTIs and dapagliflozin dosage strength.[14] In contrast to all, one study found higher incidence of UTI in SGLT2i group (33.49%), as compared to non-SGLT2 inhibitor (11.72%) and found old age and female gender as risk factors. However, there was no significant difference in UTI between the dapagliflozin and empagliflozin (34.00% and 33.03%, respectively) and with SGLT2 inhibitors risk of UTI increased by 3.70.[15]

Another review, has studied different doses, and UTI frequency was recorded 3.6%, 5.7%, 4.3%, and 3.7% of cases for dapagliflozin 2.5 mg, 5 mg, 10 mg, and placebo, respectively. It was also seen that, UTIs were the infrequent (0.3%) cause of treatment cessations and majority of infections that were identified were mild to severe and were treated with conventional antibiotics.[16] While another study found that frequency of urinary tract infection was 0.09% in diabetics using 10 mg dapagliflozin.[10] It was reported earlier that, UTIs are more common in people with type 2 diabetes who use dapagliflozin, particularly if the medication is taken for more than 24 weeks and at a dosage of 10 mg per day, p < 0.0001.[17] Genital tract infections are linked to a higher risk while using SGLT-2 inhibitors however, UTIs are not.[18]

Limitations of this study include, potential biases due to non-probability consecutive sampling, absence of comparison group, and single centered study limiting the generalizability of the findings.

Cocnlusion:

It is concluded that, type 2 diabetics taking dapagliflozin 10mg are at low risk of developing UTI. Patients with increase age, prolonged duration of diabetes, family history of UTI and uncontrolled diabetes and female gender are at risk for developing UTI.

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Authors Contribution

CAAA: Conceptualization of Project
RI: Data Collection
SMNA: Literature Search
SBS: Statistical Analysis
QUA: Drafting, Revision
SK: Writing of Manuscript