Original Article

Frequency Of Urinary Tract Infections In Type 2 Diabetes Patients Taking Sodium-Glucose Co-Transporter-2 (SGLT2) Inhibitors To Regulate Their Blood Sugar Level

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Abstract

Objective: Study of the prevalence of genitourinary infections in diabetic patients on SGLT2 inhibitors

Study design: A cross-sectional study

Place and Duration: This study was conducted at Services Institute of Medical Sciences Lahore **hospital from January 2018 to January 2019**

Methodology: The SGLT-2 inhibitors drugs given to the patients were empagliflozin and dapagliflozin as a combination or monotherapy over three months. The patients were asked for a detailed medical history and their medical records were observed to assess the genitourinary infections. The questionnaire included queries related to pain during micturition, frequency of micturition, the urgency of micturition, itching, vaginal or penile discharge, redness, soreness, abdominal pain, back pain, suprapubic pain, vomiting, diarrhea, fever, chills, discomfort around the perianal area, tenderness in the costovertebral angle and sepsis

Results: A total of 1050 patients were considered, out of which 504 (48%) were commenced on dapagliflozin while 546 (52%) were commenced on empagliflozin. Out of 504 patients taking dapagliflozin, 327 (64.88%) were male and 177 (35.11%) were female. On the other hand, 393 (71.97%) male patients and 153 (28.02%) female patients were among those 546 that were using empagliflozin. The risk of urinary tract infection in the patients using dapagliflozin was 22 (4.3%) and it was 34 (6.74%) in those using empagliflozin. Similarly, the risk of genital tract infections in the patients using dapagliflozin was 19 (3.76%) and those using empagliflozin were 23 (4.56%). The predominance of genital infections and urinary infections was more in females than males in both empagliflozin and dapagliflozin users. The correlation between uncontrolled diabetes and female gender with the frequency of genitourinary infection was significant with a p-value of 0.003 and 0.001, respectively.

Conclusion: Diabetic patients are more prone to have genitourinary infections than healthy individuals. Patients taking SGLT-2 inhibitors have been shown to have a higher prevalence of catching genitourinary infections. SGLT-2 inhibitors intake is related to genitourinary infections in patients of diabetes mellitus type 2.

Keywords: Genitourinary infections, Diabetes mellitus, dapagliflozin, empagliflozin, SGLT-2 inhibitors

Introduction

Diabetes mellitus is a global burden and Pakistan comes in 7th number among the countries with the highest number of diabetic patients according to the surveys of the World Health Organization (WHO) [1]. This burden will drastically increase if appropriate measures are not taken in time. One of the main causes of this increase in burden is the scarcity of resources in the healthcare system of Pakistan [2]. For the management of an optimum range of blood sugar levels in diabetic patients, mainly seven groups of drugs are used. Out of these drug groups, SGLT-2 inhibitors are considered to be an innovative and effective drug group. The drugs in this group are used as a monotherapy as well as in combination with other drugs [3].

The drugs of this group that are approved by the FDA for the management of diabetes mellitus are empagliflozin, dapagliflozin, ertugliflozin, and canagliflozin [4]. These drugs have shown excellent tolerability and safety with no risk of lowering blood sugar below the optimum level [5]. SGLT-2 inhibitors have shown promising effects in lowering and maintaining the blood glucose level, lipid profile, blood pressure, body weight, and HbA1C [6]. Another phenomenal feature of this drug group is that these drugs are also cardio-protective because they improve the function of endothelial tissues [7].

The SGLT-2 inhibitors function by inhibiting the reabsorption of glucose from the proximal convoluted tubule of the kidney [8]. It is not yet clear whether the genitourinary infections in diabetic patients taking SGLT-2 inhibitors are related to the drug or not [9]. Generally, diabetic patients are more prone to catch a genitourinary infection than normal individuals, which happens due to the compromised immunity of diabetic patients [10]. Similarly, vaginitis is also more common in diabetic patients comparatively [11]. The present study is conducted to find out the prevalence of these infections in diabetic patients and their correlation with SGLT-2 inhibitors.

Methodology

The present study is a cross-sectional study that was conducted to assess the correlation of genitourinary infections with the intake of SGLT-2 inhibitors in patients with diabetes mellitus type 2. Written informed consent was taken from all the participants before the conduct of the study. The patients considered in the present study were those who were taking SGLT-2 inhibitors as a monotherapy or in combination with any other hypoglycemic drug for three months. As per the exclusion criteria of the study, patients having diabetes mellitus type 1, gestational diabetes mellitus, and no diabetes at all, were excluded from the study.

A careful personal and clinical history was taken from all the participants of the study. A specially designed proforma and questionnaire were filled out by the clinical assistants after taking the history. The proforma also included information regarding the symptoms of genital tract infections and urinary tract infections in the participants, during taking SGLT-2 inhibitors.

The questionnaire included queries related to pain during micturition, frequency of micturition, the urgency of micturition, itching, vaginal or penile discharge, redness, soreness, abdominal pain, back pain, suprapubic pain, vomiting, diarrhea, fever, chills, discomfort around the perianal area, tenderness in the costovertebral angle and sepsis. Any history of genitourinary infections that occurred before the commencement of the SGLT-2 inhibitors, was also recorded.

After taking a detailed history of the patients, laboratory data of the patients was also recorded that included blood sugar level, lipid profile, HbA1C, urine complete examination, urea, and creatinine. Those patients showing the pet symptoms of infection such as dysuria, pain, fever, sepsis, urgency, and frequency of urination, also underwent urine culture tests. Patients having positive urine culture reports were said to have genitourinary infections.

The data regarding the patients were collected, studied, and analyzed in IBM SPSS version 26. The data were expressed in terms of frequencies and percentages. The chi-square test was utilized to assess the relationship between certain categories.

Results

A total of 1050 patients were added in the present cross-sectional study. The mean age of the patients was 37±11 years. A total of 720 (68.57%) out of 1050 patients were male while 330 (31.43%) were female. The basic demographic data has been demonstrated in Table 1.

Out of 1050 patients, 504 (48%) were commenced on dapagliflozin while 546 (52%) were commenced on empagliflozin. The risk of urinary tract infection in the patients using dapagliflozin was 22 (4.3%) and it was 34 (6.74%) in those using empagliflozin. Similarly, the risk of genital tract infections in the patients using dapagliflozin was 19 (3.76%) and those using empagliflozin were 23 (4.56%).

The predominance of genital and urinary tract infections was seen more in women compared to men. The frequencies and percentages of the infections according to gender distribution, have been shown in Table 2.

It can be observed from Table 2 that a significant correlation is present between the female gender and the prevalence of genital and urinary tract infections. Table 3 shows the correlation of genitourinary infections with other variables of the study

Table 1. Demographic data of the patients involved in the study

Variables	**Total (n=1050)**
Gender	
Male	720 (68.57%)
Female	330 (31.43%)
Mean age (years)	37±11
Mean BMI (kg/m^2)	28.3±5.6
The mean duration of diabetes (years)	6.1±2.6
History of UTI	52 (4.95%)
Mean HbA1C	7.8±2.4

Table 2. Prevalence of infections according to the gender of the patients

Variables		**Patients taking dapagliflozin (n=504)**		**Patients taking empagliflozin (n=546)**	
		Frequency	**Percentage**	**Frequency**	**Percentage**
Urinary infections	**Total**	22	4.3	34	6.74
	Female	15	68.18	12	35.29
	Male	700	31.82	22	64.71
Genital infections	**Total**	19	3.76	23	4.56
	Female	7	36.84	8	34.78
	Male	12	63.16	15	65.22

Table 3. Correlation of other variables of the study with the prevalence of genitourinary infections

Variables	**Genitourinary infections (n=98)**	**p-value**
BMI (more than 30 kg/m^2)	15 (15.30%)	0.233
Duration of diabetes (more than 5 years)	14 (14.28%)	0.162
HbA1C (more than 8.5%)	69 (70.4%)	0.003
Female gender	42 (42.86%)	0.001
Previous history of genitourinary infections	12 (12.25%)	0.464

Discussion

The present study has been conducted to assess the association of SGLT-2 inhibitors with the increased frequency of genitourinary infections in patients with type 2 diabetes mellitus. The study shows that the correlation is not significant, however, female diabetic patients are more prone to have infections compared to male patients. Genitourinary infections are generally more common in diabetic patients compared to normal individuals. Khan et al conducted a study for the evaluation of the connection between urinary tract infections and diabetes mellitus type 2. The sample size of their study was 350. All the participants had diabetes mellitus type 2. The overall prevalence of UTI in those patients was almost 47%. They concluded that patients with diabetes are more susceptible to having a UTI [12].

Khan et al conducted a cross-sectional study in which 400 patients took dapagliflozin in doses of 5mg and 10 mg for the treatment of diabetes. Blood and urine samples were taken for the evaluation of genitourinary infections. A total of 5.3% of those patients were seen to have urinary tract infections. They concluded that the infections were mild to moderate. The extent of the infection was not severe enough to indicate a discontinuation of the drug [13].

A meta-analysis was conducted by Singh et al in which they aimed to determine the safety of SGLT-2 inhibitor drugs in diabetic patients. Initially, they included 1042 studies in their analysis from the year 2012 to the year 2017. After the screening, 27 studies were included in their final analysis. They concluded that the administration of these drugs warrants close monitoring of their side effects, including diabetic ketoacidosis and UTIs [14].

Rauf et al conducted a study similar to the present study. However, their study was a retrospective one. They closely studied the medical records of 57 patients taking SGLT-2 inhibitors for the management of their diabetes. Their study showed that patients who had been taking the drug for four months had a higher prevalence of UTIs. They have also concluded that the association of UTIs with the female gender was significant [15].

Conclusion

Diabetic patients are more prone to have genitourinary infections than healthy individuals. Patients taking SGLT-2 inhibitors have been shown to have a higher prevalence of catching genitourinary infections. The prevalence is more prominent in female patients taking SGLT-2 inhibitors and patients with uncontrolled diabetes.

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None

Conflict

No conflict of interest

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