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SGLT2 Inhibitors and the Associated Risk of Genito Mycotic Infections – A Narrative Review

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ABSTRACT: The increased prevalence of Diabetes mellitus, the comorbid associations and complications among the global population has led to a dependency for treatment options with multiple modalities. One such option is the SGLT2 inhibitor (SGLT2i) class of drugs. SGLT2i have been demonstrated to improve glycemic control while providing cardiovascular (CV) and renal benefits in patients with T2DM. SGLT2 inhibitors comprising of canagliflozin, dapagliflozin, empagliflozin, ertugliflozin and remogliflozin are indicated in T2DM individuals with CV complications or chronic kidney disease (CKD). Although generally well tolerated, they pose some important safety concerns. The most common side effect of SGLT2i administration being Genital Mycotic Infections (GMI) and Symptomatic Volume Depletion. Meta-analysis and large clinical trials have reported an incidence of 2.5% to 6.5% of GMI, and a 4-6-fold increased risk of GMI among patients on SGLT2i.
This narrative review evaluates the recent literature on SGLT2i and the incidence and severity of GMI. The review aims to help guide health care professionals involved in clinical care for patients on SGLT2 inhibitors.
The existing literature evidence suggests that the GMI associated with SGLT2i therapy are generally mild and respond well to the conventional treatment. Major risk factors of infection are female, poor hygiene, prior infection, and uncircumscribed men. Perineal hygiene and treatment with standard antifungal agents could effectively decrease the incidence of such infections and may not warrant strict discontinuation of SGLT2i therapy. Active patient participation and awareness during treatment initiation is helpful in early recognition of symptoms and timely interventions.

KEY WORDS: Antifungals, Genito Mycotic Infections, Perineal Hygiene, Sodium-glucose transport protein 2 (SGLT2) inhibitors.

INTRODUCTION

Diabetes Mellitus condition has emerged as an overwhelming global health concern with an expected prevalence projected to rise to 10.2% (578 million) by 2030. India with an 8.9% prevalence of DM constitutes the largest (87%) proportion of the South-East Asian diabetic population [1]. About 90 % of diabetic patients have chronic type 2 diabetes associated with multiple comorbidities, including atherosclerotic cardiovascular disease (ASCVD), heart failure (HF) and chronic kidney disease (CKD) [2]. Therefore, treatment requires multiple modalities which further increased the risk of associated adverse events [3,4]. Hence, for clinicians, drugs such as SGLT2i that could help manage multiple conditions are often desirable options.

SGLT2 inhibitors comprising of canagliflozin, dapagliflozin, empagliflozin, ertugliflozin and remogliflozin are indicated in T2DM individuals with high risk for CV complications or chronic kidney disease (CKD). SGLT2i have been demonstrated to improve glycemic control while providing CV and renal benefits in patients with T2DM. Although generally well tolerated, they pose some important safety concerns. The most common side effect of SGLT2i administration are Genital Mycotic Infections (GMI) and Symptomatic Volume Depletion. Other serious concerns include diabetic ketoacidosis, increased risk of bone fracture, lower limb amputation, increased risk of cancer & acute kidney injury [5].

SGLT2 inhibitors (SGLT2is) block glucose and sodium reabsorption in the proximal tubule of the kidney, causing glucosuria and osmotic diuresis. The resulting significant glycosuria contributes to an increased risk of GMI. The reported prevalence of genital infections is 2.5% to 6.5% in large clinical trials [6-8] whereas meta-analyses of trial data show a 4–6-fold increased risk of genital infection with SGLT2 inhibitors [9,10]. Female sex, prior history of genital infections, uncircumscribed males and postmenopausal

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women are at higher risk of SGLT2 inhibitor induced GMI [11,12]. Patients with T2DM have 26% increased risk of genital infection. Genital infections in diabetes are often of mycotic origin caused by *Candida* species. In females, a glucose-inducible protein, produced by *C. glabrata*, enables the fungi to adhere strongly to the vaginal epithelium and multiply, thereby making *C. glabrata* as most common fungus causing vaginal candidiasis [13]. These infections are generally mild and responsive to antifungal treatment. Since practicing perineal hygiene and the standard of care antifungal regimen are effective in the management of genital infections, it may not be required to o discontinue SGLT2i therapy in most scenario. A patient centric approach with early recognition of the risk could help minimize the incidences of genital infections. Active patient participation and awareness during treatment initiation is helpful in identifying those at higher risk of developing genital infections. This narrative review aims to help guide health care professionals involved in clinical care for patients on SGLT2 inhibitors.

METHODOLOGY

The search was performed in the PUBMED database using the key words "SGLT2 inhibitors" or "Canagliflozin", "Dapagliflozin", "Empagliflozin", "Type 2 diabetes mellitus", "Genital mycotic infections". We restricted our screening to clinical trials and systematic review articles with no restriction for the years. We chose the literature based on the appropriateness of the content and relevance to the specific aim of the study pertaining to the extent of available evidence on the incidence of genital mycotic infections, their severity in patients undergoing treatment with SGLT2 inhibitors.

REVIEW

SGLT2 receptors

SGLT2 inhibitors are the first class of glucose lowering agents which act through SGLT2 receptors. There are two types of SGLT receptors - SGLT1 and SGLT2 that are high and low affinity glucose co-transporters, respectively [14-18]. SGLT1 is expressed in the small intestines and mediate 5% of glucose reabsorption in the S3 (distal) segment of the proximal tubule [14,15] [16]. SGLT2 receptors are expressed in the S1 and S2 proximal convoluted tubule of the kidneys facilitates reabsorption of about 95% of glucose. Therefore, by selectively blocking SGLT2 receptors, SGLT2 inhibits glucose reabsorption in the proximal tubule of the kidney, causing glycosuria. These transporters therefore remain as an ideal target for the treatment of diabetes [14,15,17,18].

SGLT2 inhibition, a novel therapeutic approach:

The class of drugs, SGLT2 inhibitors comprises of Canagliflozin, dapagliflozin, empagliflozin, ertugliflozin and remogliflozin. Canagliflozin, the first of the four SGLT2 inhibitors that was introduced in the US market in 2013 to lower blood glucose levels in adults with T2DM [19-22]. FDA has also approved SGLT2 use in combination with other drugs as canagliflozin/metformin (Invokamet®), dapagliflozin/metformin (Xigduo XR®), empagliflozin/metformin (Synjardy®) and empagliflozin/linagliptin (Glyxambi®). Table 1 lists the classes of SGLT2 drugs, their available dose and administration.

In addition to the glycemic benefits, SGLT2 inhibitors have pleotropic effects with significant metabolic, cardiovascular, and renal benefits without increasing hypoglycemic risk [19-24]. In Europe, administration of Dapagliflozin with insulin has been approved for patients with type 1 DM. Newly emerging evidence suggest possible benefits of SGLT2 inhibitors in heart failure with reduced ejection fraction and in chronic kidney disease even in patients without diabetes [25].

Table 1: List of Current SGLT inhibitors and their prescribing information

Generic Name	FDA approved	Available Doses (mg)	Administration
Canagliflozin	29 March 2013	100 300	qam before 1st meal
Dapagliflozin	May 3, 2021	5 10	Qam
Empagliflozin	Dec 2, 2016	10 25	Qam

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Canagliflozin/metformin		50/500 50/1000 150/500 150/1000	BID with meals, max dose 300 mg/2000mg
Dapagliflozin/ metformin		5/500 5/1000 10/500 10/1000	Qam with food, max dose 10 mg/ 2000mg
Empagliflozin/ metformin		5/500 5/1000 12.5/500 12.5/1000	BID with meals, max dose 25mg/2000mg
Empagliflozin/linagliptin		10/5 25/5	qam
Ipragliflozin		25 50	Qam, max dose 100 mg
Tofogliflozin		20	qam
Iuseogliflozin			
Remogliflozin etabonate	26 April 2019 by DCGI		
Ertugliflozin	22 Dec 2017		
Sotagliflozin			

FDA and EMA approved,qam-taken once daily in the morning; BID twice daily.

CV benefits of SGLT2 inhibitors

Till date, there have been four large RCTs involving 38,723 participants across six continents, which evaluated the role of SGLT2 inhibitors in T2DM patients (Table 2). Among these three trials, EMPA-REG OUTCOME (empagliflozin) [26], the CANVAS Program (CANVAS and CANVAS-R trials; canagliflozin) [7] and DECLARE-TIMI (dapagliflozin) [8] assessed the CV outcomes. The primary outcome measures were incidences of adverse cardiovascular events, including myocardial infarction or stroke and mortality. In contrast, the CREDENCE trial was specifically designed to evaluate the effect of SGLT2 inhibition on renal outcomes in patients with established diabetic kidney disease [27]. The study findings evinced that compared to placebo, SGLT2 inhibitors favored a proportional risk reduction of about 10% imparting a moderate beneficial effect on major adverse cardiovascular events. In EMPAREG OUTCOME study, 7020 participants with established cardiovascular disease demonstrated a 38% relative risk reduction in death from cardiovascular causes in the empagliflozin group, versus the placebo group [26]. A 2019 meta-analysis of these trials suggested that the effect was primarily observed in those with established atherosclerotic cardiovascular disease [28]. Further, there seemed to be consistent evidence of reno-protection with proportional risk reductions of greater than 30% in each trial compared to placebo. SGLT2 inhibitors also mediated a pre-specified or post hoc effects on a composite kidney outcome, including doubling of serum creatinine or 40% decline in estimated glomerular filtration rate (eGFR), [27,29,30] thus offering added benefits.

Table 2: Summary of the major randomized controlled trials of sodium-glucose cotransporter -2 inhibitors [31]

Study characteristics	EMPA.REG OUTCOME n=7020	CANVAS program n=10142	DECLARE-TIMI 58 n= 17160	CREDENCE N=4401
Drug	Empagliflozin	Canagliflozin	Dapagliflozin	Canagliflozin
Dose, mg	10 or 25	100 or 300	10	100
Age, mean ± SD in years	63.1±8.7	63.3±8.3	63.9±6.8	63.0±9.2

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Sex, female	2004(28.5)	3633(35.8)	6422(37.4)	1494(33.9)
Follow-up time, median in years	3.1	2.4	4.2	2.6
History of cardiovascular disease	7020(100.0)	6656(65.6)	6974(40.6)	2220(50.4)
History of heart failure	706(10.1)	1461(14.4)	1724(10.0)	652(14.8)
eGFR < 60 mL/min/1.73 m^2Ɨ	1819(25.9)	2039(20.1)	1265(7.4)	2631(59.8)
Micro-or macroalbuminuria	2782(39.6)	3026(29.8)	5199(30.3)	4370(99.3)
Primary outcome(s)	MACE	MACE	MACE and Hospitalization for heart failure or CV death	Elevated (twice) serum creatinine levels, end stage kidney disease, CV or renal caused mortality.

CV=Cardiovascular, eGFR= estimate glomerular filtration rate, MACE=major adverse cardiovascular events (nonfatal myocardial infarction, nonfatal stroke, or CV death).

Evidence on SGLT2 inhibitors & Guidelines

In 2018, several clinical practice guidelines for the treatment of T2DM such as a consensus report by the American Diabetes Association [32] and the European Association for the Study of Diabetes, [33] the American College of Cardiology's Expert Consensus Decision Pathway [34] and Diabetes Canada's clinical practice guideline [35] were updated to reflect the latest evidence of cardiovascular and kidney protection with specific glucose-lowering agents.

Although there is limited evidence on reduction in the risk of CV outcomes or progression of kidney diseases, metformin remains as first-line pharmacotherapy in T2DM patients owing to its reduced cost, favorable tolerability, and safety profile [36]. SGLT2 inhibitors and GLP-1 receptor are recommended as second-line agents in patients with T2DM established cardiovascular disease [32-35].

The 2018 consensus report by the American Diabetes Association and European Association for the Study of Diabetes and the American Diabetes Association's 2019 standards of care added recommendations on the use of SGLT2 inhibitors in patients with heart failure and chronic kidney disease [33,37]. Considering data from CREDENCE trial, the 2019 standards of care recommended SGLT2 inhibitors for the prevention of kidney failure and cardiovascular events in patients with T2DM and an eGFR down to 30 mL/min/1.73 m2, particularly in those with macroalbuminuria [37].

As per the 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases, SGLT2 inhibitors (empagliflozin, canagliflozin or dapagliflozin) are recommended in patients with T2DM and CVD or with a high CV risk (38) Empagliflozin is recommended in patients with T2DM and CVD to reduce the mortality risk. Also, SGLT2 inhibitors are recommended to lower risk of hospitalization due to heart failure (Figure 3).

Safety/ Challenges associated with SGLT2i

Despite the well-established tolerability and safety profile with added CV and renal benefits, SGLT2 inhibitors pose adverse events that majorly include the risk of genital mycotic infection (GMI; balanitis in men and vulvovaginitis in women) and volume depletion-related events, which are consistent with the mechanism of action of this drug class [5]. Another uncommon but potentially serious adverse effects, as observed in CANVAS program were ketoacidosis [39], an increased risk of amputation of the lower extremities and a slight increase in risk of fracture [7]. However, combined results from EMPA-REG OUTCOME or DECLARE-TIMI, did not show any significant increase in urinary tract infections (UTIs), events were consistent with volume depletion, acute kidney injury (AKI), bone fractures or amputations (Table 3) [8,26].

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Table 3: Summary of potential adverse events associated with SGLT2i

More common adverse events	Less common adverse events
Genital mycotic infections	Diabetic ketoacidosis
Urinary tract infection	Lower limb amputation
Hypoglycemia	Bladder cancer
Volume depletion	Bone fracture
	Fournier's gangrene
	Acute kidney injury

Table 4: Adverse events of genital infection – Results from EMPA-REG OUTCOME (from Zinman et al., 2015).

	Placebo	Empagliflozin	
		10 mg	25 mg
Total N	2333	2345	2342
	Events in N (%)	Event in N (%)	Events in N (%)
Total population	42 (1.8)	153 (6.5)	148 (6.3)
Male	25 (1.5)	89 (5.4)	77 (4.6)
Female	17 (2.6)	64 (9.2)	71 (10.8)

Genital Mycotic Infections and Sodium-glucose Cotransporter 2 Inhibitor Therapy:

The risk of GMI in patients taking SGLT2 is increased by 4 to 8-fold compared to patients on placebo or other hypoglycemic agents [8,9,27,40-42]. The onset of GMI infections occur during the first 3 to 6 months of treatment with SGLT2 inhibitors and the associated risks persist with on-going treatment [43,44]. Renal glucosuria resulting from pharmacological administration of SGLT2 inhibitors leads to a conducive environment for pathogens like Candida species leading to genital infections [Table 5] [45,46]. Large outcome trials have evidence proving the phenomenon of increased incidence of GMI with prolonged or increased used of SGLT2 inhibitors.

Microbiological rationale is that the increase in urinary glucose concentration approaches the composition of Sabouraud agar, the medium permissible for growth of yeast. The ensuing mechanisms of increased adherence of *Candida sp.*to the genital tract and the co-existing reduced host immune response status in T2DM patients augments the risk of GMI [44], as evidenced in large outcome trials.

Table 5: Prevalence of genital infection in Type 2 diabetes mellitus patients on sodium-glucose cotransporter-2 inhibitors therapy

SGLT2 inhibitor	Study	Total study population (n)	Test dosage	Incidence of genital infection
Dapagliflozin	Yabe *et al.* [47]	16,664	Not available	2.46%-4.99%
	Yabe *et al.* [48]	1708		3.2% Female: 8.2% Male: 0.8%
	Johnsson *et al.* [49]			
	Bailey *et al.* [50]	4545	2.5mg(*n*=814), 5mg(*n*=1145), or 10mg(*n*=1193)	4.1%, 5.7%, 4.8%
	Kaku *et al.* [51]	546	2.5mg(*n*=137), 5mg(*n*=137), or 10mg(*n*=135)	8%, 13%, 9%

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		279	1mg(*n*=59), 2.5mg(*n*=56), 5mg(*n*=58), or 10mg(*n*=52)	0%, 1.7% 1.7% 0%
Canagliflozin	Prasanna Kumar *et al.* [52] Bode *et al.* [53] Stenlof *et al.* [54]	9439 714 195	100mg(*n*=3092) or 300mg(*n*=3085) 100mg(*n*=241) or 300mg(*n*=236) 100 mg (n=195) 300 mg (n = 197)	3.4%, 4.5% 14.5%, 14.45% 8.8% 7.4%
Empagliflozin	Zinman *et al.* [26] Kohler *et al.* [55]	6563 12283	10mg(*n*=2345) or 25mg(*n*=2342) 10mg (n = 3806) or 25mg (n = 4782)	6.5%, 6.3% 4.7%, 5%

SGLT2: Sodium-glucose cotransporter-2

A network meta-analysis of SGLT2 inhibitors and the associated risk of GMI that included 52 trials and other studies indicated an odds ratio of 3.6 to 5, that is fairly similar to that of placebo (Table 6) [7,26,56]. In the EMPA-REG trial, [26] empagliflozin-treated patients showed a significantly higher incidence of genital infections than those receiving placebo (6.4% vs. 1.8% of patients) with a substantially higher incidence in women (empagliflozin vs. placebo, 10.1% vs. 2.6%) than men (5.0% vs. 1.5%; P<0.001 for all). The meta-analysis cited above further reinforces this and demonstrates risk ratios of 3.3(95% CI, 2.74–3.99), and 2.86 (95% CI, 2.00–4.10) [23] for genital infection in association with SGLT2 inhibitor. More recently, a potential association between SGLT2 inhibitor administration and Fournier's gangrene - a rare but potentially fatal condition characterized by necrotizing fasciitis of the perineal soft tissues - was reported [57]. Fifty-five cases of Fournier's gangrene were identified over the six-year period up to January 2019 [58]. FDA has therefore included a warning in the prescribing information and patient medication guides of all SGLT2 inhibitors on the risk of Fournier's gangrene [59].

Table 6: SGLT-2 inhibitors and genital mycotic infections- Results from a network meta-analysis of 52 RCTs [56]

SGLT-2 inhibitor	Genital mycotic infections Odds Ratio (95% CI)
Canagliflozin	5.0 (3.7, 6.7)
Dapagliflozin	4.5 (3.4,6.0)
Empagliflozin	3.6 (2.4, 4.6)

Risk factors for higher genital infection risk

Genital Infection in Special Populations on Sodium-glucose Co-transporter-2 Inhibitor Therapy

Certain special populations including postmenopausal women and uncircumcised men with diabetes are anticipated to experience more genital infections than others (Table 7). It has been hypothesized that hormonal changes during and post menopause are related

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to diminished local immunity in the female reproductive tract which increases the chances of having genital infections [60]. Similarly, circumcision in men is associated with better maintenance of genital hygiene which is indirectly related to lower incidence of genital infection [61]. Pooled data from eight studies (n = 9439) with longer mean exposure (68 weeks of canagliflozin, 64 weeks of placebo) showed that the rate of male genital mycotic infection was more common among uncircumcised men (11%) than circumcised men (3%) [62]. Although evidence is scarce, studies conducted in Japanese population highlight the benefits of practicing better hygiene in combating the risk of genital infections. Even though the literature is scarce, a few researchers claim that Japanese men with diabetes exhibit a considerably lower incidence of genital infections due to better hygiene. In an efficacy and safety study of dapagliflozin as a monotherapy in Japanese patients with T2DM (*n* = 279), only two patients (one case each in the dapagliflozin 2.5- and 5-mg groups) reported clinical features and investigations suggestive of genital infection [63]. In addition, women with a prior history of genital infection are more prone to infections while on SGLT2 inhibitor therapy. In addition, older age, uncontrolled diabetes, increased BMI & CKD, are all considered independent risk factors for GUI [11,64]. This could lead to cautious initiation of SGLT2i in these populations.

Table 7: SGLT2 inhibitors and GMI- High risk population

Female Sex,
Poor Perineal Hygiene
History Of Prior Genital Infection
Postmenopausal Women
Uncircumscribed Men
Older age
Uncontrolled Diabetes
Increased BMI
CKD

Prevention measures to reduce the SGLT2i therapy mediated risk of Genital Infection in Patients with Diabetes

Proper counselling on the pros and cons of SGLT2i and patient education on routine practice of perineal hygiene are the primitive steps in reducing the risk of genito-urinary infections in patients with diabetes [Figure 1].

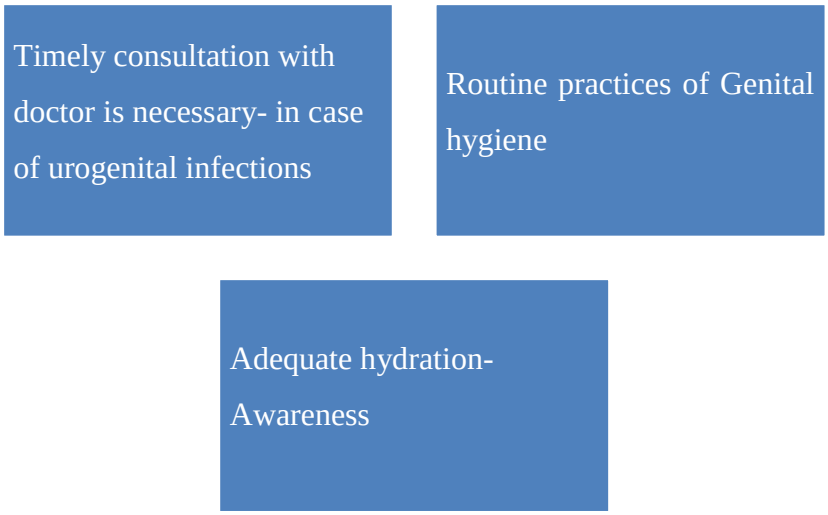

Figure 1: Overview of steps to prevent genital infections

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Perineal hygiene

Patient education on perineal hygiene is an essential pre-emptive measure for all individuals with diabetes. Regular washing of genital organs following urination or defecation and routine use of hygienic wipes are suggested measures. With regard to practice, women should be advised to wash from front-to-back. Men should retract the prepuce prior to cleaning the areas. They should be advised to use clean water for washing or mild soap if required, and not alcohol-based disinfectants [49].

A study conducted in an outpatient setting highlighted the importance of building awareness of perineal hygiene like rinsing the genital area with water after every void and before going to bed. The results indicated that within the first six months of commencing the SGLT2 inhibitor treatment, only 4.8% of the patients who were advised on the perineal hygiene developed GMI versus a 41% of patients who did not receive the hygiene advice [65]. In addition to practicing perineal hygiene, as a preventive measure in especially high-risk women with a prior history of candidiasis, it has been recommended to frequently change pads/ tampons and to wear cotton underwear rather than tight synthetic underwear [66].

Treatment of Genital Infection in Patients on Sodium-glucose Cotransporter-2 Inhibitor Therapy

Although the chances of genital infections in patients with T2DM are considerably high, with prompt treatment, a better prognosis can be achieved [11,67]. Genital infections reported in the study population with SGLT2 inhibitors, are often mild to moderate in severity and respond well to conventional therapy [50,68]. The clinical practice guidelines for the management of candidiasis and treatment of uncomplicated *Candida* vulvovaginitis by the Infectious Diseases Society of America 2016 and The Society of Obstetricians and Gynecologists of Canada, 2015, recommends topical antifungal azoles such as miconazole and clotrimazole (Table 8 and 9) [11]. In addition, for effective management of recurrent VVC, initial therapy should be followed by weekly oral fluconazole 150 mg weekly for a period of up to 6 months [69,70].

Table 8: Treatment for vulvovaginal candidiasis

Genital infection	Treatment recommendations
Strong recommendations with high quality evidence	
Candida vulvovaginitis	Any topical antifungal agents, or a single oral dose (150-mg) of fluconazole
Severe acute *Candida* vulvovaginitis	Two to three oral doses (150 mg each) of fluconazole, given every 72 h.
Recurrent infections of vulvovaginal candidiasis	Topical treatment for 10-14 days, followed by fluconazole (150 mg) weekly for a period of 6 months
Strong recommendations with low quality evidence	
Candida glabrata vulvovaginitis that is unresponsive to oral azoles	Topical intravaginal boric acid (600 mg gelatin capsule) OR Nystatin intravaginal suppositories, 100,000 units daily for 14 days Topical 17% flucytosine cream with or without 3% AmpB cream daily for for 14 days

Table 9: Topical antifungal options for the treatment of vaginal candidiasis

Medicine	Preparation
Clotrimazole cream 1%	5 g single application at bedtime for 7-14 days
Clotrimazole vaginal suppository 100 mg	1 suppository at bedtime for 7 days
Clotrimazole vaginal suppository 200 mg	1 suppository at bedtime for 3 days
Miconazole cream 2%	5 g single application at bedtime for 7 days
Miconazole vaginal suppository 100 mg	1 suppository at bedtime for 7 days
Miconazole vaginal suppository 200 mg	1 suppository at bedtime for 3 days

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Treatment of *Candida* Balanitis

Infection due to *Candida* balanitis is associated with poor hygiene. Along with frequent normal saline washes, it has been recommended to apply clotrimazole cream 1% or Miconazole cream 2%, twice a day for 10 days. Topical steroids, like 1% hydrocortisone can be added in cases of marked inflammation. Topical therapy is usually sufficient in most of the cases of *Candida* balanitis [71].

Continuation of Sodium-glucose Cotransporter-2 Inhibitor Therapy After an Episode of Genital Infection

These mild to moderate genital infections do not mandate discontinuation of SGLT2 therapy due to good response to standard management. [44,50,72,73]. However, the incidence of genital infections within the first month of treatment were associated with a greater adjusted risk for subsequent discontinuation with SGLT2i (19.4% without discontinued versus 31.8% with by 1 year; adjusted HR 1.48; 95% CI 1.21 to 1.81) [50]. It has been observed that discontinuation of therapy during an episode of genital infection is not related to better prognosis [44,72,73].

CLINICAL IMPLICATIONS

Females and patients with past history of infections are sub-groups that are at high risk of developing genital infections when on SGLTi therapy. Stratifying risk based on such simple clinical parameters can aid in targeted counselling and informed treatment decisions. The high-risk patients who are started on SGLTi should be carefully counselled on genital hygiene and probable need for antifungal medications in the future.

CONCLUSION

The anticipated association of SGLT2 inhibitors and increased risk of genital infection is a major cause of concern for diabetologists. Major risk factors of infection are female sex, poor hygiene, prior infection, and uncircumscribed men. Genital infections following SGLT2 inhibitor therapy are mild to moderate in nature which respond well to the conventional therapy. Adequate counselling might help in preventing genital infections in patients with diabetes on SGLT2i treatment. It was also noted that incidence of genital infections and their progression can be significantly reduced by maintaining perineal hygiene and standard antifungal therapy.

RECOMMENDATIONS

Treatment with SGLT2 inhibitors may predispose the patients to developing mild GMIs. Specifically, female population and patients with history of prior infection are subgroups at greatly increased risk of genital infections with SGLT2i therapy. Taking preventive measures and following personal hygiene are advised in patients treated with SGLT2 inhibitors. However, the proven benefits of SGLT2 inhibitors, including the reduction of cardiovascular and renal risks make them a preferred choice in specific populations. Therefore, a conscientious choice that weighs the benefit to harm in individuals is warranted prior to the treatment with SGLT2 inhibitors, especially in the high-risk population. This narrative review can assist healthcare professionals in discussions with patients regarding benefits and risks of starting SGLTi therapy, and in managing probable future complications.

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