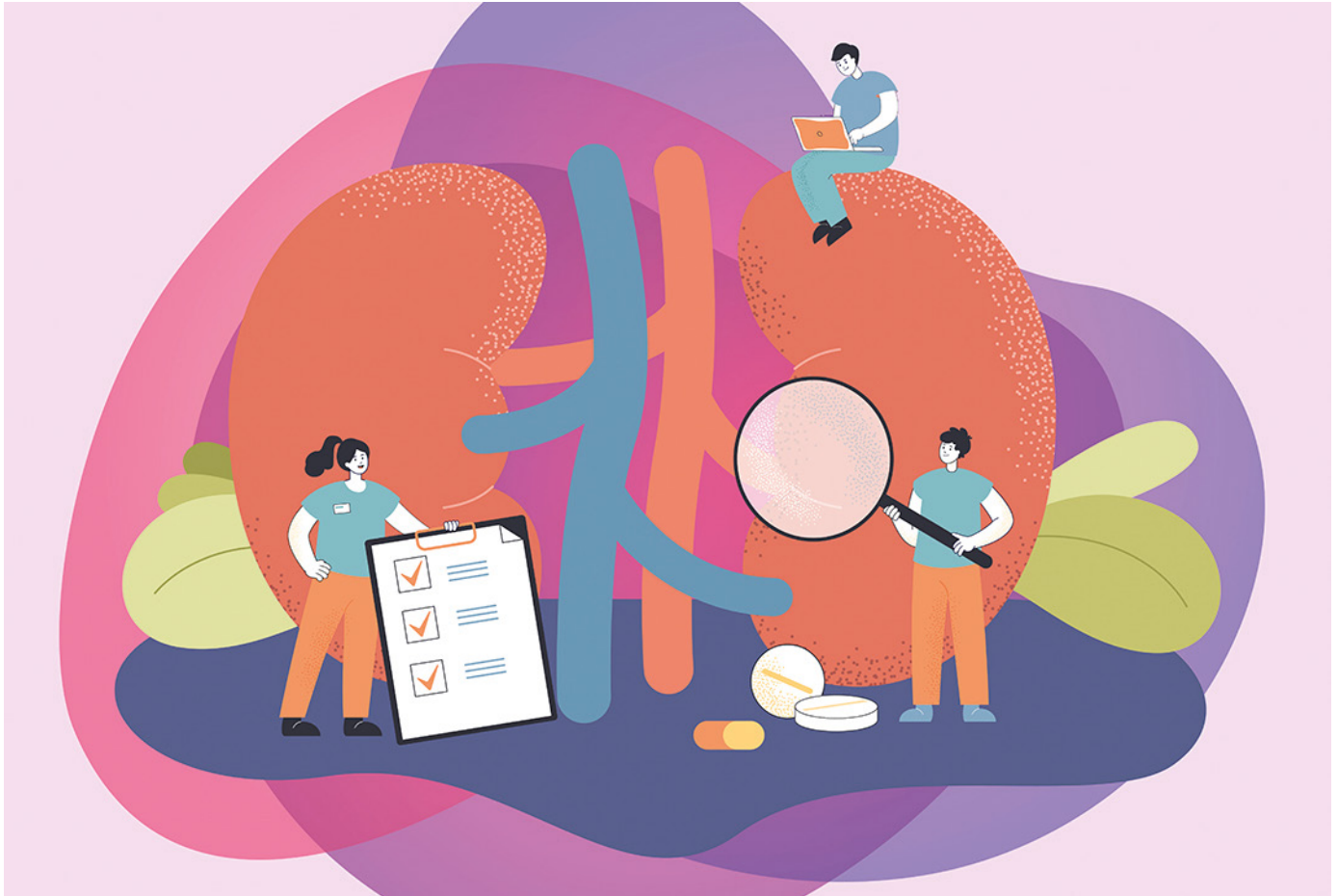**Dr. Óscar Baro Pato.**
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Update on the Management of Urinary Tract Infections in People with Diabetes

Urinary tract infection (hereinafter UTI) is considered a common infectious pathology, but is it as frequent as we think? And if so, in patients with type 2 diabetes mellitus (T2DM), what happens? Does it have the same frequency, prognosis, complications, or treatment?

This article aims to answer all these questions by providing a retrospective review of this disease and updating its contents.

An article published in 1998 considered that UTI in the general population was the second most common cause of consultations in primary care for infectious pathology, after respiratory infections. It also showed a prevalence of bacteriuria in women with T2DM three times higher than in the general population (1).

Another article from 2010 assessed the incidence of UTI in patients with T2DM, concluding that they were more frequent in women and older patients (over 70 years old), regardless of sex (2).

Now, let's analyze a report from 2012, an observational study that compared the incidence and risk of UTI in patients with and without diabetes; at the 1-year follow-up, the risk of UTI was 2.08 for patients with diabetes. It also showed that, in clinical practice, regardless of gender and age, the risk of developing a UTI is higher for patients with T2DM vs patients without the disease (3).

In a new 2017 article, which followed up for 9 years, it was concluded that T2DM was associated with a higher risk of any genitourinary, genital, and UTI infections, with UTI incidence rates being higher than genital infections, and showing a similar pattern when stratified by sex (4).

Regarding the severity of UTIs and data strictly from Spain, an article published in 2020 evaluated hospital admissions from 2001 to 2018 for this reason, revealing that the incidence of admissions for UTI was more than four times higher in patients with T2DM than in patients without diabetes (5).

At this point, and starting in 2020, a noticeable change in studies and articles published caught attention, clearly related to the emergence of a new class of drugs, sodium-glucose **cotransporter type 2 inhibitors (SGLT2i)**. This partly motivates the structure of this article, attempting to show the precedents and the current situation regarding this pathology in people with T2DM.

That said, let's focus now on an article publi-

shed in 2021, which, after confirming that **UTI is one of the main acute complications of T2DM**, centers its content on **their treatment**, concluding **that it should be the same for patients with and without diabetes, and in neither case should asymptomatic bacteriuria be examined or treated** (6).

Lastly, it shows that the use of SGLT2 inhibitors (SGLT2i) significantly increased the incidence of genital tract infections, but not of UTI, pyelonephritis, or urological sepsis.

Then, in 2022, we found a real-life observational study conducted between 2019 and 2021 in Thailand, concluding the high incidence of UTI in patients with T2DM using SGLT2i (specifically dapagliflozin and empagliflozin) vs those not using this pharmacological group. There was also higher incidence in this patient group with older age and associated with the female gender. However, no differences were found in the incidence rates of UTI between one drug (dapagliflozin) and the other (empagliflozin) (7).

Nearly concluding this review, I would like to highlight two very comprehensive studies published recently:

On one hand, we have a study published in September 2023, which specifically evaluates the **particularities of UTIs in patients with diabetes**, reaching the following conclusions: **they evolve more frequently to bacteremia, present an increase in hospitalizations, and have higher rates of recurrence and mortality vs UTIs reported in patients without diabetes**. A series of **risk factors** were identified, such as: **female sex**, **advanced age**, a **UTI in the previous 6 months, poor glycemic control, and the duration of diabetes**. Bacterial strains involved in UTIs of patients with diabetes and their susceptibility to antibiotics are similar to those of patients without diabetes (8).

In any case, the duration of treatment should be that of a complicated UTI.

This study also evaluates the peculiarities of treatment with SGLT2i, highlighting that UTIs occur when this treatment is initiated, recurrent infection was infrequent in these patients, and the treatment with usual antibiotics was mostly effective. Similarly, treatment with SGLT2i did not increase the risk of developing pyelonephritis or urological sepsis.

THE PRESENCE OF A URINARY TRACT INFECTION IN A DIABETIC PATIENT MAY PRESENT WITH DYSPURIA, POLYURIA, URGENCY, HEMATURIA, SUPRAPUBIC PAIN, AND SENSITIVITY IN THE PELVIS, WITHOUT DIFFERENCES FROM THE SYMPTOMS IN NON–DIABETIC PATIENTS

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» On the other hand, the study published in October 2023 specifically assesses the association of SGLT2i with UTI in patients with T2DM. It recommends performing a urine culture in these cases for proper selection of antibacterial treatment; it also concludes that the relationship between SGLT2i use and UTIs is independent of the patient's hemoglobin A1c and body mass index (9).

Finally, I would like to comment on the conclusions of an article published in March 2024, which reviews the association between diabetes, the use of SGLT2i, and UTIs, and concludes that there is more evidence associating SGLT2i with genitourinary infections than with UTIs. Therefore, more research is still needed today to clearly understand the relationships between SGLT2i, genital infections, and UTIs (10).

Once the literature has been broken down, what conclusions do we reach? Or, in other words, what takeaways can I bring home?

It is evident **that people with diabetes have a higher prevalence and incidence of UTIs, especially women, with a female/male UTI ratio of 4:1** (11). Similarly, the prevalence of asymptomatic bacteriuria is also increased in women with diabetes.

As for the risk factors for developing a UTI in patients with diabetes, they do not differ from those in patients without diabetes.

When specifically talking about patients with diabetes, there is a higher risk depending on the duration of the condition (if it is longer than 5-10 years) and if certain pharmacological treatments are received. On the other hand, the relationship with the degree of glycemic control, in ranges without hyperglycemic decompensation, is inconsistent, though it is somewhat higher in patients with poorer glycemic control (hemoglobin A1c > 8%-9%).

Regarding symptoms, the presence of a UTI in a patient with diabetes can present dysuria, pollakiuria, urinary urgency, hematuria, suprapubic pain, and pelvic tenderness, with no differences vs the symptoms of patients without diabetes. If we review the prevalence of asymptomatic bacteriuria, it will be increased in women with diabetes, although it is usually mild, does not persist, and does **not require treatment**. In fact, screening for **asymptomatic bacteriuria** is unnecessary in diabetic patients.

The approach to treatment would be as follows: in the case of a typical UTI in a woman, with dysuria and pollakiuria present, without other symptoms or signs suggesting complications, treatment should begin without further complementary tests. If only one symptom of infection is present, it is recommended to perform a combur test for confirmation. As for the urine culture, it should be reserved for cases where the diagnosis is unclear, the »

» re is suspicion of antibiotic resistance, or we are facing a patient relapse.

Regarding post-treatment management, urine culture follow-up is not necessary if the patient is asymptomatic, although it is recommended for patients with immunosuppression, advanced age, recent infection treated with antibiotics, or the presence of resistant germs in the initial urine culture. On the other hand, **in the male population, a follow-up urine culture should be performed**.

When prescribing treatment, short antibiotic regimens are recommended, i.e., from 1 to 5 days, as there are no differences in the outcomes vs 7-10 day regimens, and side effects and treatment adherence are improved. The **treatments of choice** are: fosfomycin 3g, in a single dose, and nitrofurantoin 50 mg, every 12 hours for 5 days.

The reasons for hospital referral include very poor control with blood glucose > 400 mg/dL, not responding to the initiated antibiotic treatment, fever > 39ºC associated with or suspected of ketoacidosis.

Finally, what can we contribute in terms of SGLT2i? The data we have is fairly consistent and shows that treatment **with SGLT2i is associated with a small increase in symptomatic UTIs in both men and women, although the rates are lower in the former**.

The characteristics of infections associated with SGLT2i, their clinical presentation, and the microorganisms involved are similar to those in other patients, with no increased severity or recurrence, and they respond to the standard treatment previously explained. Similarly, discontinuation of SGLT2i treatment due to urinary infections is rare and considered an exceptional situation. **D**

CONCLUSIONS:

■ Urinary Tract Infections (UTIs) are one of the most frequent acute complications in T2DM.

■ UTIs in patients with T2DM are more likely to progress into bacteremia, hospitalization, recurrence, and mortality than in patients without T2DM.

■ Asymptomatic bacteriuria does not require screening or treatment.

■ In asymptomatic women, post-treatment follow-up is not necessary, but in men, a follow-up urine culture should be performed after treatment.

■ The treatment of choice is the same as for UTIs in patients without diabetes: fosfomycin 3g in a single dose or nitrofurantoin 50 mg every 12 hours for 5 days.

■ The emergence of the pharmacological class of sodium-glucose cotransporter 2 inhibitors (SGLT2i) has increased the number of UTIs, but without greater severity in clinical presentations and with a good response to the treatment of choice.

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