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SEXUAL HEALTH

Sweet urine, bitter outcome: Empagliflozin and balanoposthitis

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5 minutes to Read



Urine loaded with sugar offers an excellent growth medium for fungi and bacteria [Image: Mikhail Nilov on Pexels]

Sexual health specialist **Massimo Giola** continues his series of short, mostly clinical case-based sexual health articles. This year, he has in mind a mix of transgender medicine and sexology topics, but he starts with a genital dermatology issue he has seen a few times recently

Key points

- Sodium-glucose cotransporter-2 inhibitors (dapagliflozin and empagliflozin) work by causing glycosuria.
- Urinary tract infections and genital fungal infections are reported side effects of SGLT2 inhibitors.
- Particularly among uncircumcised people with penises, specific advice should be given, and care should be taken, to avoid irreversible scarring of the prepuce resulting in inability to pull the foreskin back.



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Nurses may also find that reading this article and reflecting on their learning can count as a professional development activity with the Nursing Council of New Zealand (up to 0.25 PD hours).

John is a 38-year-old man with type 2 diabetes, on treatment with metformin + empagliflozin. He used to be on metformin alone, but his GP added the sodium-glucose cotransporter-2 (SGLT2) inhibitor approximately one year ago for insufficient control of the diabetes. He is overweight (BMI of 31kg/m²) but otherwise well, and he does not take any other regular medications.

His GP refers him to the sexual health service for “refractory balanoposthitis with ?phimosis”. When I meet John, he tells me things have got progressively worse, and he is now unable to retract his foreskin. He has been in a monogamous heterosexual relationship with the same partner for the past 10 years, but they have been unable to have sex for the past three months as erections have become painful for John, due to the tight foreskin.

Looking at his laboratory results, he has had several sexually transmitted infection screenings (always negative) and penile swabs taken from the glans (sometimes showing growth of *Candida albicans*, sometimes of normal skin flora only).

His GP tried several topical creams: clotrimazole 1 per cent; miconazole 2 per cent + hydrocortisone 1 per cent; and a three-drug topical combination of hydrocortisone + natamycin + neomycin.

John has tried to apply the creams as he was told to do, but it has become increasingly difficult as the opening of the foreskin has become smaller and tighter. Recently, he has only been able to smear a tiny amount of cream on the edge of the foreskin. He went back to his GP to explain that, and he was then prescribed oral fluconazole with no clear response either.

Combinations of topical agents

For quite a while, I thought I was the only grumpy old doctor in New Zealand ranting all the time about these combinations. Then (much to my relief) world-famous dermatologist Amanda Oakley wrote an article for *New Zealand Doctor* about the worst mistakes in dermatology, quoting routine prescription of the three-drug combination listed above as one of them (see “**Dermatology**”, 11 May 2022). Topical neomycin, in particular, is well known to cause reactive dermatitis and even genital ulcers, and it should be avoided at all costs.

Personally, I am very conservative in using topical agents for balanitis/balanoposthitis – the vast majority of mild to moderate, non-specific balanoposthitis cases respond very well to simple genital skin hygiene recommendations (one, maximum two, showers per day; short showers less than five minutes; warm, not hot, water; avoidance of all liquid body washes and use instead of a bar of simple, white, unscented soap; avoidance of friction trauma during sex or masturbation by using lubricant gel or creams) and, in some cases, using emulsifying ointment as a skin protection while showering. I do not like aqueous cream as it is an emulsion of water and oil (as the name suggests) and can cause maceration of the genital skin, which tends already to be more moist than other areas of the body.

If it is moderate to severe and very typical for *Candida* balanoposthitis (a minority of cases, mostly among people with diabetes or with other medical conditions affecting the immune response), I use clotrimazole for a short time. I never use combinations of topical agents (nor oral fluconazole for superficial fungal infections).

Very seldom, there might be a good argument for using a different class of antifungal (in practice, nystatin rather than an azole) for non-*albicans* *Candida* species or for azole-resistant *C. albicans*.

Back to John

On examination, John has a circumferential tight white scar of the prepuce approximately 1cm from the opening. It is now impossible to retract the foreskin. Through the tiny remaining opening, I can glimpse, in the fold between foreskin and glans, a white, clumpy exudate sitting on a red, inflamed glans.

John is shocked to hear that at this stage, the only possible solution is a circumcision as no medical treatment would be able to restore the normal prepuce anatomy and stretchiness. While waiting for urology to see him, I suggest applying clotrimazole cream on the glans and under the foreskin using a cotton bud swab gently inserted through the tiny opening that remains.

I ask John what kind of instructions he was given when the SGLT2 inhibitor was started. He vaguely remembers being given a patient information leaflet suggesting to “keep your genitals clean” ([healthify.nz/medicines-a-z/e/empagliflozin](https://www.healthify.nz/medicines-a-z/e/empagliflozin)), which he found a bit offensive as he has a shower, perhaps two, every day.

Is it enough to “keep your genitals clean”?

I don't think so. John is not the only case of severe and refractory genital candidiasis we have seen in the last couple of years among people with diabetes on SGLT2 inhibitors – both men and women.

Suggesting to “keep your genitals clean” is suboptimal and (I agree with John) a bit patronising and offensive. Most genital skin problems arise in people who are squeaky clean, and are normally associated with excessive cleaning, not with being “unclean”.

The root cause of the issue here is the excretion of urine loaded with sugar, which offers an excellent growth medium for fungi and bacteria.¹ It is not such an uncommon side effect either – the analysis of pooled data from eight studies (9439 patients) showed 11 per cent of uncircumcised men treated with an SGLT2 inhibitor developed a mycotic balanoposthitis.²

Particularly in people with a foreskin, any stagnating sugary urine after micturition, even a few drops, is to be avoided. We need to be much more explicit and detailed in our advice.

Uncircumcised men started on SGLT2 inhibitors need to fully retract the foreskin before each micturition (to avoid drops of urine spilling into the foreskin fold), and to rinse with water and pat dry the glans before allowing the prepuce to roll back up. Ideally, circumcised men (and women) need to rinse with water after every micturition and then pat dry the glans (or vulva), or if rinsing is not an option, at least pat dry with toilet paper.

Apart from giving good preventive advice when starting people on SGLT2 inhibitors, providers need to promptly act if problems develop while on these drugs, review the objective state of the genital skin regularly, and consider alternative treatment for diabetes if clinically indicated.

Details have been changed to protect patient confidentiality

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- Are there any skills you need to develop to apply this learning effectively?

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References

1. Johnsson KM, Ptaszynska A, Schmitz B, et al. Vulvovaginitis and balanitis in patients with diabetes treated with dapagliflozin. *J Diabetes Complications* 2013;27(5):479–84.
2. Nyirjesy P, Sobel JD, Fung A, et al. Genital mycotic infections with canagliflozin, a sodium glucose co-transporter 2 inhibitor, in patients with type 2 diabetes mellitus: a pooled analysis of clinical studies. *Curr Med Res Opin* 2014;30(6):1109–19.