Dapagliflozin and recurrent Fournier's gangrene: The role of the pharmacist

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Background:

Type 2 diabetes mellitus (T2DM) is a condition affecting around 4.5% of the Australian population, with almost 1.2 million hospital admissions related to T2DM in 2019-20.[1] Reducing the number of hospital admissions by avoiding complications is important for management of T2DM and reducing costs to the healthcare system. Sodium-glucose co-transporter-2 (SGLT2) inhibitors are commonly used in clinical practice for management of T2DM as a second agent, added onto standard metformin therapy.[2] Despite their ability to improve overall survival and rates of death from CV causes, reduce incidence of heart failure hospitalisations, cause modest weight reduction, and contribute to improving blood pressure control, there are some adverse effects that can limit its use.[2] Post marketing reports of euglycemic ketoacidosis and severe genital infections including perineal necrotising fasciitis, aka Fournier's gangrene (FG), have occurred and are important rare adverse effects patients should be counselled on to avoid related hospital admissions.[2,3]

Aim:

To discuss a case of recurring Fournier's gangrene in a patient on SGLT2 inhibitor dapagliflozin and the pharmacist's role in identifying the potential adverse drug reaction (ADR).

Clinical features:

54 year old female, presenting febrile, worsening pelvic pain and swelling with abscess of mons pubis, DKA.

PMHx:
T2DM, IHD (prior MI), pAF, OSA, asthma, obesity, HTN, GORD.

Diabetic home meds:
Metformin 1g XR BD
Dapagliflozin 5mg BD
Semaglutide 1mg SC weekly

Outcomes:

- ICU admission for DKA management. Local DKA protocol followed.
- IV amoxicillin + clavulanic acid 1.2g q8h + vancomycin 1.5g BD started.
- ID team impression: "Fournier's gangrene spectrum illness."
- Pharmacist routine medication Hx and reconciliation performed.
- Review of PMHx showed previous ICU admission in Dec 2016 for perineal necrotising fasciitis of unknown cause.
- Pharmacist confirmed starting date of dapagliflozin as Jan 2016, using Medicare dispensing records, GP records and electronic medical record.
- Pharmacist identified previous case reports of SGLT2 inhibitors and FG.
- Pharmacist notified ICU and treating team with recommendation to cease SGLT2 inhibitor dapagliflozin permanently given recurrent episodes of FG and DKA.[4] Recommendation accepted.
- Medical consult and diabetes educator referral put into place for optimisation of diabetes management for patient. HbA1c 11%.
- Surgical intervention: Washout and debridement of pelvic abscess.
- Diagnosis of Fournier's gangrene confirmed during admission.

12 unique cases of Fournier's gangrene in patients on SGLT2 inhibitors reported to FDA from March 2013 - Jan 2019.[5]

Naranjo score 3 = Possible adverse drug reaction[6]

Patients with diabetes at high risk of FG in trial data.[4,5]

AMH: Perineal necrotising fasciitis rare adverse effect of SGLT2 inhibitors.[3]

Meta-analysis unable to identify causal link between SGLT2 inhibitor and FG.[5]

Conclusion:

There has not been an established causal link between the use of SGLT2 inhibitors and Fournier's gangrene due to the limitations of possible underreporting and inability to establish incidence[5], however several post marketing case reports have been made of FG in patients on SGLT2 inhibitors.[4,5] This case highlights the role of the pharmacist in identifying a possible severe adverse drug reaction. Counselling patients on rare adverse events such as signs of euglycemic DKA and FG could prevent avoidable hospital admissions in patients on SGLT2 inhibitors and help reduce the burden on the healthcare system.

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