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EUGLYCAEMIC DIABETIC KETOACIDOSIS ASSOCIATED WITH SODIUM GLUCOSE CO-TRANSPORTER 2 INHIBITORS (SGLT2 INHIBITORS)

WebAIRS has received three reports over the last 18 months where Sodium glucose co-transporter 2 inhibitors (SGLT2), also known as Flosins, have led to euglycaemic diabetic ketoacidosis (EuDKA). In the webAIRS cases, the patients presented for emergency surgery and the SGLT2 inhibitors had not been ceased beforehand. Fortunately, all three patients were managed appropriately, and it was possible to mitigate the degree of harm. The blood glucose levels were 3.4, 5.7 and 14 mmol/L and the plasma ketones were 1.4, 1.0 and 6.9 mmol/L respectively (Normal < 0.6 mmol/L). Two cases were managed in intensive care and one case by an endocrinologist on the ward. All three cases in this series ultimately had a satisfactory outcome but experienced ketoacidosis of varying severity. However, poorly treated DKA can be associated with significant risk of severe harm or death.

SGLT2 inhibitors act by reducing the renal uptake of glucose and thereby increasing glucose excretion in the urine. This mode of action has the potential for diabetic ketoacidosis to develop associated with normal or with moderately raised blood glucose levels. This is known as EuDKA, although it should be noted that the definition includes blood glucose levels up to 14 mmol/L which is above the normal range. There have been several articles and safety alerts relating to the issue of EuDKA published since 2015.¹⁻⁴ Perioperative management can be divided into the risk factors, methods

for prevention and if DKA occurs then escalating the management.

Risk factors

- Patient factors – Management of diabetes with SGLT2 inhibitors, dehydration, low carbohydrate diet, acute illness, sepsis and the stress response to injury or surgery.
- Task factors – Fasting for a procedure, bowel preparation for a procedure, emergency case and medical or surgical procedures especially major surgery.
- Caregiver factors – Knowledge of the risks of SGLT2i, following an accepted management plan and communication between team members.
- System factors – Adequacy of protocols and adequacy of preoperative instructions.

Prevention

- Assessment – Identify the use of SGLT2i at least 3 days before admission and on the day of admission. If taking SGLT2i, check both plasma blood glucose and plasma ketones by fingerprick or laboratory test.
- Planning – Ensure that management protocols are in place for the perioperative management of patients taking SGLT2i. This should include protocols for elective cases, emergency cases, and where DKA is identified on admission. It is normally recommended that SGLT2i should be ceased 3 days prior to a procedure and not recommenced until dietary intake has completely returned to normal. If dieting is recommended prior to a procedure, for instance, in morbidly obese patients, then the SGLT2i should also be ceased.

Escalate

- Where DKA is detected, enact protocols for management, including a specialist physician, endocrinologist or intensive care specialist. Consider management in a high dependency (HDU) or intensive care unit (IDU). Where emergency surgery must proceed, stabilise as much as possible before the procedure.

This article is intended to raise the level of awareness of the problem with SGLT2 inhibitors and DKA, especially euDKA where blood glucose levels are either normal, or mild to moderately elevated. However, it is beyond the scope of this article to provide a detailed summary of the issues involved and the management of DKA. It is strongly advised that the following references are read¹⁻⁴ and that all institutions develop their own customised protocols and management plans.

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References

1. Severe Euglycaemic Ketoacidosis with SGLT2 Inhibitor Use in the Perioperative Period <http://www.anzca.edu.au/fellows/safety-and-quality/safety-alerts> Accessed 21/10/19.
2. Severe Euglycaemic Ketoacidosis with SGLT2 Inhibitor Use in the Perioperative Period. Dr Roger Traill. <http://www.anzca.edu.au/documents/alert-dka-and-oral-hypoglycaemics-20180215.pdf> Accessed 21/10/19.
3. Safety advisory - diabetic ketoacidosis and surgical procedures: Sodium glucose co-transporter 2 inhibitors. 18th July 2018. <https://www.tga.gov.au/alert/sodium-glucose-co-transporter-2-inhibitors> Accessed 21/10/19.
4. D.A. Milder, T.Y. Milder and P.C.A. Kam. 'Sodium-glucose co-transporter type-2 inhibitors: pharmacology and peri-operative considerations'. *Anaesthesia* 2018, 73, 1008-1018 (doi:10.1111/anae.14251).