



Patient Safety Alert: Risk of possible harm from the use of Sodium-glucose cotransporter-2 (SGLT-2) inhibitors in patients planned for or post-Bariatric Surgery

Background:

Sodium-glucose co-transporter-2 inhibitors (SGLT-2i) (loosely known as gliflozins) are a group of drugs that are commonly used for patients with Type 2 Diabetes Mellitus [1]. They have recently gained popularity due to their cardio-renal protective benefits in patients with and without type 2 diabetes mellitus [2]. However, they are also known to be associated with euglycemic and hyperglycaemic diabetic ketoacidosis (DKA) and the Food and Drug Administration of the United States of America issued a warning on this in 2015 [3]. In the United Kingdom, NICE recommends checking whether the person may be at increased risk of DKA, for example on a very low carbohydrate or ketogenic diet, before starting an SGLT2i [4]. The American Academy of Clinical Endocrinologists currently recommends that SGLT-2 inhibitors should be withheld for at least 24 hours before elective surgery and until patients can tolerate a normal diet [5].

Mechanism of action of SGLT-2:

These drugs (Canagliflozin, Dapagliflozin, and Empagliflozin) inhibit renal Sodium/Glucose co-transporters, thereby reducing the reabsorption of glucose in the kidney and serum glucose levels [1]. Because of their mechanism of action and their impact on reducing insulin (due to decreasing glucose) and increasing glucagon levels, patients, especially those with severely reduced oral intake (such as in those pre and post-op bariatric surgery) are predisposed to dehydration and ketosis.

Risks of SGLT2i use in patients undergoing Bariatric Surgery:

The risks include increased genital and urinary tract infections, and rarely Fournier's gangrene and euglycemic (or hyperglycaemic) DKA [1]. The diagnosis of euglycemic DKA is confirmed by the presence of metabolic acidosis, ketosis, bicarbonate less than 15 mmol/L, and a glucose level that is usually less than 11 mmol/L [6,7]. In contrast, in hyperglycaemic DKA, the blood glucose is significantly elevated and is usually > 15 mmol/L. Patients undergoing bariatric surgery are usually advised to go on a liver-reducing low (<1200kcal per day) or very low-calorie diet (<800kcal per day) before surgery. For many patients, this will be a sudden and significant reduction in their habitual dietary intake. Moreover, in the first few weeks after bariatric surgery, most patients will be consuming only around 600 kcal per day and some struggle to meet their fluid requirements. All these factors place them at a higher risk of developing ketosis.

The literature on SGLT2i induced DKA in post-bariatric surgery patients is small but growing [8,9,10]. There appears to be a small but significant risk of DKA in patients on SGLT-2i undergoing bariatric surgery [1,8,9,10]. Several cases have been reported with different agents and different procedures

[1,12]. Cases have also come to the attention of the Patient Safety Committee at British Obesity and Metabolic Surgery Society (BOMSS) of DKA in post-bariatric surgery patients in the United Kingdom where SGLT2 inhibitors were implicated.

This alert will help bariatric teams, anaesthetists, and General Practitioners manage the risks of SGLT-2 inhibitors in patients pre or post-bariatric surgery.

Recommendations:

- 1) Bariatric teams should stop any SGLT2i 48 hours before starting any preoperative diet and communicate this to the patient's General Practitioner (GP)
- 2) Bariatric teams should stop any SGLT2i 48 hours before bariatric surgery even if no preoperative diet is recommended and communicate this to the GP
- 3) Patients who have had bariatric surgery should not be started on SGLT2i without a full discussion of the pros and cons and other treatment options. The risk of DKA in the long term will vary from procedure to procedure, duration after surgery, and patient's dietary intake.
- 4) The risk of DKA due to SGLT2i in people without type 2 diabetes mellitus is very rare. However, initiation of these agents for their cardio-renal benefits in patients who have had bariatric surgery should only be after a full discussion of the pros and cons.
- 5) SGLT-2i should be withheld in any patient hospitalised for major surgery or acute serious illness. Ketones levels should be monitored daily, even if asymptomatic with normal blood glucose levels, and the drugs should only be restarted once the clinical condition has stabilised and normal oral intake established [11]. If a decision is taken to commence them at a later stage or permanently omit them, this should be communicated to the GP.

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