Risk Factors for Diabetic Ketoacidosis (DKA) for Patients on Sodium/Glucose Cotransporter-2 inhibitor (SGLT2i) Therapy

Introduction

Possible increased risk of DKA is reported on SGLT2i therapy, with increasing speculation regarding the pathophysiology of this process.

Six admissions for DKA occurred in patients on SGLT2i therapy at the Royal Bournemouth Hospital over a 12 month period, we present commonalities between each case and current literature.

Method

Admissions coded for DKA and type 2 diabetes were identified, and their notes reviewed to identify SGLT2i use. Retrospective review of notes was used to identify common presenting symptoms and possible risk factors.

We conducted a brief literature search to compare our cases to current evidence.

Patient Cases

Case 1 (Underlined text used to highlight possible similarities)

A 42 year old female with type 2 diabetes presented to A+E with dyspnoea, reduced oral intake and vomiting. She had experienced 5 stone weight loss over a period of 8 months, prior to admission.

Her pH was 6.81, her glucose was 13.6mmol/L and her ketones were 4.0mmol/L.

She was on Empagliflozin and Metformin.

Following discharge her anti-GAD and Islet cell antibodies were tested and were positive.

Case 2

A 53 year old female was admitted twice with ketoacidosis. On her first admission she presented with a facial abscess. Her pH was 6.82, her glucose was 29mmol/L and her ketones were 3.9mmol/L.

She was on a combination of Dapagliflozin and Metformin. Dapagliflozin was not stopped, likely as a result of her hospital transfer for abscess drainage.

She represented 2 months later with a 3 day history of vomiting and poor oral intake. Her pH was 6.88, her glucose was 19.2mmol/L. Her Dapagliflozin was stopped.

Case 3

A 52 year old male presented with a 5 day history of vomiting and reduced oral intake.

On admission his pH was 7.09 and his glucose was 31.7 mmol/L.

He was taking Dapagliflozin and metformin, as well as Lantus, Novorapid and Exenatide.

He had previously been diagnosed with latent autoimmune diabetes of adulthood (LADA).

Case 4

A 41 year old female had 2 admissions with ketoacidosis. On her first admission she presented with coryzal symptoms. Her pH was 6.84 and her glucose was 12mmol/L. She was on Empagliflozin and Metformin. Her diabetes started initially in pregnancy as gestational diabetes, and it later persisted.

Her Empagliflozin was stopped initially but restarted in immunology clinic for unclear reasons.

A few months later she represented with mild ketoacidosis with a pH of 7.28, glucose of 7.8mmol/L and ketones of 5mmol/L.

Key similarities

- In total there were 6 admissions to hospital between 4 patients.
- In 4 of these admissions, vomiting and reduced oral intake were one of the main presenting symptoms.
- In 4 admissions the glucose level was less than 20mmol/L on admission.
- In 5 admissions the pH was less than 7.10 on admission.
- All patients were also taking Metformin.
- There was a possible link with auto-immune diabetes, with 2 patients having LADA. One patient had also developed type 2 diabetes following gestational diabetes, for which pathophysiology is not yet clear but may possibly be auto-immune related.

Discussion and Summary

We conducted a brief literature review looking at links between SGLT2i therapy and development of DKA. Autoimmune diabetes was associated with development of ketoacidosis in our cohort. This is also seen in the literature which is often suggestive of a link with impaired pancreatic endocrine function, which would be expected in our patients with LADA. This may have implications for recent guidance suggesting SGLT2i therapy might be used in patients with Type 1 diabetes. Further research is needed to explore this.

Other common features both in the literature and in our patients were presentation with nausea, vomiting, reduced carbohydrate intake and lower than expected glucose levels on admission. Reduced carbohydrate intake is also of possible concern, as SGLT2i therapy is often prescribed to patients trying to lose weight.

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