COMMENT ON HAMBLIN ET AL.

Capillary Ketone Concentrations at the Time of Colonoscopy: A Cross-Sectional Study With Implications for SGLT2 Inhibitor–Treated Type 2 Diabetes. Diabetes Care 2021;44:e124–e126

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The study on sodium–glucose cotransporter 2 inhibitor (SGLT2i) therapy by Hamblin et al. (1) advocates for increasing β-hydroxybutyrate (BHB) to 1.7 mmol/L for hyperketonemia, in contrast to our previously suggested threshold of 1.0 mmol/L (2). This change is premature, since the new cutoff is based on a nonnormally distributed data set, the risk of developing ketoacidosis is different in patients with diabetes compared with patients without diabetes, and a higher BHB threshold may increase the false-negative rate of early ketoacidosis.

The new threshold is based on a central 95% reference range on a healthy normoglycemic cohort, where 91% (138 of 151) of the values were below 1.0 mmol/L. The data presented are not normally distributed and, hence, are prone to high variability and are less reliable (3).

Providers cannot assume the risk of progression to ketoacidosis is identical in patients with and without diabetes. SGLT2 inhibition results in a proketogenic state due to urinary caloric losses and a decreased insulin-to-glucagon ratio, stimulating lipid utilization. The superimposed effects of diet modifications, prolonged fasting when scheduled later in the colonoscopy list, bowel preparation, and inappropriate precolonoscopy handling of SGLT2i pose an increased risk of ketoacidosis in this group.

Further, BHB values >1.0 mmol/L are usually considered hyperketonemic thresholds in the perioperative period (4). Having different cutoffs for colonoscopy and noncolonoscopy procedures might add an element of confusion among clinicians.

Finally, the inconvenience of the lower threshold is overstated. We have suggested that this threshold should prompt acid–base analysis in those who have not sufficiently withheld their SGLT2i and insulin dextrose infusions if required, not automatic cancellation of colonoscopy. We agree that colonoscopies are low-risk procedures that can be safely undertaken unless the BHB values are close to the diabetic ketoacidosis (DKA) threshold, i.e., 3.0 mmol/L, as evident from our case series (2). Applying a cutoff of 1.0 mmol/L, we observed an 18% (14 of 77) incidence of hyperketonemia among SGLT2i-treated patients. There was one euglycemic DKA (EDKA) episode for every five hyperketonemic presentations, yet colonoscopies were successfully performed in all our patients, including those manifesting EDKA.

In situations where the consequences of missing a diagnosis such as EDKA are serious compared with the minimal harm associated with an insulin and dextrose treatment, a low specificity may be preferable. A higher BHB threshold may increase the false-negative rate in patients in ketosis who are at high risk of developing ketoacidosis. Conversely, although a low BHB threshold comes with the burden of identifying benign ketosis, ketoacidosis is unlikely to be missed with this strategy. This was evident in our EDKA series, where patient number 1 presented with a BHB of 1.6 mmol/L (below the 1.7 mmol/L cutoff) before colonoscopy, increasing to 2.0 mmol/L postprocedure, reiterating the significance of a postcolonoscopy measurement (2).

Since the new BHB threshold from a central data set may give a false impression that ketoacidosis is not evolving and it deviates from the existing cutoffs, a BHB threshold of 1.0 mmol/L in this subgroup should trigger evaluation of clinical and acid–base indices, which, in most cases, will allow colonoscopy to proceed. Prospective multicenter research on this topic is required.

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