RESPONSE TO COMMENT ON RUBINO ET AL.

Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations. Diabetes Care 2016;39:861–877

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On behalf of the 48 coauthors from our article reporting the findings and recommendations of the 2nd Diabetes Surgery Summit (DSS-II) (1), we sincerely thank Aberle and Göke (2) for their insightful comments about the consideration of sodium–glucose cotransporter 2 (SGLT2) inhibitors to treat type 2 diabetes (T2D) shortly after bariatric/metabolic surgery.

The DSS-II was a consensus development conference, culminating a yearlong effort to generate new guidelines for the use of "bariatric" operations to expressly treat T2D (i.e., "metabolic surgery"), including among patients not obese enough to qualify for surgery according to traditional BMI-based criteria. Among our 32 position statements, which all had a high consensus rate, one recommendation endorsed the usage of diabetes medications with low risk for hypoglycemia—including SGLT2 inhibitors—in early postmetabolic surgery patients because metabolic surgery itself powerfully lowers glucose levels. Aberle and Göke argue that SGLT2 inhibitors should not be used in this setting because both SGLT2 inhibitors and metabolic surgery increase the risk of ketoacidosis.

Indeed, SGLT2 inhibitors typically generate a state of mild, persistent hyperketonemia and can occasionally precipitate euglycemic diabetic ketoacidosis (DKA) (3–5). By reducing the renal threshold for glucose reabsorption and increasing urinary glucose excretion, SGLT2 inhibitors lessen the glucose pool, lowering insulin and raising glucagon levels. Such conditions decrease oxidative and nonoxidative glucose disposal, prompting a compensatory increase in lipid oxidation. This carbohydrate-to-lipid shift in substrate utilization generates ketones, which are byproducts of lipid catabolism.

Similarly, any state of energy deficit, including the acute perioperative caloric restriction that accompanies bariatric/metabolic surgery, can enhance lipolysis and generate hyperketonemia, dubbed "fasting ketosis." Aberle and Göke cite a report of 12 cases of DKA occurring shortly after bariatric/metabolic surgery, suggesting that this intervention can sometimes precipitate that adverse outcome (6). However, eight of those cases were in people with type 1 diabetes, most of whom received inadequate postoperative insulin, and four of them (0.2% incidence among all bariatric/metabolic operations surveyed) were in patients with T2D whose DKA was triggered by infection, inadequate insulin, and/or dehydration. All of these cases represented traditional hyperglycemic DKA (P.R. Schauer, personal communication) rather than the lower-than-expected glycemic DKA associated with SGLT2 inhibitor use, and none of the patients were taking SGLT2 inhibitors.

Nevertheless, in the spirit of caution, and according to our shared oath, primum non nocere, we agree with Aberle and Göke overall. There is precious little evidence to support the use of one versus another diabetes medication in postmetabolic surgery patients, and the DSS-II recommendations provide ample options lacking the theoretical concerns of SGLT2 inhibitors discussed here. So for now, we feel SGLT2 inhibitors may be less preferable than available alternatives in the immediate postoperative period. However, there is little reason to worry about enhanced DKA risk later after surgery, and the median onset among cases reported to date was 12 postoperative days, with a range of 0–61 days. Hence, at >2 months after surgery, it seems safe to consider SGLT2 inhibitors as options in postmetabolic surgery patients. Fortunately, this is usually not even an issue, as diabetes remits in a large majority of cases after surgery (1).

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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