Response to Letter to the Editor from Banerjee and Mondal: Management of Hyperglycemia in Hospitalized Adult Patients in Non-Critical Care Settings: An Endocrine Society Clinical Practice Guideline

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Dear Editor

We would like to thank Dr. Banerjee and Dr. Mondal for their interest in the recently published clinical guideline addressing management of hyperglycemia in non-critically ill-hospitalized adult patients (1,2). We welcome the opportunity to respond to the issues raised regarding inpatient use of non-insulin therapies, for which we agree that the lack of high certainty evidence keeps the debate open for use of these agents in the hospital setting.

The three classes of glucose lowering agents highlighted by Banerjee and Mondal are the glucagon like peptide 1 receptor agonists (GLP-1RA), metformin, and sodium glucose cotransporter 2 inhibitors (SGLT2i). There are currently two studies examining the use of GLP-1RA in hospitalized patients. Fayfman et al demonstrated improved glycemic measures in patients receiving exenatide combined with basal and correctional insulin but not when exenatide was used with correctional insulin alone (3). The two groups receiving exenatide experienced more nausea and vomiting prompting a higher dropout rate. Kaneko et al initiated therapy with liraglutide one week prior to scheduled surgical procedures that allowed titration of this medication in the outpatient setting prior to admission (4). Additionally, the primary outcome of this study was the difference in insulin use rather than glycemic measures, which the guideline development panel prioritized to determine benefit. There is a need for more studies investigating the initiation or continuation of longer acting GLP-1RA in hospitalized patients to determine their efficacy and safety.

Regarding metformin, we agree that the risk for metformin associated lactic acidosis is low. However, we were unable to identify any studies investigating the safety and efficacy of using metformin in hospitalized patients and agree that there is a need for studies using metformin in hospitalized patients (5).

The question raised regarding inpatient use of SGLT2i is an important one given the significant benefits observed when initiated during or following hospitalization for patients with and without type 2 diabetes admitted with acute heart failure (6). The purpose of this guideline was to address management of hyperglycemia in the hospital and not to address non-glycemic outcomes in specific
patient populations with diabetes and cardiovascular disease. Regarding pre-operative discontinuation of SGLT2i, current evidence suggests that discontinuation of these agents 3-4 days prior to even minor elective surgical procedures mitigates risk for euglycemic DKA, a condition that can go unrecognized in the absence of severe hyperglycemia with potential for adverse clinical outcomes (7).

In conclusion, we agree that there is a need for more studies investigating the safety, efficacy and potential beneficial effects of continuing or initiating non-insulin agents in hospitalized patients with type 2 diabetes. The recommendations made in the guideline were based on a comprehensive and robust assessment of benefits compared with harms following the GRADE process (8). The summary of findings table published with the guideline includes literature addressing other important concerns including cost-effectiveness (1). Overall, given the available published science, we found that, on balance, potential harms outweighed potential benefits of using these medications for glycemic control during hospitalization.
References


