



COMMENT

Is Incretin-Based Therapy Ready for the Care of Hospitalized Patients With Type 2 Diabetes?

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We read with interest the narratives by Schwartz and DeFronzo (1) and Umpierrez and Korytkowski (2) relating to the use of incretin-based therapy in the care of hospitalized patients with hyperglycemia. We have performed a number of mechanistic studies to evaluate incretin-based therapies in the critically ill that were not referenced (3–5). In these articles, exogenous glucagon-like peptide 1 (GLP-1) was shown to attenuate the glycemic response to enteral nutrient in mechanically ventilated critically ill patients both with and without preexisting type 2 diabetes, and was associated with stimulation of serum insulin and suppression of plasma glucagon (3,5). Enteral nutrition can be administered directly into the stomach or small intestine, and the route of feeding is a major determinant of glucose-lowering that occurs with GLP-1. We observed that GLP-1 slows gastric emptying when the emptying rate is relatively “normal,” but not when emptying is already abnormally slow, which is often the case in the critically ill (4).

It is recognized that the use of insulin has substantial limitations, particularly as excess dosing precipitates hypoglycemia and, despite sophisticated algorithms, glycemic variability remains a major problem (1,6). GLP-1 also has potential

advantages over insulin, including putative beneficial cardiac effects, and its use has the capacity to reduce nursing workloads (1,2). Neither narrative, however, discussed the concept that hyperglycemia is not the same insult in every patient, rather, that patients with critical illness–induced hyperglycemia should potentially be treated differently to those patients with preexisting hyperglycemia associated with diabetes, which is exacerbated by critical illness (6). Rapid glucose lowering with or without overt hypoglycemia may indeed be harmful in the latter group, and the capacity of GLP-1 to lower glycemia more gradually may lead to improved outcomes (6). Another potential advantage is that there is no impediment to intravenous administration of an agent in the critically ill. Nauck et al. (7) have recently summarized the evidence that intravenous administration of GLP-1 or its agonists may be more effective, with less adverse events, than subcutaneous administration. While the “normalization” of glycemia did not occur in all critically ill patients we studied, we have not observed hypoglycemia or vomiting following intravenous administration of GLP-1 in this group (3–5).

While we agree with Schwartz and DeFronzo (1) that the use of incretin-based therapies in hospitalized patients

is appealing, our experience would support the view of Umpierrez and Korytkowski (2) that insulin is a proven therapy, albeit one with major limitations, and should currently remain the treatment of choice. We suggest that additional data relating to 1) optimizing incretin-based regimens, such as whether the intact peptide, agonists, dipeptidyl peptidase-4 inhibitors, and/or glucose-dependent insulinotropic polypeptide should be used; 2) whether GLP-1 and its agonists are effective as monotherapy (which we would favor) and, if so, which patients respond or which are more appropriately treated using GLP-1 and its agonists in combination with insulin; and 3) cardiovascular safety should be sought promptly, as this information is important prior to widespread use of incretin-based regimens in hospitalized patients.

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