RESPONSE TO COMMENT

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

Stanley Schwartz[1] *and Ralph A. DeFronzo*[2]

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We thank Drs. Deane and Horowitz (1) for bringing this work to our attention. Their results provide further support for our contention that glucagon-like peptide 1 (GLP-1) therapy represents a safe and effective intervention to improve glycemic control in critically ill, hospitalized patients both with and without preexisting type 2 diabetes. In agreement with us (2), they recognize that "insulin has substantial limitations, particularly as excess dosing precipitates hypoglycemia" (1), and a number of recent trials have failed to demonstrate any benefit in morbidity or mortality in critically ill hospitalized patients who receive intensive insulin therapy (3–5).

We are unaware of published data demonstrating that the basic pathophysiologic disturbances responsible for hyperglycemia in nondiabetic "patients with critical illness–induced hyperglycemia" are different from those in "patients with preexisting hyperglycemia associated with diabetes" (1). In either case, we agree with Deane and Horowitz that a gentler reduction in glycemia with avoidance of hypoglycemia "may lead to improved outcomes." We also agree that "there is no impediment to intravenous administration of GLP-1," as reviewed by Nauck et al. (6). Further, as we pointed out (2), if GLP-1 therapy does not achieve the desired level of glycemic control, basal insulin therapy (both exenatide and liraglutide are approved with basal insulin) can be added without revising currently approved protocols for in-hospital insulin therapy.

With all of this agreement between ourselves and Deane and Horowitz and with the recognition by Deane and Horowitz that insulin has "major limitations," we are surprised that they conclude that insulin should "remain the treatment of choice" and then continue on to state that GLP-1 and its agonists are effective as monotherapy and that they favor this approach. We do disagree with Deane and Horowitz that "insulin is a proven therapy" in critically ill hospitalized patients. To the contrary, many recent studies have shown no proven benefit or even an increase in morbidity and mortality with intensive insulin therapy (3–5).

Last, as pointed out in the concluding statement of our narrative (2) and in agreement with Deane and Horowitz (1), additional well-designed, large-scale, prospective clinical trials comparing GLP-1 agonists versus insulin are warranted to delineate the advantages and disadvantages of each therapeutic approach.

Duality of Interest. S.S. has served on the advisory boards for Eli Lilly, Amylin, Santarus, Janssen, Merck, and Sanofi and on the speaker's bureau for Eli Lilly, Amylin, Santarus, Merck, Sanofi, Novo Nordisk, Boehringer Ingelheim, Bristol-Myers Squibb, and AstraZeneca. R.A.D. has served on the advisory boards for Takeda, Amylin, Bristol-Myers Squibb, Boehringer Ingelheim, Novo Nordisk, Janssen, and Lexicon and on the speaker's bureau for Novo Nordisk. R.A.D. has received grants from Takeda and Bristol-Myers Squibb. No other potential conflicts of interest relevant to this article were reported.

References

1. Deane AM, Horowitz M. Comment. Is incretin-based therapy ready for the care of hospitalized patients with type 2 diabetes? (Letter). Diabetes Care 2014;37:e40–e41. DOI: 10.2337/dc13-1616
2. Schwartz S, DeFronzo RA. Is incretin-based therapy ready for the care of hospitalized patients with type 2 diabetes? The time has come for GLP-1 receptor agonists! Diabetes Care 2013;36:2107–2111
3. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. N Engl J Med 2006;354:449–461
4. Brunkhorst FM, Engel C, Bloos F, et al.; German Competence Network Sepsis (SepNet). Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med 2008;358:125–139
5. Preiser JC, Devos P, Ruiz-Santana S, et al. A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study. Intensive Care Med 2009;35:1738–1748
6. Nauck MA, Baranov O, Ritzel RA, Meier JJ. Do current incretin mimetics exploit the full therapeutic potential inherent in GLP-1 receptor stimulation? Diabetologia 2013;56: 1878–1883

[1]*Main Line Health System, University of Pennsylvania, Philadelphia, PA*
[2]*Diabetes Division, University of Texas Health Science Center at San Antonio, San Antonio, TX*
Corresponding author: Ralph A. DeFronzo, albarado@uthscsa.edu.