There Are Great New Medications Out There—Why Aren't We Using Them?

Stephen Brunton, Editor-in-Chief

When I heard more than a decade ago that a new class of medication—glucagon-like peptide 1 (GLP-1) receptor agonists—would soon become available and that drugs in this new class cause impressive A1C reduction, result in negligible hypoglycemia, are easy to titrate, and—best of all—result in significant weight loss, I knew that they were going to be a winner with my primary care colleagues. Although GLP-1 receptor agonists are injectables, I was reassured that the needles would be a small gauge and easily tolerated. Many years ago, before the basal insulin revolution, it was unusual for primary care clinicians to initiate, let alone titrate, insulin. Now, most health care providers are familiar with basal insulin, and many are also comfortable with basal-bolus insulin regimens. I thus surmised that GLP-1 receptor agonists would be like training wheels for those not yet comfortable with insulin.

So, what happened?

Although these drugs were launched with much fanfare, there has been reticence about using them; today, less than half of primary care providers prescribe them. Is there confusion regarding the incretin system? Do some clinicians think dipeptidyl peptidase-4 inhibitors (another diabetes drug class) are basically oral GLP-1 receptor agonists? (They aren't.) Is the hesitation because GLP-1 receptor agonists need to be injected (despite the widespread use of injectable insulin)? Is it the side-effect profile? Is reimbursement an issue?

Considering the ease of use of GLP-1 receptor agonists, as well as their therapeutic benefits, positive cardiovascular outcomes data, synergistic action with insulin, and improving reimbursement and formulary coverage, this continuing lack of utilization is perplexing.

Sodium–glucose cotransporter 2 (SGLT2) inhibitors are an even more recent addition to the pharmaceutical armamentarium for diabetes. Although the oral agents in this class have been on the market for only a little more than 3 years, they have had greater uptake than GLP-1 receptor agonists, albeit still not as much as would be anticipated. A drug that causes glycosuria seems counterintuitive to our physiology education, which suggests that glucose in the urine is a reflection of uncontrolled diabetes rather than a mechanism to lower both glucose and calories. Perhaps the 1-800-BAD-DRUG advertisements have had a chilling effect on enthusiasm for these agents, but wouldn't the recently reported positive results of cardiovascular outcomes trials counter this concern?

I have always maintained that safety trumps efficacy, and the lack of utilization may be a manifestation of this truism. Perhaps many of us are waiting to see if there are any unidentified long-term adverse events.

In the meantime, therapy options continue to expand. Articles in this issue by Aroda et al. (p. 138), Wysham

Primary Care Metabolic Group, Los Angeles, CA

Corresponding author: Stephen Brunton, sbrunton@pceconsortium.com

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et al. (p. 149), and Skolnik et al. (p. 174) evaluate the efficacy and safety of two new options: fixed-ratio co-formulations of a GLP-1 receptor agonist and a basal insulin (insulin degludec/liraglutide and insulin glargine/lixisenatide) (1–3). These articles review data from randomized clinical trials of these combination injectable products, summarize the benefits of and limitations to their use, and discuss how they may help to address barriers to treatment intensification.

As I have said previously, this is an exciting time to manage diabetes. With ~40 medications now at our disposal, we have many alternatives to tailor therapy to our patients' specific needs and preferences. That said, early in my career, I received some worthy advice: "Never be the first nor the last to use a new medication."

Duality of Interest

The author serves on advisory boards and/or as a speakers bureau member for Abbott Diabetes, AstraZeneca, Becton Dickinson, Boehringer Ingelheim, Janssen, Eli Lilly and Company, Novo Nordisk, and Sanofi. No other potential conflicts of interest relevant to this article were reported.

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