Editor’s Message
Optimizing Treatment for Patients With Diabetes Mellitus: Glycemic and Nonglycemic Effects
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Despite an array of medications available in the United States to treat patients with type 2 diabetes mellitus (T2DM), physicians still have not achieved optimal control of this disease. In the present supplement to JAOA—The Journal of the American Osteopathic Association, we look at 3 contributing factors to this phenomenon. Mark D. Baldwin, DO, addresses the topic of cardiovascular risk associated with diabetes mellitus. Steven H. Barag, DO, discusses the advantages of using insulin early in the treatment of patients with T2DM. Finally, Alan J. Garber, MD, PhD, explores incretin-based agents, including their unique nonglycemic benefits.

Dr Baldwin provides evidence to support the claim that diabetes mellitus is a cardiovascular risk equivalent. Furthermore, he reviews the outcomes of the major intensive glucose-lowering trials that evaluated cardiovascular outcomes—the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial,1 the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial,2 and the Veterans Affairs Diabetes Trial (VADT).3 Dr Baldwin then balances these findings with the long-term outcomes from the epidemiologic follow-ups of the United Kingdom Prospective Diabetes Study (UKPDS)4 and the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study.5 He reviews glucose-lowering effects, nonglycemic benefits, and risks of available agents and discusses how these agents contribute to cardiovascular risk modification.

Dr Barag covers various aspects of the early introduction of insulin in T2DM management. He offers compelling evidence of the benefit of this approach. He also explores patient and physician barriers to insulin use, noting how a proactive physician can overcome these barriers. Finally, Dr Barag provides physicians with a number of treatment algorithms6-8 to initiate and proactively titrate insulin doses with the goal of achieving glycemic control quickly and safely.

Dr Garber reviews the pathophysiologic mechanisms of the incretin system in the development of T2DM. He further examines how to achieve glucose control while maintaining or even advancing other metabolic benefits. He provides an overview of glucagon-like peptide-1, or GLP-1, receptor agonists, including their effects on glucose levels, weight, and blood pressure. Dr Garber also reviews data on dipeptidyl peptidase-4, or DPP-4, inhibitors, an oral class of agents that

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have effects on the incretin system. Incretin-based agents offer a novel pathophysiologic mechanism with which to address T2DM, and their nonglycemic benefits (eg, increasing β-cell proliferation and decreasing β-cell apoptosis, increasing central nervous system-mediated satiety, exerting neuroprotective effects) also appear to be clinically useful.

Only approximately half of individuals with T2DM meet national glucose control standards. More importantly, the majority of people with T2DM are likely to die from cardiovascular disease as a complication of T2DM. We know that many traditional medications (metformin being an exception) have limited benefits for cardiovascular disease prevention. Therefore, to be successful, physicians may need to become less “glycemic-centric.” With the various options of glucose-controlling agents available, physicians can consider the nonglycemic effects of these medications in an effort to truly individualize treatment plans.

Evidence is building to support the idea that early aggressive intervention is most important in the treatment of patients with T2DM. In light of the progressive nature of T2DM, it is crucial to achieve and maintain glucose control early—rather than trying to chase this disease after the patient becomes glucotoxic and lipotoxic. After reading this JAOA supplement, physicians will gain new information to help them select agents to manage diabetes mellitus early and aggressively, resulting in not only successful glucose control but also the prevention of cardiovascular morbidity and mortality.

References