

Managing Type 2 Diabetes: Balancing HbA1c and Body Weight

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Abstract: Most patients with type 2 diabetes present with comorbid overweight or obesity. Reaching and maintaining acceptable glycemic control is more difficult in overweight and obese patients, and these conditions are associated with increased risk for cardiovascular and other diseases. Glycemic management for these patients is complicated by the fact that insulin and many of the oral medications available to treat type 2 diabetes produce additional weight gain.

However, an increasing number of therapeutic options are available that are weight neutral or lead to weight loss in addition to their glycemic benefits. This article evaluates the evidence from clinical trials regarding the relative glycemic benefits, measured in terms of glycated hemoglobin change, versus the impact on body weight of each medication currently approved for type 2 diabetes. In general, the sulfonylureas, thiazolidinediones, and D-phenylalanine derivatives have been shown to promote weight gain. The dipeptidyl peptidase-4 inhibitors are weight neutral, while the biguanides, incretin mimetics, and amylin mimetics promote weight loss. Trials examining the glycemic benefits of the weight loss agents orlistat and sibutramine are also examined. Awareness of this evidence base can be used to inform medication selection in support of weight management goals for patients with type 2 diabetes.

Summary: The management of type 2 diabetes should not only facilitate glycemic control resulting in improved HbA1c, but should also take into consideration the effects of medication on weight. The classes of diabetes drugs discussed previously achieve HbA1c reduction by different mechanisms of action and have a variety of effects on body weight. The SUs, TZDs, D-phenylalanines, and meglitinides have variable effects on weight gain, while biguanides, α -glucosidase inhibitors, incretin mimetics, DPP-4 inhibitors, and amylin mimetics tend to be weight neutral or induce weight loss. The weight loss medications orlistat and sibutramine are also associated with reduction of HbA1c.

The management of type 2 diabetes requires a multidisciplinary approach that targets the treatment of not only blood glucose levels, but also associated cardiovascular risk factors, including dyslipidemia, blood pressure, inflammation, and hypercoagulability. Weight reduction has been shown to improve glycemic control and reduce cardiovascular risk factors independent of drug effect, whereas weight gain can exacerbate insulin resistance and worsen glycemic control. Weight gain can also worsen hypertension and increase cardiovascular risk factors. Unfortunately, many antihyperglycemic agents and insulin promote weight gain, and this information should be factored into the risk/benefit analysis in selecting medications. Before 1995, the only available drugs for diabetes management in the United States were insulin and SUs. However, over the past decade we have seen an increased selection of available antidiabetic agents that improve glycemic control and are also weight neutral or even promote weight loss. Future studies are needed to define whether additional metabolic and cardiovascular benefits are derived from agents with these properties.

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