Case Study Responses

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Note: Readers are encouraged to visit www.InsulinJournal.com to review the details of a Case Study published in the April 2008 issue of *Insulin*.

This was the case of a 58-year-old, obese man with type 2 diabetes mellitus (DM), uncontrolled cardiovascular risk factors, and recently diagnosed, nonobstructive coronary disease. The patient's internist prescribed metformin 850 mg twice daily for his diabetes and referred him for a pharmacologic stress test. Results of a myocardial perfusion test were equivocal, with mild ischemia in the inferior wall. A subsequent coronary angiogram revealed mild, diffuse disease. The interventionist started the patient on aspirin 81 mg and ramipril 5 mg and referred him for aggressive risk-factor management.

Question 1. What is the first step that you would recommend to improve this patient's cardiometabolic risk profile?
Answer: a. Initiate therapeutic lifestyle modifications for weight loss, including diet, exercise, and smoking cessation.

The first step for our patient, who is obese and a smoker, is clearly to initiate a program of therapeutic lifestyle modifications targeting weight loss and smoking cessation. The possible benefits of diet and exercise for patients with type 2 DM are substantial. Several long-term studies have demonstrated consistent beneficial effects of regular exercise training on carbohydrate metabolism and insulin sensitivity, which can be maintained for at least 5 years. Improvements in glycosylated hemoglobin (A1C) levels are generally 10% to 20% of baseline. The multiple benefits of smoking cessation on cardiovascular and overall health are well known. In the Steno-2 study,[1] such aggressive lifestyle modifications, along with appropriately aggressive medical therapy, decreased cardiovascular events by almost 50%.

Rimonabant, a selective cannabinoid (CB1) receptor antagonist, has been shown to produce favorable metabolic effects directly and by inducing weight loss.[2] Rimonabant is approved in Europe for use in conjunction with diet and exercise. In the United States, however, a committee advising the US Food and Drug Administration has voted not to recommend approval of the drug primarily because of concerns regarding increased incidences of suicide, seizures, and depression. Gastric bypass procedures induce weight loss of 65% to 80% of excess body weight, correcting hyperlipidemia and hypertension in >70% of patients and reversing diabetes in up to 90% of patients.[3] For obvious reasons, this cannot be the first step for the patient in this case study. Initiation of statin therapy is indicated for this patient, although not necessarily as the first step.

Question 2. With sustained weight loss, you would expect the following in this patient:
Answer: d. All of the above (better glycemic control, better blood pressure control, and improvement in lipid profile).

Weight loss is an important goal for patients with type 2 DM (especially if they are overweight or obese) because of its beneficial effects on glycemic control. Moderate weight loss (5% reduction in body weight) can improve insulin action, decrease fasting blood glucose levels, and reduce the need for diabetes medications. A linear relation exists between the amount of weight lost and the extent of improvement in fasting blood glucose levels. Weight loss also improves other risk factors for cardiovascular disease by reducing blood pressure, improving serum lipid concentrations (decreases in serum triglycerides [TG], total cholesterol [TC], and low-density lipoprotein [LDL] cholesterol and an increase in serum high-density lipoprotein [HDL] cholesterol concentrations), and reducing serum markers of inflammation.[4]

Question 3. Weight loss would have the following effect on the patient's lipid profile:
Answer: c. Increased HDL, decreased LDL, decreased very low-density lipoprotein (VLDL), decreased TG.

In a meta-analysis of 70 studies,[5] it was shown that for every kilogram (2.2 lb) decrease in body weight there were significant ($P \leq 0.05$) decreases in TC, LDL, and TG and a significant ($P < 0.01$) increase in HDL.

Question 4. What other evidence-based therapies would be beneficial in improving this patient's cardiometabolic risk profile?

A large body of literature exists regarding use of medications to reduce blood pressure to 130/80 mm Hg. For this patient with an elevated blood pressure of 150/88 mm Hg, ramipril should be titrated upward to the 10-mg dose that was shown to be cardioprotective in the Heart Outcomes Prevention Evaluation (HOPE) study.[6] In view of the findings of the recent ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial (ONTARGET),[7] the angiotensin-receptor blocker telmisartan might also be an option. Results of the recent Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial[8] have shown the importance of aggressive lowering of blood pressure using perindopril (an angiotensin-converting enzyme inhibitor) and indapamide (a diuretic) in patients with type 2 DM. Statin therapy should be initiated for this patient to address his dyslipidemia. After a few months of statin therapy, the patient's lipid levels should be reevaluated and use of a fibrate drug should be considered if the hypertriglyceridemia and low HDL levels persist.

Although the effect of aggressive glycemic control (A1C <7.0%) on macrovascular events remains unclear, lowering the patient's A1C to a moderate level (7.0%) would clearly be evidence based for reduction of macrovascular and microvascular events. Use of sulfonylureas, gliptins, exenatide, or insulin should be considered.

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