Is Weight Loss a Cure for Type 2 Diabetes?

It has been estimated that ~10% of the U.S. population will be diagnosed with type 2 diabetes by the year 2010. Cardiovascular disease accounts for 75% of all related deaths in diabetic patients. While the use of HMG CoA reductase inhibitors has contributed to a marked reduction in mortality in cardiovascular deaths, the benefit in type 2 diabetes has been disappointing. Patients with type 2 diabetes have a sixfold increased risk of a first-time myocardial infarction compared with nondiabetic patients (1). Additionally, diabetic patients have twice the risk of myocardial infarction. As cardiovascular mortality is the leading single cause of death in the U.S. and because patients with type 2 diabetes have a three- to eightfold increased risk of death, new treatment strategies need to be considered for this disease and its prevention (1).

Dixon and O'Brien (2) describe the effects of laparoscopic adjustable gastric band surgery on the development of type 2 diabetes. All patients had severe obesity (BMI ≥35.0 kg/m^2). One year after surgery, 64% patients had remission of diabetes. The prevalence of diabetes decreased from 10 to 5.6%. An additional 26% of patients with diabetes had an improvement in their control of diabetes. Gastric band surgery resulted in an average weight loss of 27 kg. HbA_{1c} was reduced from 7.8 to 6.2%. The 1.6% fall in HbA_{1c} was also associated with a 58-mg/dl decrease in fasting blood glucose concentration. Sjostrom et al.(3) demonstrated that over an 8-year period, the prevalence of type 2 diabetes increased from 8 to 25% in patients with severe obesity. However, unlike the short-term benefits described in the Dixon and O'Brien study, the prevalence of diabetes was 11% at baseline and 11% at 8 years after a 40-lb sustained weight loss. This would suggest that weight loss alone is not a cure for type 2 diabetes. However, a larger amount of weight loss (100 lbs) reduces the prevalence of type 2 diabetes from 27 to 9% after 6 years of follow-up (4). Clearly, more clinical research is needed to determine which diabetic patients will undergo remission with weight loss. For example, are those patients who fail to undergo remission antibody-positive patients or patients with maturity-onset diabetes of the young?

Probably more important than the treatment of type 2 diabetes, weight loss reduced the incidence of a new diagnosis of type 2 diabetes from 19% to only 3.6% at 8 years (3). In patients with impaired glucose tolerance (IGT), the incidence of type 2 diabetes occurred in only 1% after 7.6 years (4). In the Dixon and O'Brien study, no one with impaired fasting glucose progressed to develop diabetes during follow-up (2). In addition, impaired fasting glucose resolved in 89% of patients at 1 year and 100% at 2 years.

In Dixon and O'Brien's study, weight loss improved insulin sensitivity and β-cell capacity (78 to 119%), as determined by the homeostasis model assessment method (HOMA). In type 2 diabetes, the β-cell loses ~4% of its capacity to secrete insulin per year (5). Improvement in β-cell capacity to secret insulin may delay the diagnosis of type 2 diabetes. Sulfonylureas have been shown to increase β-cell function, but the loss of the β-cell remains at 4% per year (6). If, as predicted by the HOMA, the β-cell capacity increases by 41%, then substantial weight loss should delay the onset of diabetes by ~10 years.

As with all surgical procedures, there are risks. In Dixon and O'Brien's report, three patients had early postoperative complications, and 30% required surgical revision due to gastric prolapse (20%), band erosion (6%), or tube leakage (4%). In comparison, the open gastric bypass surgery has a 1.5% mortality and an 8.5% complication rate (4).

In Dixon and O'Brien's report, weight loss was associated with an increase in serum HDL cholesterol (1.03 to 1.22 mmol/l or 39.8 to 47.2 mg/dl) and a reduction in serum triglyceride concentration (2.43 to 1.39 mmol/l or 215 to 123 mg/dl). As might be expected, there was no effect on LDL cholesterol (3.45 to 3.67 mmol/l or 133 to 142 mg/dl).

In addition to the improvement in the lipid profile, liver function tests improved. AST, ALT, and GGT all decreased by 40–50%. We know that 15% of patients with nonalcoholic hepatic steatosis (NASH) progress to cirrhosis of the liver. The normalization of the LFTs suggests that weight loss may prevent the progression from NASH to cirrhosis.

In a self-reported questionnaire, 15 of the 35 diabetic patients reported having sleep apnea. All 15 patients reported resolution of sleep apnea symptoms at 1 year after surgery.

These authors have studied a total of 500 patients, and the report in the journal documents the effect of weight loss in 50 patients with severe obesity and type 2 diabetes. In addition to these 50 patients with type 2 diabetes, the authors reported results for 67 patients with the diagnosis of impaired fasting glucose (110–125 mg/dl). Patients with impaired fasting glucose may progress to type 2 diabetes at a faster rate than IGT. Using IGT, only 24% of Pima Indians progress to type 2 diabetes at 5 years (7). However, using the newer impaired fasting glucose criteria, 37% progress to type 2 diabetes at 5 years, or 7.4% per year (7). As mentioned above, Dixon and O'Brien report that 91% of the patients with impaired fasting glucose had a normal fasting glucose when measured 1 year after surgery. Only 6 of 67 patients remained with an impaired fasting glucose at 1 year. Of those followed-up at 2 and 3 years, none of the patients had impaired fasting glucose. Also, none of the 67 patients went on to develop type 2 diabetes.

In the Nurses Health study, the risk for development of type 2 diabetes is increased 38-fold if one has morbid obesity (BMI ≥35 kg/m^2). Risk for type 2 diabetes is increased 20.1-fold in patients with obesity (BMI of 30.0–34.9 kg/m^2) (8). As little as a 4.2-kg loss in body weight sustained for a average of 3.2 years can re-

duce the progression to type 2 diabetes by ~50% (9). Over a 4-year period, only 11% of those with IGT progressed to type 2 diabetes compared with 23% in the control group (9). In Dixon and O'Brien's study, no one with impaired fasting glucose progressed to type 2 diabetes after laparoscopic surgery. In fact, 91% of those with impaired fasting glucose had normal fasting glucose at 1 year.

While gastric banding surgery may be hopeful for the severely obese, it must be tested prospectively in obese individuals before it can be recommended as a treatment for type 2 diabetes. More importantly, new strategies are needed to prevent the progression of impaired fasting glucose and impaired glucose tolerance to type 2 diabetes. Laparoscopic gastric band surgery maybe the first to offer promise.

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