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Very-low-energy diet for type 2 diabetes: An underutilized therapy?

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ABSTRACT

Background: Current approaches to the management of type 2 diabetes focus on the early initiation of novel pharmacologic therapies and bariatric surgery.
Objective: The purpose of this study was to revisit the use of intensive, outpatient, behavioral weight management programs for the management of type 2 diabetes.
Design: Prospective observational study of 66 patients with type 2 diabetes and BMI ≥32 kg/m^2 who enrolled in a program designed to produce 15% weight reduction over 12 weeks using total meal replacement and low- to moderate-intensity physical activity.
Results: Patients were 53 ± 7 years of age (mean ± SD) and 53% were men. After 12 weeks, BMI fell from 40.1 ± 6.6 to 35.1 ± 6.5 kg/m^2. HbA1c fell from 7.4% ± 1.3% to 6.5% ± 1.2% (57.4 ± 12.3 to 47.7 ± 12.9 mmol/mol) in patients with established diabetes: 76% of patients with established diabetes and 100% of patients with newly diagnosed diabetes achieved HbA1c <7.0% (53.0 mmol/mol). Improvement in HbA1c over 12 weeks was associated with higher baseline HbA1c and greater reduction in BMI.
Conclusions: An intensive, outpatient, behavioral weight management program significantly improved HbA1c in patients with type 2 diabetes over 12 weeks. The use of such programs should be encouraged among obese patients with type 2 diabetes.

1. Introduction

In response to the evidence that near-normal glycemia can reduce the long-term complications of type 2 diabetes and the approval of new classes of antihyperglycemic medications, consensus guidelines have been published for the management of type 2 diabetes. Although essentially all of them recognize the role of overnutrition, physical inactivity, and obesity in the pathogenesis of type 2 diabetes, few, if any, recommend lifestyle intervention as first line therapy for its management. Indeed, in 2008, the American Diabetes Association and the European Association for the Study of Diabetes concluded that because lifestyle interventions often fail to achieve or maintain glycemic goals either because of failure to lose weight, weight regain, progressive disease, or a combination of factors, metformin therapy should be initiated at the diagnosis of type 2 diabetes (Nathan et al., 2009). More recently, Roux-en-Y gastric bypass (RYGB), now termed "metabolic surgery", has been proposed as first line therapy for obese patients (body mass index (BMI) >30 kg/m^2) with type 2 diabetes (Cohen et al., 2012; Pories, Swanson, MacDonald, et al., 1995). Although a recent trial demonstrated that 12 months of medical therapy plus bariatric surgery achieved better glycemic outcomes than medical therapy alone in obese patients with uncontrolled type 2 diabetes (Schauer et al., 2012), another small, short-term, clinical trial suggested that a very-low-energy diet, similar to those consumed by patients following RYGB, can produce similar improvements in glycemia, beta-cell function, and insulin sensitivity as RYGB (Jackness et al., 2013).

The purpose of this study was to determine if 12 weeks of a very-low-energy diet combined with physical activity of low- to moderate-intensity was effective for the management of type 2 diabetes. Our hypothesis was that although traditional low intensity lifestyle interventions may fail to achieve glycemic goals, more intensive, outpatient,

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multidisciplinary, behavioral obesity management programs may be an appropriate first-line treatment for type 2 diabetes.

2. Methods

The University of Michigan Investigational Weight Management Program is a 2-year, outpatient, multidisciplinary, behavioral, obesity management program. The program is offered to obese members of a managed care health plan who are required to participate in one of three weight management programs in order to receive enhanced benefits (Rothberg, McEwen, Fraser, Burant, & Herman, 2013) and to patients referred by University of Michigan-affiliated health care providers. To be eligible, patients must have BMI >32 kg/m^2 with a diagnosis of type 2 diabetes or BMI >35 kg/m^2. The study was reviewed and approved by the University of Michigan Institutional Review Board and all patients provided written informed consent.

Patients are seen by an endocrinologist for an initial assessment, once in the first month, and quarterly thereafter. At the first visit, antihyperglycemic medication regimens are reviewed and modified. Sulfonylureas and thiazolidinediones are tapered and discontinued. When necessary, weight neutral or weight negative medications are substituted for weight potentiating medications. If patients are taking fewer than 15 units of insulin per day, insulin is discontinued. For patients taking ≥15 units of insulin per day, short-acting insulin analogues are discontinued and the dose of long-acting insulin analogues is reduced by 50%. GLP-1 agonists were substituted for insulin in 3 patients who discontinued insulin. Metformin is discontinued only if the HbA1c is ≤6.5% (47.5 mmol/mol) and the patient requests that metformin be discontinued.

Patients are seen by a dietitian weekly for the first month, every other week for the next 2 months, and monthly thereafter. The initial focus of the program is on 15% weight reduction over 12 weeks using intensive energy restriction. Most patients receive intensive caloric restriction (800 kcal/day) in the form of total meal replacement (HMR®, Boston, MA) employing chocolate or vanilla shakes or chicken soup (160–170 kcal/per packet). Additional calories are prescribed for those who weigh more than 160 kg (an additional 160–170 kcal/day for every 23 kg over 160 kg). Patients are asked to gradually increase their physical activity (low to moderate intensity) to 40 min per day (either in divided bouts or all at once) over the first 12 weeks. Patients are asked to keep diaries listing the number of shakes they consume, deviations from the prescribed diet, hunger/satiety, and physical activity. Diaries are reviewed weekly with the dietitian. After approximately 12 weeks, patients continue to receive intensive behavioral counseling, are transitioned to regular foodstuffs, and are asked to perform 40 to 90 min of moderate to vigorous physical activity per day for weight maintenance.

Glucose and HbA1c were measured by the Chemistry Laboratory of the Michigan Diabetes Research Center. Glucose assays were performed using a Cobas Mira Chemistry Analyzer (Roche Diagnostics Corporation, Indianapolis, IN). Intra-assay coefficients of variation are 2% at 84 and 283 mg/dl (4.7 and 15.7 mmol/l). Inter-assay coefficients of variation are 3.6% at 92 mg/dl (5.1 mmol/l) and 2.8% at 310 mg/dl (17.2 mmol/l). HbA1c was measured using a Tosoh G7 HPLC Analyzer (Tosoh Biosciences Inc, South San Francisco, CA). The method uses a non-porous ion exchange column and a high performance liquid chromatography system. At an HbA1c of 5.8% (39.9 mmol/mol), the day-to-day coefficient of variation of the assay is 1.7% and at an HbA1c of 9.7% (82.5 mmol/mol), it is 1.6%.

The demographic and clinical characteristics of the study population were described using means ± standard deviation (SD) or number (%). The demographic and clinical characteristics of patients included in the study vs. those excluded from the study and those with established diabetes vs. those with newly diagnosed diabetes were compared using t-tests or chi-square tests. BMI, weight, and measures of glycemia at baseline and follow-up were described using means ± standard deviation or number (%) and then compared using paired t-tests. To examine the demographic and clinical factors associated with a change in HbA1c between baseline and follow-up, we used analysis of variance. We used stepwise regression with a p-value to enter the model set at 0.15 and a p-value to stay in the model set at 0.05 to further examine factors associated with change in HbA1c. All analyses were performed using SAS 9.3 (SAS Institute, Cary, NC).

3. Results

Between 2010 and 2013, 367 patients enrolled in the Investigational Weight Management Program and completed at least 12 weeks of follow-up. Of these, 93 (25%) were diagnosed with type 2 diabetes. Sixty-six (71%) had baseline HbA1c or blood glucose levels and HbA1c levels measured 3 to 6 months after baseline and are the focus of this study. Twenty-seven (29%) were missing baseline or follow-up measures of glycemia and were excluded from the study. Those excluded did not differ from those included with respect to age, sex, race/ethnicity, baseline or follow-up BMI. They did, however, have slightly shorter durations of diabetes (3.4 ± 5.0 years) compared to those included in the study (6.2 ± 6.1 years) ($p = 0.03$).

Of the 66 patients included in this study, 58 had established diabetes and had baseline and follow-up measures of HbA1c. Eight were newly diagnosed with diabetes based on standard 75 g oral glucose tolerance tests. They did not have baseline measurements of HbA1c but had follow-up measures of HbA1c. Table 1 shows the characteristics of the study population including the total population ($n = 66$), those with established diabetes ($n = 58$), and those with

Table 1
Characteristics of the study population.

	People with baseline HbA1c or OGTT and follow-up HbA1c (n = 66)	Established diabetes (n = 58)	Newly diagnosed diabetes (n = 8)	p-value (established vs. newly diagnosed diabetes)
Age (years)	53 ± 7	53 ± 7	53 ± 8	0.8268
Sex				0.4591
Male	35 (53%)	32 (55%)	3 (38%)	
Female	31 (47%)	26 (45%)	5 (63%)	
Race/ethnicity				1.00
Non-Hispanic White	60 (91%)	52 (90%)	8 (100%)	
Other (Hispanic, Black, or Asian)	6 (9%)	6 (10%)	0	
Education (missing 4)				0.7952
<College degree	20 (31%)	17 (29%)	3 (38%)	
College degree	21 (32%)	18 (32%)	3 (38%)	
Professional or graduate degree	24 (37%)	22 (39%)	2 (25%)	
Smoking				1.00
Current smoker	2 (3%)	2 (3%)	0	
Never smoker/ex-smoker	90 (97%)	56 (97%)	8 (100%)	
Duration of diabetes (years) (missing 4)	6.2 ± 6.1	7.1 ± 6.0	0.2 ± 0.2	0.0020