Reduction in Glycemic Variability and Hyperglycemia with a Low-Glycemic Index Portion-Controlled Diet in Persons with Type 2 Diabetes

Anthony N. Fabricatore
Nutrisystem, Inc., Fort Washington, PA
Louise A. Hesson **Thomas A. Wadden**
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, PA

Background

- Two previous trials found statistically and clinically significant reductions in HbA1c among overweight and obese subjects with type 2 diabetes who were treated with a commercially-available portion-controlled low-glycemic index diet (i.e., Nutrisystem D) in conjunction with lifestyle counseling sessions.[1-2]
- Although HbA1c is the primary predictor of complications in persons with diabetes, it is limited by its inability to measure glycemic variability, an independent risk factor for diabetes-related complications.[3]
- Indicators of glycemic variability – but not HbA1c and fasting glucose – are strongly associated with oxidative stress, which is thought to be a mechanism by which diabetes increases the risk of micro- and macrovascular diseases.[4-5]
- While several sophisticated glycemic variability metrics have been developed, they are highly correlated with simple measures of variability and stability, such as the standard deviation of blood glucose values and the percentage of time in the euglycemic range.[6]

Objective
This study employed continuous glucose monitoring (CGM) to assess multiple measures of glycemic variability and stability in a sample of overweight and obese adults during consumption of a low-glycemic index portion-controlled diet, compared to usual diet, in a randomized cross-over trial.

Method

Participants
Overweight and obese individuals (BMI ≥ 27 kg/m^2), aged 18-65 years, with type 2 diabetes were eligible to participate. Exclusion criteria included use of insulin or warfarin, weight change ≥ 5% in the previous 3 months, binge eating disorder, pregnancy or lactation, allergies to soy or peanuts, and regular use of acetaminophen (due to interference with the glucose monitoring device).

Twelve participants were randomized to receive first either the portion-controlled diet or their usual diet. Two participants who were assigned to receive the portion-controlled diet first refused to return to their usual diet during the second test diet period and were excluded from analyses. Characteristics of the final sample of 10 participants (6 women, 4 men) are shown in ***Table 1***.

Method, continued

Table 1. Participant Characteristics.

	Mean (SD)
Age (y)	55.4 (11.6)
Diabetes duration (y)	4.9 (5.9)
Diabetes medications (number)	1.3 (1.0)
HbA1c (%)	6.8 (0.9)
Glucose (mg/dl)	122.7 (33.3)
Insulin (μIU/ml)	9.8 (8.7)
HOMA2-IR (score)	1.4 (1.1)
Weight (kg)	108.0 (16.1)
Body Mass Index (kg/m^2)	37.8 (2.9)
Waist (cm)	118.3 (12.0)
Systolic Blood Pressure (mmHg)	134.1 (12.8)
Diastolic Blood Pressure (mmHg)	72.5 (7.6)
Total Cholesterol (mg/dl)	194.6 (32.9)
HDL Cholesterol (mg/dl)	55.1 (13.1)
LDL Cholesterol (mg/dl)	116.1 (30.7)
Triglycerides (mg/dl)	116.7 (46.4)

Test Diets
Usual Diet (UD). Participants were told to "Eat how you would normally eat if you were not in this study." Participants received no specific instructions on foods to consume or avoid, or what quantities to consume during this period.

Portion-Controlled Diet (PCD). Participants consumed portion-controlled products from the Nutrisystem D program (Nutrisystem, Fort Washington, PA) for three entrees and one to two snacks per day. Nutrisystem D items were supplemented with grocery foods (e.g., fruits, vegetables, low-fat dairy items) according to a structured meal plan to provide approximately 1300 (women) to 1500 (men) kcal/d, with approximately 53% coming from carbohydrate, 22% from fat, and 25% from protein. The estimated glycemic index of the program is 34, which falls in the low range.

Procedure
At the start of each test diet period, participants visited the clinic to be fitted with a CGM device (SEVEN PLUS, Dexcom, San Diego, CA). This entailed insertion of a sensor, subcutaneously, into the abdomen by the study nurse practitioner. The device samples the interstitial fluid at 10-second intervals and stores an average estimate of blood glucose values every 5 minutes. Sensors can remain in place for up to 7 days.

Method, continued

The device's display was disabled so that participants did not see CGM output. However, participants were instructed to calibrate the device twice daily against a traditional glucometer (One Touch Ultra 2, LifeScan, Milpitas, CA). At the mid-point of each 14-day test diet period, participants returned to the clinic to have the CGM sensor replaced.

Participants also were instructed to keep a detailed record of food and beverage intake for three days – two consecutive weekdays and one weekend day – during each test diet period. Intake records were analyzed using Food Processor software, version 10.6.0.

Outcomes
CGM data were exported to a spreadsheet, and the following values were calculated for each day, then averaged over the 14 days of each test diet period:

1. Mean of glucose values
2. Standard deviation of glucose values
3. Interquartile range of glucose values
4. Percentage of glucose values in the hyperglycemic range, defined as > 180 mg/dl.
5. Percentage of glucose values in the euglycemic range, defined as 71-180 mg/dl.
6. Percentage of glucose value in the hypoglycemic range, defined as ≤ 70 mg/dl.

Analyses
CGM outcomes and dietary intake data during the PCD and UD periods were compared using paired t-tests. Alpha was set at 0.05 for each test.

Results

Dietary Intake
Participants' intake differed during the two diet periods as shown in ***Table 2***. Specifically, participants consumed less total energy, a smaller percentage of energy from total and saturated fat, a greater percentage of energy from protein, and more grams of fiber during the PCD period compared to UD. Energy from carbohydrate and grams of sugar did not differ significantly between diets.

Results, continued

Table 2. Dietary intake by test period

	PCD	UD	P
Energy (kcal)	1217.2 (234.9)	1673.9 (541.2)	.015
From carbohydrate (%)	54.2 (7.7)	50.8 (4.2)	.178
From fat (%)	25.9 (7.2)	32.6 (4.6)	.008
From saturated fat (%)	8.4 (2.7)	10.4 (2.8)	.001
From protein (%)	22.0 (3.1)	18.1 (2.9)	.016
Fiber (g)	25.5 (5.9)	18.6 (10.3)	.046
Sugar (g)	66.0 (16.8)	75.5 (37.0)	.479

Glycemic Outcomes
A similar number of glucose values were recorded during the PCD and UD periods (3078.1 ± 486.7 vs. 3266 ± 376.5, p = 0.21). As shown in ***Figure 1***, below, participants' mean, standard deviation, and interquartile range of blood glucose values were significantly lower during the PCD period, as compared with the UD period.

Figure 1. Mean, standard deviation, and interquartile range of glucose during UD and PCD periods.

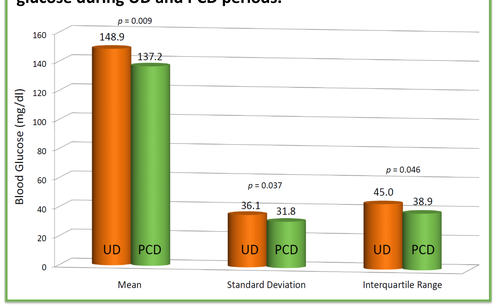
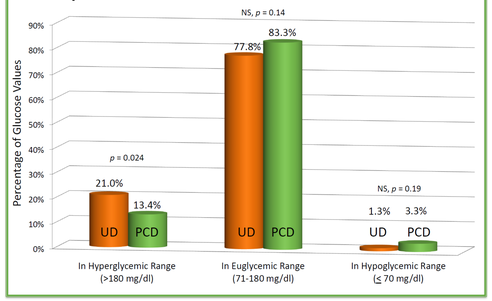


Figure 2 shows the percentage of glucose values that fell in the hyperglycemic (>180 mg/dl), euglycemic (71 – 180 mg/dl) and hypoglycemic (≤ 70 mg/dl) ranges. Participants experienced significantly less hyperglycemia during the PCD than UD (p = 0.024). Differences in hypoglycemia and euglycemia were not significant between the two diet periods.

Results, continued

Figure 2. Percentage of glucose values in three ranges during consumption of UD and PCD.



Discussion

- Glycemic variability – as measured by the standard deviation and interquartile range of CGM values – was significantly reduced during consumption of the PCD, compared with UD.
- Mean blood glucose and the percentage of readings in the hyperglycemic (> 180 mg/dl) range also were significantly lower when participants consumed the PCD.
- These effects were demonstrated at 2 weeks, suggesting the reductions in glycemic variability, mean glucose, and hyperglycemia can be achieved before significant weight loss. Additionally, they demonstrate that additional improvements can be achieved in persons with generally good glycemic control at baseline (HbA1c = 6.8%).
- A limitation of the study is the lack of nutritional equivalence of the two diet periods. The PCD provided significantly fewer calories, more protein and fiber, and less fat than participants' usual diets. Thus, the mechanisms of the effects cannot be identified.
- Strengths of the study include the large volume of glucose data obtained during each of the test diet periods and the use of a cross-over design to limit inter-individual variability.
- These findings, combined with previous research, demonstrate that the tested PCD is associated with reductions in HbA1c as well as glycemic variability, which are independent risk factors for diabetes-related complications.

References
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Correspondence to: Dr. Fabricatore, afabricatore@nutrisystem.com
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