Diabetes Care Publish Ahead of Print, published online June 18, 2009

Effects of a Higher-Carbohydrate/Lower-Fat Diet Versus a Lower-Carbohydrate/Higher-Fat-Monounsaturated Diet on Postmeal Triglyceride Concentrations and other Cardiovascular Risk Factors in Type 1 Diabetes

Irene Strychar, EdD, RD[1,2,3,4] ; Jeffrey S. Cohn, PhD[5] ; Geneviève Renier, MD, PhD[1,2,3,4] ; Michèle Rivard, PhD[6] ; Nahla Aris-Jilwan, MD[3] ; Hugues Beauregard, MD[3] ; Sara Meltzer, MD[7] ; André Belanger, MD[8] ; Richard Dumas, MD[8] ; Alain Ishac, MSc[1] ; Farouk Radwan, MD[9] ; Jean-François Yale, MD[7] .

[1]Research Center of the University of Montreal Hospital Center (CRCHUM), [2]Montreal Diabetes Research Center of the CRCHUM, [3]Service of Endocrinology, Notre-Dame Hospital of the CHUM, [4]Department of Nutrition, Faculty of Medicine, University of Montreal, Montreal, [5]Heart Research Institute, Sydney, Australia, [6]Department of Social and Preventive Medicine, University of Montreal, [7]Nutrition and Food Science Centre, Royal Victoria Hospital, McGill University Health Centre (MUHC), Montreal, [8]Laval Clinic Research Center, [9]Department of Biochemistry, Notre-Dame Hospital of the CHUM, Montreal.

Corresponding Author:
Professor Irene Strychar
E-mail : irene.strychar@umontreal.ca

Submitted 29 December 2008 and accepted 4 June 2009

Additional information for this article can be found in an online appendix at http://care.diabetesjournals.org

Objective **-** To compare the effects of two eucaloric diets, a higher-carbohydrate/lower-fat versus a lower-carbohydrate/higher-fat-monounsaturated, on postmeal triglyceride (TG) concentrations and other CVD risk factors in non-obese subjects with type 1 diabetes in good glycemic control.

Methods **-** In a parallel group design study, 30 subjects were randomly assigned and completed one of the two eucaloric diets. Assessments included: BMI, blood pressure, A1C, plasma lipids, and markers of oxidation, thrombosis, and inflammation. At 6 months, subjects were hospitalized to measure plasma TG excursions for 24-hours.

Results **-** There were no significant differences between groups other than decreased PAI-1 levels and increased weight in the lower-carbohydrate/higher-fat-monounsaturated diet group. During the 24-hour testing, the lower-carbohydrate/higher-fat-monounsaturated group had a lower plasma TG profile.

Conclusion **-** A lower-carbohydrate/higher-fat-monounsaturated diet in type 1 diabetes could offer an appropriate choice for non-obese subjects in good metabolic and weight control.

The optimal macronutrient composition of the diet in diabetes has not yet been established. Dietary recommendations for carbohydrates range from 45-60% of energy intake, and 25-35% for fat (1-2); amount of carbohydrates is usually inversely associated with amount of fat. On the one hand, higher amounts of carbohydrates are directly associated with increases in plasma triglyceride levels and postprandial glycemic levels (3), risk factors in the development of micro- and macrovascular complications in diabetes (4-5). On the other hand, higher fat diets have the potential to increase fasting and postprandial triglyceride levels, independent risk factors for macroangiopathy (5). Thus, nutrition therapy needs to address the effects of diet on both fasting and postprandial triglyceride and glycemic levels.

In type 2 diabetes, replacing carbohydrates with monounsaturated fats in eucaloric diets was associated with lower triglyceride (TG) levels and improved glycemic control (6-7), however results are contradictory in type 1 diabetes (8-9). Therefore, our objective was to compare the effects of two eucaloric diets, a higher-carbohydrate/lower-fat diet versus a lower-carbohydrate/higher-fat-monounsaturated diet, on 24-hour TG and glycemic excursions and other cardiovascular risk factors in type 1 diabetes. We expected that: the lower carbohydrate content of the higher monounsaturated fat diet would reduce VLDL-TG production, resulting in lower fasting TG levels and 24-hour TG-AUC, in line with type 2 studies (6-7); and, the higher monounsaturated fat intake would positively affect LDL-oxidation, adhesion molecules, and markers of thrombosis and inflammation (10-12).

RESEARCH DESIGN AND METHODS

Adults with type 1 diabetes on intensive insulin therapy were recruited. Exclusion criteria: BMI ≥30 kg/m^2, A1C >8.4%, and major diabetes-complications. The project received ethics approval (2003-2007).

In this parallel group design 6-month study, subjects were randomly assigned to follow a higher-carbohydrate/lower-fat or a lower-carbohydrate/higher-fat-monounsaturated eucaloric diet: 54-57% and 43-46% carbohydrates, 27-30% and 37-40% total fat (10% and 20% monounsaturated), respectively. Saturated fat (<10%) and fiber (25 g/day) contents were similar. The lower-carbohydrate/higher-fat diet had fewer starch and more fat choices, in the form of olive oil.

Dietary intake was monitored weekly by the dietitian (24-hour telephone food recall) as well as pre-meal glycemia, dietary carbohydrate meal content, and insulin doses administered. Subjects also recorded daily glycemic levels, insulin doses, grams of mealtime carbohydrates, and hypoglycemic events.

Baseline and 6-month measurements included: BMI, blood pressure, A1C, plasma lipids, adhesion molecules, and markers of oxidation, thrombosis, and inflammation. At 6-months, subjects were hospitalized for 24-hours to monitor TG and glycemic excursions. Meals were standardized according to diet assignment: breakfast and lunch were similar for the 2 groups; differences in carbohydrate/fat contents were achieved at the supper meal. Usual prescribed insulin doses were given and took into account pre-meal glycemia and carbohydrate meal content.

Mann-Whitney tests were used to compare values between the 2 diets and Wilcoxon signed rank tests used to compare values within each diet group, since many variables did not meet the normality assumption of the t-test. Significance was set as $P \leq 0.05$.

RESULTS

Thirty individuals completed the study: mean age (37.9±8.1 years), years since diagnosis (16.5±10.6), BMI (24.3±2.6 kg/m^2), A1C (7.2±0.7%), dietary carbohydrates (45.5±10.7%), total fat (36.9±10.5%), monounsaturated fat (15.5±5.7%), saturated fat (11.7±4.3%); baseline characteristics were similar in the two groups. Our subjects' carbohydrate intake was similar to that of subjects in the DCCT (intensive-treated group) (13). During the 6-month trial, subjects followed their diet prescriptions (based on 24-hour recalls) and appropriately assessed carbohydrate intake at meals (±10%), for insulin dose adjustments. There were no differences between groups for insulin doses, glycemic levels, and hypo/hyperglycemic episodes.

Clinical and biochemical results (Table 1) indicate no significant differences between the two groups at baseline and at 6-months, except for absolute change scores where subjects on the lower-carbohydrate/higher-fat-monounsaturated diet had a 2% increase in weight and a 16% decrease in PAI-1 levels.

During the 24-hour testing, TG profiles tended to be lower in the lower-carbohydrate/higher-fat-monounsaturated group (see Supplemental Figure 1A-1B in the online appendix available at http://care.diabetesjournals.org) while glycemic levels after supper were higher in the higher-carbohydrate/lower-fat group. Since weight change affects TG levels, analyses were repeated with subjects maintaining stable weight (±2kg) throughout the study (see Supplemental Figure 2A-2B). Many significantly lower TG levels were observed in the lower-carbohydrate/higher-fat-monounsaturated group, resulting in a smaller TG-AUC (P=0.05).

DISCUSSION

In a sample of non-obese adults with well controlled, uncomplicated type 1 diabetes on intensive insulin therapy, the lower-carbohydrate/higher-fat-monounsaturated diet was found to have a positive effect on thrombotic factor PAI-1, and no adverse effects on lipid control. A small increase in BMI in the lower-carbohydrate/higher-fat-monounsaturated group may be due a lower meal-induced thermogenesis because of its higher fat content (14); longer term studies are needed.

In the higher-carbohydrate/lower-fat group, where individuals had increased carbohydrate intake by approximately 20%, the higher fasting TG levels are in keeping with an associated increase of VLDL-TG production, as shown in type 2 diabetes studies (6-7). In the lower-carbohydrate/higher-fat-monounsaturated group, fasting TG levels remained steady, despite a small weight gain. Insulin doses were unlikely to have determined fasting TG levels, since doses administered were comparable in the two groups and appropriately adjusted to carbohydrate intake to maintain A1C levels close to the recommended range.

During the 24-hour test period, higher TG levels were observed in the higher-carbohydrate/lower-fat diet group. The finding that 'carbohydrate-induced lipemia' rather than 'fat-induced lipemia' (3) may have a dominant influence on triglyceridemia in the diabetic state in day-to-day conditions has clinical relevance. Our subjects had normal TG values; further research is warranted with individuals in poor lipid control.

Higher glycemic levels after supper on the higher-carbohydrate/lower-fat diet during the 24-hour testing were observed, despite appropriate adjustment of insulin doses to carbohydrate meal content. Lower glycemic levels after the higher-fat-monounsaturated supper meal may be due to slower gastric emptying in the presence of olive oil (15).

Limitations include small sample size and short study duration. Our results are in keeping with the American Diabetes Association statement that it is unlikely that an optimal mix of macronutrients exists for the diabetic state (1).

CONCLUSION

A lower-carbohydrate/higher-fat-monounsaturated diet is an appropriate nutrition therapy for individuals with type 1 diabetes in good metabolic and weight control.

ACKNOWLEDGMENTS

This research project was funded by the Canadian Institutes of Health Research, Institute of Nutrition and Metabolism, Canada (MOP 62854). Lifescan Canada supplied patients with Ultra Smart glucose meters plus strips for daily blood glucose testing during the study period. Special thanks are extended to patients who participated in this study. We acknowledge the valuable assistance of doctors, nurses, and personnel of Notre-Dame Hospital of the Univeristy of Montreal Research Center (CHUM), the McGill University Health Centre (MUHC), and the Laval Clinic Research Center.

Disclosures: The project was funded by the Canadian Institutes of Health Research, Nutrition and Metabolism Institute (MOP 62854)**.** Lifescan Canada supplied patients with Ultra Smart glucose meters plus strips for daily blood glucose testing during the study period.

REFERENCES

1. American Diabetes Association. Nutrition recommendations and interventions for diabetes. A position statement of the American Diabetes Association. *Diabetes Care* 31(January, Supplement 1):S61-S78, 2008

2. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Nutrition Therapy. *Canadian Journal of Diabetes* 32(Supplement 1):S40-S45, 2008

3. Parks EJ, Hellerstein MK. Carbohydrate-induced hypertriacylglycerolemia: Historical perspective and review of biological mechanisms. *Am J Clin Nutr* 71:412-433, 2000

4. Ceriello A. The post-prandial state and cardiovascular disease: Relevance to diabetes mellitus. *Diabetes/Metabolism Research and Reviews* 16:125-132, 2000

5. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy. *N Engl J Med* 342;381-389, 2000

6. Garg A. High-monounsaturated-fat diets for patients with diabetes mellitus: A meta-analysis. *Am J Clin Nutr* 67:577S-582S, 1998

7. Chen YDI, Coulston AM, Zhou MY, Hollenbeck CB, Reaven GM: Why Do Low-Fat High-Carbohydrate Diets Accentuate Postprandial Lipemia in Patients with NIDDM? *Diabetes Care* 18:10-16, 1995

8. Georgopoulos A, Bantle JP, Noutsou M, Hoover HA: A High Carbohydrate Versus a High Monounsaturated Fatty Acid Diet Lowers the Atherogenic Potential of Big VLDL Particles in Patients with Type 1 Diabetes. *J Nutr* 130:2503-2507, 2000

9. Georgopoulos A, Bantle JP, Noutsou M, Swaim WR, Parker SJ: Differences in the Metabolism of Postprandial Lipoproteins after a High-Monounsaturated-Fat Versus a High-Carbohydrate Diet in Patients with Type 1 Diabetes Mellitus. *Arterioscl Thromb Vasc Biol* 18:773-782, 1998

10. Giugliano D, Esposito K. Mediterranean Diet and Cardiovascular Health. *Ann NY Acad Sci* 1056:253-260, 2005

11. Ruano J, Lopez-Miranda J, de la Torre R, Delgado_Lista J, Fernandez J, Caballero J, Covas MC, Jiménez Y, Pérez-Martinez P, Marin C, Fuentes F, Pérez-Jiménez P. Intake of phenol-rich virgin olive oil improves the postprandial prothrombotic profile in hypercholesterolemic patients. *Am J Clin Nutr* 86:341-346, 2007

12. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiento M, D'Andrea F, Giugliano D. Effect of a Mediterranean-Style Diet on Endothelial Dysfunction and Markers of Vascular Inflammation in the Metabolic Syndrome: A Randomized Trial. *JAMA* 292:1440-1446, 2004

13. Delahanty LM, Nathan DM, Lachin JM, Hu FB, Cleary PA, Ziegler GK, Wylie-Rosett J, Wexler DJ, for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications. Association of diet with glycated hemoglobin during intensive treatment of type 1 diabetes in the Diabetes Control and Complications Trial. *Am J Clin Nutr* 89:518-524, 2009

14. Rasmussen LG, Larsen TM, Mortensen PK, Due A, Astrup. Effect on a 24-hr energy expenditure of a moderate-fat diet high in monounsaturated fatty acids compared with that of a low-fat, carbohydrate-rich diet: A 6-month controlled dietary intervention trial. *Am J Clin Nutr* 85:1014-1022, 2007

15. Gentilcore D, Chaikomin R, Jones KL, Russo A, Feinle_Bisset C, Wishart JM, Rayner CK, Horowitz. Effects of fat on gastric emptying of and the glycemic, insulin, and incretin responses to a carbohydrate meal in type 2 diabetes. *J Clin Endocrinol Metab* 91:2062-2067, 2006

Table 1 - ***Glycemic, anthropometric, blood pressure, fasting plasma lipid and oxidative, thrombotic, inflammatory markers throughout the dietary trial for the higher-carbohydrate/lower-fat diet group (n=15) and lower-carbohydrate/higher-fat-monounsaturated diet group (n=15)***

Variables	Higher-carbohydrate/lower-fat diet*			Lower-carbohydrate/higher-fat-monounsaturated diet*		
	Baseline†	6-Months‡	Absolute change	Baseline†	6-Months‡	Absolute change
A1C (%)	7.3±0.7	7.2±0.7	-0.2±0.5	7.0±0.7	7.1±0.9	+0.1±0.6
BMI (kg/m^2)	24.3±2.6	24.1±2.6	-0.24±1.0 ∫	24.3±2.7	24.8±2.7	+0.56±0.6 ∫
Weight (kg)	71.1±13.7	70.3±13.1	-0.83±3.0 ∫	71.8±13.4	73.4±13.6	+1.6±1.8 ∫
Body Fat (%)	25.3±7.6	23.8±7.0	-1.6±3.8 ∫	23.9±7.6	25.3±7.4	+1.4±2.1∫
Fat-Free-Mass (%)	36.6±5.5	37.6±5.3	+1.0±2.4	36.3±4.7	36.5±5.6	+0.24±2.2
Systolic blood pressure (mm hg)	116±15	120±10	+3.9±14.4	122±15	122±16	-0.2±21.1
Diastolic blood pressure (mm hg)	72±7	77±8	+4.7±11.0	78±7	75±8	-2.6±8.9
Triglycerides (mmol/L)	0.72±0.30	0.86±0.55	+0.14 ± 0.46	0.68±0.34	0.65±0.20	-0.03 ± 0.22
Total-cholesterol (mmol/L)	4.40±0.66	4.28±0.78	-0.12 ± 0.66	4.48 ± 0.88	4.25±0.64	-0.24 ± 0.66
HDL-cholesterol (mmol/L)	1.47±0.35	1.53±0.35	+0.06 ± 0.27	1.64±0.33	1.63±0.38	-0.01 ± 0.22
Total-cholesterol/HDL-cholesterol ratio	3.12±0.77	2.90±0.78	-0.22 ± 0.55	2.80±0.67	2.67±0.48	-0.13± 0.37
LDL-cholesterol (mmol/L)	2.60±0.63	2.35±0.75	-0.25 ± 0.70	2.53±0.73	2.31±0.46	-0.21 ± 0.57
Apo B (g/L)	0.78±0.17	0.76±0.22	-0.01 ± 0.12	0.75±0.12	0.72±0.11	-0.04 ± 0.07
8-iso PGF (pg/ml)	239±147	267±167	+27.9±132.6	243±132	210±138	-32.1±68.3
PAI-1 (ng/ml)	55.0±23.2	69.2±23.1	+14.2±24.5 ∫	78.5±37.7	65.7±28.7	-12.8±27.0 ∫
E-selectin (ng/ml)	22.5±14.7	21.7±13.9	-0.8±3.5	23.8±15.5	25.0±14.5	+1.2±3.0
s-ICAM-1 (ng/ml)	314±59	315±58	+0.2±37	326±84	328±77	+2.0±46
hsCRP-1 (ug/ml)	7.6±8.2	9.9±12.3	+2.3±10.9	6.8±5.4	5.1±5.9	-1.7±4.8

TNF-alpha (pg/ml)	1.2±0.5	1.5±0.8	+0.3±0.8	1.4±0.5	1.4±0.9	-0.1±0.8

* Data are means ± SD.
† No significant differences were observed between diet groups at baseline (*P* > 0.05).
‡ No significant differences were observed between diet groups at 6-months (*P* > 0.05).
∫ Significantly different between diet groups for absolute change between baseline and 6-months (*P* < 0.05)