Original Article

Effect of low-glycemic load diet on changes in cardiovascular risk factors in poorly controlled diabetic patients

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ABSTRACT

Background: One dietary strategy aimed at improving both diabetes control and control of cardiovascular risk factors is the use of low glycemic index diets. These diets have been reported to be beneficial in controlling diabetes, and also increase high density lipoprotein cholesterol (HDL-C), lower serum triglyceride, and reduce glycated protein. **Aim:** Therefore, we aimed to investigate the effect of a low glycemic index–low glycemic load (GL = 67–77) diet on lipids and blood glucose of poorly controlled diabetic patients. **Materials and Methods:** In an intervention study, 100 poorly controlled diabetic patients (age 52.8 ± 4.5 years) who were taking insulin or on oral medication underwent administration of low GL diet (GL = 67–77; energy = 1800–2200 kcal, total fat = 36%, fat derived from olive oil and nuts 15%, carbohydrate = 41%, protein = 22%) for 10 weeks. Patients were recommended to follow their regular lifestyle. Total cholesterol, low density lipoprotein (LDL), HDL, triglyceride, glycated hemoglobin (HbA1c), weight, and body mass index (BMI) were measured before and 10 weeks after the intervention. **Results:** Before intervention, initial blood cholesterol and triglyceride concentrations were 205.9 ± 21.6 and 181.5 ± 22.2, respectively, and were reduced to 182.6 ± 18.2 and 161.6 ± 16.7, respectively, after 10 weeks intervention ($P < 0.001$). LDL reduced and HDL increased significantly. The HbA1c percentage reduced by 12% (from 8.85 ± 0.22% to 7.81 ± 0.27%) ($P < 0.001$), and also their weight significantly reduced from 74.0 ± 5 kg to 70.7 ± 4.6 kg ($P < 0.001$). **Conclusion:** This study demonstrated that low GL diet having lower carbohydrate amount and higher fat content is an appropriate strategy in blood lipid and glucose response control of poorly controlled diabetic patients.

Key words: Cardiovascular, glycated hemoglobin, glycemic index, glycemic load, poorly controlled diabetes

Introduction

Diabetes, especially poorly controlled (glycated hemoglobin or HbA1c >8%)[1] one, is a metabolic disease associated with a variety of micro- and macrovascular complications. Elevation of postprandial plasma glucose and insulin stimulation following ingestion of high carbohydrate diet are suggested to increase severity of diabetes and to be independent indicators of risk for atherosclerotic diseases.[2,3] As such, interventions to alleviate postprandial plasma glucose and insulin secretion by diet and lifestyle changes are the essential therapeutic objectives for diabetics.[4]

One dietary strategy aimed at improving both diabetes control and control of cardiovascular risk factors is the use of low-glycemic index (GI) diets. These approaches include diets containing 50–60% calories from carbohydrates and administration of low-glycemic load (GL) diet (100 g) (glucose equivalents per day) without elevating fat intake.[5] Conventional high carbohydrate intake recommended in diabetes, results in suboptimal glycemic control and lipoprotein profile, gradually increasing insulin and/or oral hypoglycemic medication requirement and eventually weight gain.[6]

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Some trials have produced supportive evidence of the benefits of substituting polyunsaturated fatty acids (PUFAs) for saturated fatty acids (SFAs).[7] A meta-analysis of randomized control trials (RCTs) found a 10% reduction in chronic heart disease for each 5% of energy from SFAs substituted for PUFAs,[8] while no benefits have been found by substituting carbohydrates for SFAs.[8,9]

Therefore, the aim of this study was to examine the effect of low-GL diet (GL = 67–77, 36% energy as fat, and 42% as carbohydrate), with having higher percentage of fat and lower amount of carbohydrate than conventional diabetics diet on cardiovascular risk factors changes in poorly controlled type 2 diabetic patients.

Materials and Methods

Experimental procedure

The study was a prospective observational study conducted among Caucasian patients, without having control group. The patients' biochemical data, weight, and body mass index (BMI) were compared before and after intervention. The inclusion criteria of the study were males and females of age 30–60 years with poorly controlled type 2 diabetes and having HbA1c >8%. The exclusion criteria of the study were subjects with renal, heart, chronic, metabolic (except diabetes) disease, pregnant and nursing mothers. One hundred diabetes patients who were referred to endocrine clinic during 6 months and were receiving either insulin or oral medication were recruited for this study. Before commencement of the study, patients were asked to fill a consent form, and their 7-day food dietary records were collected to estimate their usual energy intake. Patients were recommended to follow their regular lifestyle and take their medications during intervention. The procedures were followed in accordance with the ethical standards of the international guideline for human study, and the study was approved by the Human Research Ethics Committee of the Qazvin University of Medical Sciences.

Dietary plane

The energy intake varied between 1800 and 2200 kcal according to the patients' needs, which was calculated based on the "food dairy record." The GI of each food was extracted from "international table of glycemic index and glycemic load"[10] and glycemic index of Iranian foods.[11] The GL of foods was estimated using carbohydrate content (grams) of each food multiplied by GI of that food.[10] The GL of subjects' daily diet was the sum of GL of foods consumed during the day.

At baseline, patients were on high carbohydrate low fat (55–60% carbohydrate and 20% fat) conventional diabetes diet. A 10-week experimental diet consisted of ordinary food item having GI ≤55, and each main meal had GL ≤20 with overall daily GL = 67–77 (42% carbohydrate, total fat 36%, fat derived from olive oil and nuts 15%, 22% protein) [Table 1]. This was accomplished by providing a list to each individual of the recommended daily intake of commonly used foods and a substitution list allowing exchanges within food groups. The compliance with diet program and GL of consumed meals was assessed by regular fortnightly visit of a dietitian.

Laboratory methods

At baseline and 2 weeks after the diet intervention, blood samples were drawn after an overnight fast for determination of plasma glucose, HbA1c, triglyceride (TG), total cholesterol, low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C). Plasma glucose concentrations were determined by the glucose oxidase method[12] (using a Hitachi 917 analyzer, Roche Diagnostics, Biomedical Lab. Center, Florida, USA). HbA1c was determined using nephelometry (Nicocard, USA). The LDL level was measured by a homogeneous enzymatic assay (Genzyme Corp., Cambridge, MA, USA),[13] and HDL, triglycerides, and cholesterol concentrations were measured using a Hitachi 911 analyzer (Roche Diagnostics, Indianapolis, IN, USA).

Statistical analysis

Using G-Power EXE software, the sample size was calculated based on effect sizes and mean obtained for fasting blood glucose in similar studies powered at 90% and an alpha of 5%. We estimated that a sample size of 96 were enough to meet the considered powerfor our study. Data were analyzed for normality of distribution before use of parametric statistics with SPSS version 16 (SPSS Inc., Cary, NC, USA). Data were reported as mean ± SD and were analyzed by using paired Student's *t*-test and Pearson correlation to compare weight, BMI, fasting blood sugar (FBS), HbA1c, and lipid profile of patients before and after intervention.

Results

One hundred subjects (55 M, 45 F), aged 52.8 ± 4.5 years, of weight 74.0 ± 5 kg and BMI = 27.2 ± 1.9 kg/m^2, who were under treatment for a period of 11.25 ± 3 years were recruited for this study. The mean values for the data collected are shown in Table 2. FBS concentration, HbA1c percentage, weight, and BMI were significantly different between the values before and after intervention ($P < 0.001$), which reduced as follows: Fasting blood glucose by 28.1 ± 12.5 mg/dl (16.6%), HbA1c by 1.1 ± 0.3%,

Table 1: Composition of low-glycemic load diet with 1800 kcal administered to diabetic patients

Food	Weight (g)	Protein (g)	Fat (g)	Carbohydrate (g)	GI	GL	Energy (kcal)
4 Exchange from starch list, (whole wheat bread, rice, backed beans, sliced fried potato), all low GIs	Different	12	—	60	47	28	320
4 Exchange from milk list (low-fat milk, yogurt)	1000	32	20	48	30	14	480
8 Exchange from meat and meat substitutes list (lean meat, low-fat cheese, egg whites)	Different	49	21	——	—	——	440
2 Exchange from vegetable list (lettuce, cucumber, tomato)	2 Cups raw vegetable	4		10	1	1	50
4 Exchange from fruit list (fresh low-GI fruits, apple, orange)	480	——		60	40	24	240
6 Exchange from fat list (olive oil, olives, nuts, walnut)	Different		30			——	270 (15%)
Total		97 (22)	71 (36)	178 (42)		67	1800

Table 2: Lipid and blood glucose profile of diabetic patients before and after diet intervention

Patients	TG (mg/dl)	Cholesterol (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	Weight (kg)	BMI (kg/m²)	FBS (mg/dl)	HbA1c (%)
At baseline								
Male (*N*=55)	176.3±20.9	203.9±21.8	132.0±16.3	37.8±2.2	75.5±5.1	23.8±0.4	166.3±15.0	8.8±0.2
Female (*N*=45)	187.8±22.4	208.4±21.2	136.8±16.8	39.2±4.0	72.0±4.3	27.8±1.3	172.8±19.5	8.9±0.2
Total (*N*=100)	181.5±22.2	205.9±21.6	134.1±16.6	38.5±3.2	74.0±5	27.2±1.9	169±17	8.85±0.22
	CV=12.3%	CV=10.5%	CV=12.3%	CV=8.3%	CV=6.7%	CV=7%	CV=10%	CV=2%
After 10 weeks intervention								
Male (*N* = 55)	159.6±18.6	179.6±19.9	124.4±13.0	41.3±3.0	72.3±4.5	23.0±0.2	138.6±12.8	7.8±0.2
Female (*N* = 45)	166.3±13.3	186.3±15.2	128.0±13.6	42.5±5.7	68.7±4.0	26.6±1.3	144.2±11.25	7.8±0.3
Total (*N*=100)	161.6±16.7	182.6±18.2	129.5±13.4	41.4±4.4	70.7±4.6	26.0±1.8	141±12	7.81±0.27
	CV=10.3%	CV=10%	CV=10.3%	CV=10.6%	CV=6.5%	CV=7%	CV=8.5%	CV=3%
P	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001

Changes in lipids and blood glucose profiles in male and female groups and also in total patients before and after intervention were significant ($P < 0.001$)

weight by 3.3 ± 1 kg, and BMI by 1.2 ± 0.4 kg/m² ($P < 0.001$). Cholesterol and TG concentrations were 205.9 ± 21.6 mg/dl and 181.5 ± 22.2 mg/dl and reduced to 182.6 ± 18.2 and 161.6 ± 16.7, respectively ($P < 0.001$). Both LDL and HDL showed significant changes. LDL increased, while HDL decreased.

Discussion

This study showed a significant effect of low-GL diet on cardiovascular risk factors including total cholesterol, TG, LDL, HDL, FBS, and HbA1c. In our study, as we hypothesized, the administered low-GL diet suppressed the HbA1c of the patients to 7.8 ± 0.3%, which is not considered as poorly controlled level[1] and was our target in the present study.

While there is widespread concern about increasing diabetes and obesity and related health care costs, development of an appropriate diet for cardiovascular risk factor reduction and weight management is a public health issue. The reduction in cardiovascular risk factors in poorly controlled diabetic patients in our study was due to weight loss and also low GL of diet.

Although the poorly controlled diabetes patients had similar isocaloric diet before and during intervention, the low-GI, low-GL diet caused significant weight reduction after 10 weeks of intervention. Several studies have examined the effect of GI on human appetite, and most of them demonstrated increased satiety, delayed return of hunger, or decreased *ad libitum* food intake after consumption of low compared to high-GI foods.[14] In contrast, hyperinsulinemia resulting from high-GI food intake may cause weight gain by directing nutrients away from oxidation in muscle and toward storage in fat. In animal study it was shown that hyperinsulinemia elevates glucose utilization in fatty tissue, but decreases utilization in muscles, a process that results in increased food intake and weight gain.[14] In epidemiological studies, it has been reported that Pima Indian children with increased fasting insulin levels gain more weight than those children having normal insulin concentration.[15] Energy-restricted diet based on low-GI foods produced greater weight loss than did an equivalent diet based on high-GI foods, and among healthy pregnant women, high-GI diet resulted in greater weight gain at term than isocaloric low-GI diet.[16] The weight changes found in adult rats fed isoenergic, nutrient-balanced diets based on high-GI or low-GI diet

for 32 weeks were significantly different. The low-GI group had reduced weight, while the high-GI group demonstrated increased weight.[16] These diets have been reported to be beneficial as they control diabetes, increase HDL-C, lower serum TG,[17] and reduce glycated proteins.[18] In contrast, consuming high-GI diet and consequently high-GL diet was 4 times greater among women with a higher BMI,[19] which may lead to diabetes and cardiovascular disease (CVD). Also, the epidemiological studies such as the Nurses Health Study and Health Professional Follow-Up Study,[20] and also Framingham Offspring Study[21] have demonstrated the association between GL and type 2 diabetes, CVD, and metabolic syndrome.

All the above studies confirm weight reduction in diabetes subjects of our study, following low-GL diet. The present study also gains support from a study in which consumption of an *ad libitum* low-GL diet by obese adults during 6 months resulted in significant body weight reduction which was comparable with conventional restricted energy (250–500 kcal/day deficit) diet group (–7.8% and –8.4% weight reduction, respectively).[22] In our study, diabetes subjects with low GL and sufficient energy intake had 4.4% weight reduction during 10 weeks intervention. The low-GL diet in our study may have increased oxidation of nutrients in muscles rather than storing them in white tissue. In addition, the low-GL diet may have elevated satiety and reduced the intake of foods.

In epidemiologic studies, both GI and the GL of the overall diet were associated with a greater risk of type 2 diabetes in whole adult population and low-GI diet had significant effect on reducing glycosylated proteins.[19] The low-GI and low-GL diets independent of weight loss have significant effect on improving cardiovascular risk factors. In a study, *ad libitum* intake of the low-GI diet resulted in a 10% decrease in LDL-C compared with isocaloric high-GI diet after 10 weeks intervention,[23] and also *ad libitum* intake of low-GI diet showed a significantly greater mean decline in plasma triacylglycerols than did the conventional restricted diet.[22] In our present study, the LDL-C reduced by 4%, while the HDL-C increased by 8%. Beneficial effect of low-GI diet in the management of diabetes is well documented. A meta-analysis showed that after average duration of 10 weeks, subjects with type 1 and 2 diabetes who were consuming low-GI diets had HBA1c concentration of 0.4% points lower than those who were following a high-GI diet.[18] Comparing low-GI versus high-GI diet, the low-GI diet significantly improved fasting blood glucose and HbA1c of type 2 diabetes. The patients who followed low-GI diet demonstrated a reduced HbA1c level and it was 0.39% points lower than the HbA1c level of those who followed high-GI diet.[4] In our study, after 10 weeks intervention, the fasting blood glucose reduced by 28.1 ± 12.5 mg/dl (16.6%), and HbA1c by 1.1 ± 0.3%.

The mechanism underlying improvement of fasting blood glucose and HbA1c in the present study probably is the elevated whole-body glucose disposal.[4] The low-fat, high-carbohydrate diet, which causes postprandial hyperglycemia and hyperinsulinemia, has a significantly less favorable effect on circulating triacylglycerol and PAI-1 (plasminogen activator inhibitor-1; a marker of fibrinolytic capacity) concentration than does low-GL diet.[24] In turn, these episodes may enhance hepatic triacylglycerol production or reduce peripheral clearance.[24,25] Higher concentrations of triacylglycerol and PAI-1 have direct association with cardiovascular events.[26]

In our study, the moderate carbohydrate diet with GL = 67–77 g/day, including 42% carbohydrate as energy intake, and 15% of fat derived from olive oil and nuts sources was almost similar to ADA's recommendation which is more appropriate and compelling for glycemic control for long period. The GL <80 g/day is considered low-GL diet.[27] The higher the GL, the greater the glycemic effect[28] and insulinogenic effect.[10] The GL of diet in our study was even lower than maximum g/day recommendation for low-GL diet.

Conclusion

The meal plan provided by us for glycemic control and control of cardiovascular risk factors of poorly controlled diabetes subjects is appropriate. The mechanism of low GL diet for weight loss is due to its effect on oxidation elevation of nutrients in muscles rather than storing them in white adipose tissue, a process that increases satiety, delayed return of hunger, or decreased *ad libitum* food intake and weight loss.

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