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Dietary strategies for patients with type 2 diabetes in the era of multi-approaches; review and results from the Dietary Intervention Randomized Controlled Trial (DIRECT)

Sivan Ben-Avraham[a], *Ilana Harman-Boehm*[b], *Dan Schwarzfuchs*[c], *Iris Shai*[a,*]

[a] *The S. Daniel Abraham Center for Health and Nutrition, Department of Epidemilogy, Ben-Gurion University of the Negev, Beer-Sheva, Israel*
[b] *Department of Internal Unit C and Diabetes Unit, Soroka University Medical Center, Beer-Sheva, Israel*
[c] *Nuclear Research Center Negev, Dimona, Israel*

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ABSTRACT

Dietary intervention is recognized as a key component in prevention and management of type 2 diabetes (T2DM) and the debate persists: which dietary strategy is most effective. In the Dietary Intervention Randomized Controlled Trial (DIRECT) 322 moderately obese participants were randomized for 2 years to one of three diet groups: low-fat, Mediterranean and low-carbohydrate. Differential effects were observed in the sub-group of patients with T2DM at 24 months: participants randomized to the Mediterranean diet, which had the highest intake of dietary fibers and unsaturated to saturated fat ratio, achieved greater significant improvements in fasting plasma glucose and insulin levels. Patients who were randomized to the low-carbohydrate diet, which had the minimal intake of carbohydrates, achieved a significant reduction of hemoglobin A1C. Although improvements were observed in all groups, the low-fat diet was likely to be less beneficial in terms of glycemic control and lipid metabolism. Interpretation of results from different studies on dietary strategies may be complex since there is often no consistency in diet compositions, calorie restriction, intensity of intervention, dietary assessment or extent of adherence in the trial. Nevertheless, it seems that low fat restricted calorie diets are effective for weight loss and are associated with some metabolic benefits; however, some recent trials have shown that low carbohydrate diets are as efficient in inducing weight loss and in some metabolic measures such as serum triglycerides and HDL-cholesterol may be even superior to low fat diets. When addressing the issue of diet quality rather than quantity applying the glycemic index may have some added benefits. Furthermore special features of the Mediterranean diet have apparent additional favorable effects for patients with T2DM.

1. Introduction

"Diabesity" is a term that describes the joint occurrence of T2DM and obesity [1]. T2DM constitutes 85–95% of all diabetes in developed countries, and an even higher percent in developing countries, with 50 to 90% of all cases resulting from weight gain [2,3]. According to the World Health Organization it is estimated that the worldwide prevalence of diabetes will rise from 171 million in 2000 to 366 million in 2030 [4]. Data from the International Diabetes Federation indicate that in people aged 20–79 years the worldwide prevalence will rise from 5.9% in 2007 to 7.1% in 2025 [2].

Diabetes and related complications are major causes of morbidity and mortality; it is among the leading causes of

* *Address for correspondence:* Dr. Iris Shai, The S. Daniel Abraham International Center for Health and Nutrition, Department of Epidemiology and Health Systems Evaluation, Ben-Gurion University of the Negev, P.O. Box 653, Beer Sheva 84105, Israel.
E-mail address: irish@bgu.ac.il (I. Shai).

cardiovascular disease, blindness, renal failure, and lower limb amputation [3]. The cost of diabetes in the USA in 2007 was estimated at $174 billion total, of which $58 billion were spent to treat the chronic complications of diabetes [5]. Control of hyperglycemia has been repeatedly shown to decrease diabetes complications, particularly microvascular complications, making it a main target for treatment [6].

Obesity induces insulin resistance and increases glycemia; therefore weight loss is an important goal for T2DM patients. Diabetes professional and health organizations encourage weight loss by a combination of physical activity and reduced energy intake for overweight or obese individuals [7]. Moderate weight loss (5% of body weight) was shown to improve glycemic control, insulin resistance, blood pressure, and dyslipidemia in patients with T2DM [8].

2. Dietary treatment in type 2 diabetes

The use of an efficient dietary strategy is now recognized as a key component of the prevention and management of the different aspects of T2DM [8]. Nevertheless, the debate continues as to which dietary strategy is most effective [7,9–11]. The importance of carbohydrate intake for glucose tolerance was pointed out in very early studies; possible mechanisms underlying the association include suppression of free fatty acid release by carbohydrates, thus eliminating the metabolic competition to glucose utilization [12]. Studies conducted 20–40 years ago established the concept of improved control of glycemia and blood lipids in either T2DM patients or healthy subjects given high carbohydrates or high-carbohydrate high-fiber diets [12]. The accumulating evidence showing a positive effect of reduced carbohydrate intake on glycemic control, triglyceride and high density lipoprotein cholesterol (HDL-C) concentrations is contrary to these findings [13,14]. This adds up to observation on parallel decrease of fat intake and increase of obesity [15].

Diabetes Associations guidelines continue to recommend relatively high total carbohydrate (45–60% of energy) and reduced total and saturated fat intake as a weight loss strategy for obese and overweight T2DM patients [7]. However, some flexibility as to macronutrient distribution is evident. In 2008 the American Diabetes Association (ADA) declared for the first time that achieving weight loss may be possible by either low-carbohydrate or low-fat calorie restricted diets, although data for low-carbohydrate diet were limited then to up to 1 year of follow-up [16]. Current recommendations of the ADA [16], European Association for the Study of Diabetes (EASD) [17], Canadian Diabetes Association (CDA) [18], and Diabetes UK [19] are presented in Table 1.

3. The 2-year Dietary Intervention Randomized Controlled Trial (DIRECT)

Methods of the DIRECT have been published elsewhere [13]. Briefly, the DIRECT was a 2 year dietary intervention trial conducted in a workplace with an on-site medical clinic and exclusive cafeterias where food dishes were color-coded according to the different dietary strategies. Moderately obese participants (n = 322 of which 46 were T2DM patients) were randomly assigned to one of three diet groups: low fat, low carbohydrate, and Mediterranean. The low-fat calorie-restricted diet aimed for 30% of calories from fat, 10% of calories from saturated fat, and 300 mg of cholesterol per day. The Mediterranean calorie-restricted diet aimed for 35% of calories from fat, specifically adding olive oil and nuts and additional 2 portions of fish/week. The low-carbohydrate diet was based on the Atkins diet; it had no restriction on energy, protein and fat intake. The aim was to provide 20 g/day of carbohydrates for 2 months, with a gradual increase to a level which would maintain weight loss. Adherence to the diets was evaluated by a validated [20], food-frequency questionnaire [21] and in a subgroup of participants two 24-hour dietary recalls to confirm absolute intake.

4. DIRECT findings

Adherence to the study was 95% after the first year and 85% after 2 years. Baseline characteristics of the study population and baseline diet composition have been published [13] and were similar in the three arms. In general, participants were mostly men (86%) with mean age of 52 ± 7 years and mean BMI of 30.9 ± 3.6. Coronary heart disease was present in 37% and diabetes in 14% of participants.

Intake of energy (kcal/day) decreased significantly in all diet groups at 6, 12 and 24 months as compared with baseline ($P < 0.001$) [13], with no significant difference between the groups, although the low-carbohydrate diet was not calorie-restricted (Fig. 1A). There were significant differences in absolute change of carbohydrate intake (g/day) as compared with baseline between the groups at 6, 12 and 24 months (Fig. 1B), with the low-carbohydrate group having the lowest intake ($P < 0.001$) [13]. Total fat intake (g/day) decreased in all diet groups at 6, 12 and 24 months as compared with baseline (Fig. 1C). The percent of energy from fat was significantly different between the groups and higher in the low-carbohydrate group as compared with the others ($P < 0.001$) [13]. Intakes of saturated fat (g/day) and dietary cholesterol (mg/day) (Fig. 1D & 1E) decreased in the low-fat and Mediterranean diet groups and increased in the low-carbohydrate group with significant differences between groups ($P < 0.001$). Intake of dietary cholesterol (Fig. 1E) was higher in the low-carbohydrate group ($P = 0.04$) [13]. The Mediterranean-diet group had a higher (Fig. 1F) monounsaturated to saturated fat ratio ($P < 0.001$) and dietary fibers intake ($P = 0.002$) (Fig. 1G) [13].

As previously reported [13] among participants with T2DM, fasting plasma glucose at 24 months, decreased in the Mediterranean-diet group while in the low-fat group it increased ($P < 0.001$). HOMA-IR (homeostasis model assessment of insulin resistance) decrease was significantly greater in T2DM patients randomized to the Mediterranean diet than to the low-fat diet ($P = 0.04$). Changes in HbA1c from baseline are presented in Fig. 2. At 24 months there was a decrease in HbA1c in all diet groups although the change was significant only within the low-carbohydrate group ($P < 0.05$). Changes between groups, however, did not reach significant values.

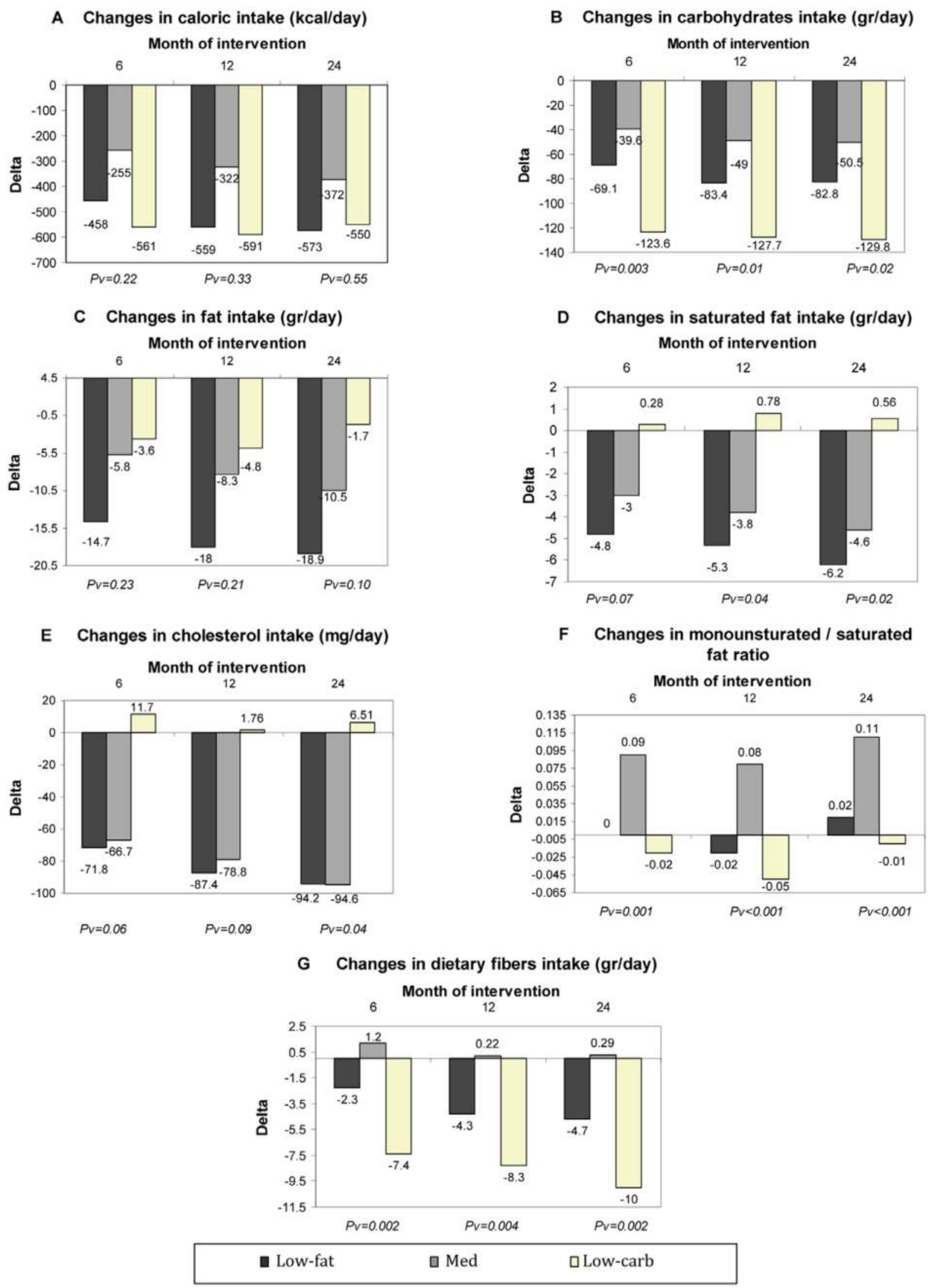

Fig. 1 – Changes in intakes of energy (A), carbohydrates (B) fat (C), saturated fat (D), cholesterol (E), monounsaturated to saturated fat ratio (F) and dietary fibers (G) at 6, 12 and 24 month of intervention as compared to baseline across low-fat, Mediterranean and low-carbohydrate diet groups. P-values (*Pv*) are between groups at each time point.

Table 1 – Current nutritional recommendations of health diabetes organizations.

Organization	Weight management	Macronutrients % of total daily energy	Source of carbohydrates	Source of fat % of total daily energy
American Diabetes Association (ADA) [16]	In overweight and obese insulin resistant individuals, modest weight loss may improve insulin resistance. For weight loss, either low-carbohydrate or low-fat calorie-restricted diets may be effective in the short term (up to 1 year).	Protein – 15–20%. The best mix of carbohydrate, protein, and fat appears to vary depending on individual circumstances. Total caloric intake must be appropriate to weight management goals.	Carbohydrate from fruits, vegetables, whole grains, legumes, and low-fat milk is encouraged for good health. The use of glycemic index and load may provide a modest additional benefit.	Saturated fat to <7% Minimize Intake of *trans* fat. Limit cholesterol to <200 mg/day. 2+ servings of fish per week to provide n-3 polyunsaturated fatty acids
European Association for the Study of Diabetes (EASD) [17]	For BMI >25 kg/m^2, reduce caloric intake and increase energy expenditure.	Protein – 10–20%. Fat – up to 35%. Carbohydrates – the remainder 45–60%.	Vegetables, legumes, fruits and wholegrain cereals. Dietary fiber and low glycemic index particularly important to individuals in the upper end of recommended range.	Saturated and trans-unsaturated fats <8–10%, monounsaturated fat 10–20% of daily energy, polyunsaturated fatty acids up to 10% 2–3 servings of fish a week and plant sources of n-3 fatty acids.
Canadian Diabetes Association (CDA) [18]	Foods should be low in energy density to optimize satiety and discourage over consumption, help attain and maintain a healthy body weight.	Protein – 15–20%. Fat – up to 35%. Carbohydrates – 45–60%.	Include vegetables, fruit, whole grains and milk. Consume low-glycemic-index foods in place of high-glycemic-index foods. Sucrose intake up to 10% of daily energy	Saturated fats <7% instead consume monounsaturated fats, restrict *trans* fat to a minimum. Polyunsaturated fat <10%, consume foods rich in polyunsaturated n-3 fatty acids.
The British Diabetic Association/Diabetes UK [19]	Weight loss and stabilization is a major priority for those who are overweight.	Protein – up to 1 g/kg body weight. Fat – up to 35%. Carbohydrates – 45–60%.	Sucrose may provide up to 10% of energy	Saturated and trans-unsaturated <10% of energy. n-6 polyunsaturated <10%. Eat fish, once or twice weekly.

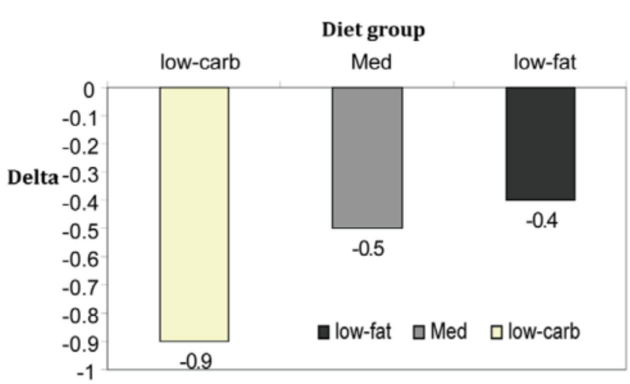

Fig. 2 – Changes in hemoglobin A1c (%) in the sub-group of subjects with type 2 diabetes at 24 months of intervention in the 3 diet groups.

5. Dietary strategies

The evaluation of dietary strategies for T2DM should explore their effects on weight, glycemic control, insulin resistance, dyslipidemia, inflammation and other cardiovascular risk factors [7]. Trying to compare different dietary strategies is complex; low fat and low carbohydrate diets were initially aimed at weight reduction and control, the Mediterranean diet originated in a food pattern observed in the Mediterranean region [11], and glycemic index and glycemic load represent a system allowing a qualitative scaling of carbohydrate containing foods [16]. Recent findings related to the various strategies and their diabetes relevance are summarized below.

5.1. *Low-fat diet*

Low fat diets were traditionally recommended for weight loss [16] based on the fact that the caloric content of fat is higher than other macronutrients. Findings from the Diabetes Prevention Program (DPP) indicated that in individuals with elevated glucose concentrations, intensive lifestyle interventions including a low fat (<25% of energy) restricted-calorie dietary modification, resulted in a 58% reduced incidence of diabetes as compared with placebo [22–24]. In a study of 136 individuals with glucose intolerance, a fat-reduced diet was compared with a control group without dietary intervention. The reduced fat group had significant short-term changes regarding reductions in total and LDL cholesterol (LDL-C), body weight and systolic blood pressures [25]. In the Women Health Initiative (n = 48,835) 40% of participants were randomized to a low fat diet (20% calories from fat) and 60% were treated according to the principles of the 1995 Dietary Guidelines for Americans by the US Departments of Agriculture and Health and Human Services [26]. Although subgroup analysis suggested that decreases in intake of energy from fat reduced diabetes risk, adjustment for weight loss indicated that weight loss was the main predictor of reduced risk rather than macronutrient composition [27]. Other trial randomized 99 individuals with T2DM to a low-fat vegan diet (~10% of energy from fat, 15% protein, and 75% carbohydrate) or a diet following the 2003 ADA guidelines (15–20% protein, <7% saturated fat, 60–70% carbohydrate and monounsaturated fats, and cholesterol ≤200 mg/day) for 74 weeks. Both diets were associated with reductions in weight and plasma lipid levels. When controlling for medication changes, the low-fat vegan diet appeared to have a more favorable effect on glycemia and plasma lipids than did the conventional diabetes low fat diet [28]. In an interventional trial (n = 42) lasting 6 weeks in a cross-over design, two types of diets were given, high-carbohydrate diet (55% energy carbohydrate, 30% fat, and 10% monounsaturated fat) and high-monounsaturated fat diet (45% energy fat, 25% monounsaturated fat, and 40% carbohydrate). Results indicated that consumption of a high-carbohydrate diet modestly raised blood pressure in T2DM patients [29].

5.2. *Mediterranean diet*

Both observational and interventional studies have found favorable effects for the Mediterranean diet on cardiovascular health, obesity and diabetes [13,30–37]. The Mediterranean diet is rich in fibers, unsaturated fats, antioxidants, polyphenols and magnesium. Several mechanisms were suggested to explain the link of these components to protection from T2DM. Fibers promote satiety through prolonged mastication, gastric distention, and increased cholecystokinin; antioxidants may reduce oxidative stress linked to insulin resistance and beta cell dysfunction; polyphenols may inhibit alpha-glucosidase in the gut and glucose transport by GLUT2; magnesium is essential for the function of enzymatic pathways linked to cellular sensitivity to insulin [11]. In the Mediterranean Diet, Cardiovascular Risks and Gene Polymorphisms (Medi-RIVAGE) study, the effects of a Mediterranean type diet or a low-fat diet on cardiovascular risk factors were evaluated in 212 men and women with moderate risk factors for cardiovascular disease. In both dietary arms there was a significant reduction in BMI, dyslipidemia, insulinemia, and glycemia, after 3 month with no significant differences between the arms [37]. The Seguimiento Universidad de Navarra (SUN) project, a large Spanish cohort study of 13,380 participants, estimated dietary intake at baseline and the relative risk for a new diagnosis of diabetes during 4.4 years of follow up. Participants who adhered closely to a Mediterranean diet had a lower risk of diabetes with relative risk adjusted for sex and age of 0.41 (95% CI: 0.19 to 0.87) for those with moderate adherence and 0.17 (0.04 to 0.75) for those with the highest adherence compared with those with low adherence [34]. In the Prevención con Dieta Mediterránea (PREDIMED) randomized clinical trial, 1224 participants were recruited to one of 3 arms in which they received quarterly education about the Mediterranean diet and either 1 L/wk of virgin olive oil or 30 g/day of mixed nuts. The control group received advice on a low-fat diet. All diets were ad libitum. At baseline, 61.4% of participants met criteria for the metabolic syndrome. The adjusted odds ratios for reversion of metabolic syndrome were 1.3 (95% confidence interval, 0.8–2.1) for the Mediterranean Diet + olive oil group and 1.7 (1.1–2.6) for the Mediterranean Diet + nuts group compared with the control diet group [35]. Another PREDIMED trial was a cohort of 339 men and 433 women aged 55 to 80 years at high cardiovascular risk (presence of diabetes or at least three cardiovascular risk factors). Food consumption was documented as well as serum concentrations of high-sensitivity C-reactive protein (CRP), interleukin-6 (IL-6), intracellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1). In a multivariate model, a higher consumption of fruits and cereals was associated with lower concentrations of IL-6 (P for trend 0.005). Subjects with the highest consumption of nuts and virgin olive oil had the lowest concentrations of VCAM-1, ICAM-1, IL-6 and CRP; although only for ICAM-1 was this difference statistically significant in the high consumers of nuts (P for trend 0.003) and for VCAM-1 in the high consumers of virgin olive oil (P for trend 0.02) [38]. In the Lyon Diet Heart Study, a randomized trial of secondary prevention in subjects after a first myocardial infarction (MI), participants were assigned to either an experimental group with a Mediterranean-type diet or control group with a western type prudent diet. In the Mediterranean diet group as compared with the western type prudent diet, death and non-fatal MI were reduced (P = 0.0001) as were unstable angina, stroke, heart failure, pulmonary or peripheral embolism (P = 0.0001) [39]. In a study comparing the effects of 3 different diets on alanine aminotransferase (ALT) concentration in obese diabetic patients (n = 259) it was found that a modified Mediterranean Diet (35% carbohydrate, 45% fat high in monounsaturated fat, 15–20% protein) was associated with the lowest ALT levels at 6 and 12 month of follow-up. The two other diets being the 2003 ADA diet (50–55% carbohydrate, 30% fat and 20% protein) and a low glycemic index diet (50–55% carbohydrate, 30% fat, 15–20% protein). When adjusted for changes in BMI, waist–hip ratio, HOMA-IR and triglycerides the evidence for the effect of the Mediterranean Diet on ALT levels persisted [33].

5.3. *Low-carbohydrate diet*

Dietary carbohydrate is the main macronutrient affecting postprandial glucose levels, therefore limiting carbohydrates might be a logical approach to lowering postprandial blood glucose levels [16]. Weight loss with low carbohydrates diets has become more common in recent years and evidence suggests that these diets are superior for short term weight loss and possibly as effective as other strategies for the long term [13,40,41]. In a meta-analysis of randomized controlled trials, comparing the effects of low-carbohydrate diets without energy restriction with low-fat energy restricted diets on weight loss in individuals with BMI $\geq$25, low-carbohydrate diets were more effective in inducing weight loss after 6 months and had more favorable effects on HDL-C and triglyceride levels. However, total cholesterol and LDL-C levels decreased more in individuals randomized to low-fat diets, and at 12 months, no significant difference was found between the diets regarding weight loss [41].

In a meta-analysis of 13 trials on restricted carbohydrate diets in subjects with T2DM levels of HbA1c, fasting glucose and triglycerides improved with lower carbohydrates diets. A greater reduction in hyperglycemia was found in the low versus high carbohydrate diets and in 9 of 11 studies evaluating HbA1c; it decreased or was reduced to a greater extent on the lower-carbohydrate diet. Although no significant relation was observed between the carbohydrate content of the diet and weight, a 10% increase in caloric intake from carbohydrates was associated with a 3.2 $\pm$1.2% increase in glucose levels (P = 0.047) and a 7.6 $\pm$ 0.6% increase in triglyceride levels (P = 0.001) [40].

The effect of a low-carbohydrate versus a low-glycemic index diet on glycemic control was tested in 84 obese subjects with T2DM who were randomized to either a low-carbohydrate diet (<20 g of carbohydrate daily); or a low-glycemic, reduced-calorie diet (500 kcal/day deficit) for 24 weeks. Both interventions led to improvements in HbA1c, fasting glucose, fasting insulin, and weight loss. The low carbohydrate diet group had a more marked improvement in HbA1c (−1.5% vs. −0.5%, P = 0.03), body weight (−11.1 kg vs. −6.9 kg, P = 0.008), and HDL-C (+5.6 mg/dL vs. 0 mg/dL, $P < 0.001$) compared with the low glycemic index diet group. Additionally, diabetes medications were reduced or eliminated in 95.2% of low carbohydrate vs. 62% of low glycemic index participants ($P < 0.01$) [42]. In another randomized trial 132 obese adults of whom 83% had diabetes or the metabolic syndrome, received counseling to either restrict carbohydrate intake to <30 g/day (low-carbohydrate diet) or to restrict caloric intake by 500 calories/day with <30% of calories from fat (conventional diet). After one year, mean weight change was similar in the two diet groups but in the low-carbohydrate diet, triglyceride levels decreased more (P = 0.044) and HDL-C levels decreased less (P = 0.025). In the subgroup of diabetic patients (n = 54) after adjustment for covariates (including weight loss), HbA1c levels improved more in the low-carbohydrate diet group [43]. A meta-analysis evaluating the effect of the proportions of fat and carbohydrates in the diet on glucose and lipid parameters, examined two kinds of diets – a low-fat/high-carbohydrate diet (58% of calories from carbohydrates and 24% from fat) and a high-fat/low-carbohydrate diet (40% of calories from carbohydrates and 40% from fat). No difference was found in values for HbA1c, fasting plasma glucose, and total and LDL-C between the groups. However, in the low-fat/high-carbohydrate diet, fasting insulin and triglyceride levels were significantly elevated (P = 0.02 and $P < 0.001$ respectively) as compared with the high-fat/low-carbohydrate diet [14]. In two recent 2-year dietary intervention studies [13,44], a low-carbohydrate diet was associated with a greater decrease in triglycerides and insulin and greater increase in HDL-C as compared with a low-fat diet.

5.4. *Low-glycemic-index/load diet*

The glycemic index (GI) was defined as the area under the postprandial blood glucose curve of a food containing carbohydrate, relative to the area under the curve after ingestion of the same amount of carbohydrate as a reference food (typically glucose or white bread) [16,45]. The GI may be considered as a measure of carbohydrate quality [46] with different foods having different influence on postprandial blood glucose level, thus making it possible to grade them by using the GI. Low GI foods may contribute to glycemic control by allowing a gradual supply of glucose to the blood and lower insulin release as compared with higher GI foods [9]. Dietary components tending to lower glycemic response are fibers, fructose, lactose, and fat. Some examples of food items with low GI are: oats, barley, bulgur, legumes, pasta, apples, oranges, yogurt, and ice cream [16]. The glycemic load represents the overall glycemic effect of a diet and is calculated by multiplying the GI by the amount of carbohydrates in each food component consumed and then totaling the values for all food items [9,16]. In a 6 month dietary intervention study comparing low GI with high cereal fiber diets, it was found that the low GI diet lowered HbA1c to a greater extent and in contradiction to the high cereal fiber diet, increased HDL-C [47]. In a recent review of randomized controlled trials with interventions 4 weeks to 12 month long, low GI diets significantly improved diabetes control, in less than ideally controlled individuals, by lowering HbA1c levels by a clinically significant 0.5%. This reduction in HbA1c was associated with a decrease in hypoglycemic events and an increase in insulin sensitivity [9]. In an intervention trial of 12 weeks of energy restriction, 53 overweight subjects were given a four week run-in period of a high saturated fat (SFA) diet (1540 kcal/day, 17% SFA) after which they were randomly assigned to either a high- or low-GI diet (1440 kcal/day, 60% carbohydrate, 5% SFA) for eight weeks. Subjects were divided into three groups of low, median and high glucose tolerance. Weight loss was not different between low and high-GI diets. However, HbA1c was reduced twofold more in subjects consuming a low-GI diet as compared to subjects consuming a high-GI diet, but the finding was not statistically significant. LDL-C concentrations were also reduced more in subjects with low glucose tolerance on the low-GI diet (P = 0.02) [48]. In a one year intervention trial patients with T2DM, managed by diet alone (n = 162) were randomly assigned to receive high-carbohydrate/high-glycemic-index (high-GI), high-carbohydrate/low-glycemic-index (low-GI), or low-carbohydrate/high-monounsaturated-fat (low-CHO) diets. The high-GI, low-GI, and low-CHO diets included respectively, 47%, 52%, and 39% of energy as carbohydrate and 31%, 27%, and 40% of energy as fat. Body weight and HbA1c did not differ significantly between diets. Fasting glucose was higher (P = 0.041), but 2-h post load glucose was lower (P = 0.010) after 12 month of the low-GI diet. With the low-GI diet, overall mean triglycerides were 12% higher and HDL cholesterol 4% lower than with the low-CHO diet ($P < 0.05$). Overall mean CRP with the low-GI diet, was 30% less than that with the high-GI diet, (P = 0.0078); CRP concentration with the low-CHO diet, was intermediate [49].

In addition to these findings there are inconsistent reports of GI effects on glycemic and metabolic control. These inconsistent findings may be due to practical and methodological problems, for instance the large individual variability in responses to carbohydrate-containing foods and the inability to predict mixed meal responses [16,46]. Nevertheless, individuals with poor glycemic control on a high GI diet may have some benefits in glycemic control when applying low GI diets [9,16].

6. Conclusions

Interpretation of results from different studies on dietary strategies may be complex since there is often no consistency in diet composition. Nevertheless, it seems that low fat diets are effective for weight loss and are associated with some metabolic benefits; however, some recent trials have shown that low carbohydrate diets are as efficient in inducing weight loss and in some metabolic measures such as serum triglycerides and HDL-C may be even superior to low fat diets. When addressing the issue of diet quality rather than quantity applying the glycemic index may have some added benefits. Furthermore special features of the Mediterranean Diet have apparent additional favorable effects for patients with T2DM.

Conflict of interest

All authors declare to have no conflict of interest.

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