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Original Paper

Utility of a Short-Term 25% Carbohydrate Diet on Improving Glycemic Control in Type 2 Diabetes Mellitus

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Key words: type 2 diabetes mellitus, carbohydrate, hemoglobin A_{1c}, glycemia, diet

Objective: To determine if introduction of a low carbohydrate diet might be a useful option for type 2 diabetic patients who do not achieve glucose target levels despite conventional treatment.

Methods: Subjects with type 2 diabetes, either treated with diet alone (n=9) or second generation sulfonylurea agents (n=19), which were discontinued, were placed on a diet based on ideal body weight and comprised of 25% carbohydrate. After a mean of 8 weeks, they were then switched to a calorically equivalent diet, but composed of 55% carbohydrate.

Results: Compared to baseline diet, after 8 weeks of a 25% diet, subjects showed significantly improved glycemia as evidenced by fasting blood glucose values ($p<0.005$) and hemoglobin A_{1c} levels ($p<0.05$). Those previously treated with oral hypoglycemic agents showed, in addition, a significant decrease in weight and diastolic blood pressure despite the discontinuation of the oral agent. When then placed on a 55% carbohydrate diet, the hemoglobin A_{1c} rose significantly over the ensuing next 12 weeks ($p<0.05$).

Conclusion: A low carbohydrate, calorically-restricted diet has beneficial short-term effects in subjects with type 2 who have failed either diet or sulfonylurea therapy and may obviate the necessity for insulin. Our study also affirms the need for reassessing the role of diet whenever type 2 diabetic patients manifests hyperglycemia, despite conventional oral treatment or diet management.

INTRODUCTION

A study was undertaken to determine if introduction of a low carbohydrate diet might be a useful option for patients with type 2 diabetes mellitus who were not achieving glucose target levels on standard therapy. The two groups of patients were evaluated: 1) subjects maintained on a standard dietary regimen of 55 to 60% carbohydrate; and 2) subjects who were considered to be secondary failures of oral hypoglycemic therapy with sulfonylurea agents [1–3].

BACKGROUND

Dietary treatment and exercise comprise the basic recommendations of health care professionals for persons with type 2 diabetes. The form those recommendations takes is highly variable and remains controversial [4]. Furthermore, these approaches tend to be more time consuming than prescribing of oral hypoglycemic agents and in a busy practice tend to be

given little attention. Up until 1994, the nutrition guidelines of the American Diabetes Association advocated diets comprised of 55 to 60% carbohydrate, 12 to 20% protein and <30% fat [5–7]. These guidelines were developed as an extension of the “prudent diet” guidelines for the general population regarding avoidance of coronary vascular disease without specific study of the resultant glycemia achieved with these diets for persons type 2 diabetes [8–12] or independent of weight loss which is known to impact glucose tolerance and risk for vascular disease [13]. Unfortunately, few therapeutic approaches to type 2 diabetes reliably result in sustained weight loss [14]. The new recommendation of The American Diabetes Association allows for individualization of the diet to achieve and maintain normoglycemia [15]. The carbohydrate distribution may therefore be adjusted to achieve the desired glucose targets.

The clinical course of type 2 diabetes generally is one of progressive escalation of therapies culminating in the introduction of insulin treatment [16]. The role of insulin in the initiation and/or propagation of complications related to type 2

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diabetes is of concern and remains an area of intense investigation [17]. We hypothesized that rather than escalate therapy with oral agents in persons who “failed diet” or with insulin in persons who “failed sulfonylureas”, we might be more successful by returning to dietary instruction, but this time with a low carbohydrate diet, extending the new nutritional guidelines of The American Diabetes Association [15] to become the mainstay of therapy. The results of these efforts are reported here.

STUDY POPULATION

We obtained approval by appropriate institutional review for all studies and informed witnessed consent from each subject. The subject population consisted of eight males and 20 females with the primary diagnosis of type 2 diabetes mellitus (Table 1). The inclusion criteria included a history of diagnosis of diabetes after 40 years of age, treatment for over a year with diet or oral hypoglycemic agents, a C-peptide value above the normal range, and considered a “failure” to achieve treatment goals of a hemoglobin A_{1c} less than 7%. In addition, patients with documented glucose values exceeding 200 mg/dl by self blood monitoring or random testing in a health care facility were included. Exclusion criteria included subjects treated with insulin, those with a history of severe hyperlipidemia requiring treatment or those with documented abnormalities in renal, thyroid, or hepatic function by standard tests. Each subject was seen weekly during the study, during which time diaries were collected, blood drawn, blood pressure and weight recorded, and dietary instruction given. Subjects were followed for a

Table 1. Demographic of the 2 Groups (Previously Treated and Not Previously Treated with Oral Hypoglycemic Agents Groups) of Type 2 Diabetic Subjects Included in the Study

	Previously treated with sulfonylureas (n=19) ^a	Not previously treated with sulfonylureas (n=9) ^a	Significance
Age	67±6.2	65.2±6.9	NS
Gender n (%)			
Female	13 (68.4%)	7 (78%)	NS
Male	6 (31.6%)	2 (22%)	NS
Height (cm)	163.0±11.1	163.9±8.0	NS
Weight (kg)	76.0±15.1	81.7±20.1	NS
Diabetes duration (years)	8.2±7.6	4.3±3.6	NS
Previous history of hypertension n (%)	12 (63%)	4 (44%)	NS
Ethnicity			
Caucasians	12	5	
Latinos	6	4	
Oriental	1	0	

NS=not significant.

^a Values are mean±standard deviation determined with the unpaired Student’s t-test.

mean of 7.9±2.7 weeks during the 25% carbohydrate diet. The subjects were then placed on a 55% carbohydrate for a mean of 12±3 weeks.

MATERIALS AND METHODS

Diet

Subjects qualifying for the study were entered and taught a diet consisting of 25% carbohydrate (85% complex carbohydrates and 15% simple carbohydrates), 45% protein, and 30% fat with an emphasis on unsaturated fat. Portion sizes were illustrated with sample meal plans and pictures of sample meals. Compliance was documented by asking the patients to record all ingested foods which was reviewed weekly by the nutritionist on our team. Alcohol was eliminated from the diet. The recommended caloric intake was based on ideal body weight [18]. The diet was introduced by modifying the American Diabetes Association Exchange Lists for Meal Planning [19] to substitute all starch and milk portions by protein portions and by selecting only one fruit portion a day, advocating fruits such as apples with a relatively high fiber content. After a mean 7.9±2.7 weeks, the 28 patients were placed on a energy equivalent 55% carbohydrate, 20% protein, 25% fat diet, referred to as an “ADA” diet for a mean of 12±3 weeks.

Discontinuation of Oral Hypoglycemic Agents

Sulfonylurea agents were gradually tapered at a rate of approximately 5 mg per week. The rate of adjustment was monitored weekly and could be accelerated or slowed depending on home blood glucose monitoring values in the hypo- or hyperglycemic ranges, respectively.

Home Blood Glucose Monitoring

Capillary home blood glucose monitoring (One Touch II, Lifescan, Milpitas, CA) was performed by all subjects at least four times per day: before breakfast and 1 hour after the beginning of breakfast, lunch, and dinner. Subjects were also encouraged to document blood glucose readings if they felt hypoglycemic or “funny”.

Laboratory Studies

Hemoglobin A_{1c} levels were measured at baseline, at the end of the 25% carbohydrate diet, and then again after completion of the 55% carbohydrate diet. Hemoglobin A_{1c} levels were measured by boronate affinity high performance liquid chromatography with inter- and intra-assay coefficients of variation <3% (Primus Corporation, Kansas City, MO). Fasting blood glucose measurements utilized a glucose oxidase method (HemoCue D, Mission Viejo, CA).

Data Analysis

The comparison of the different variables at baseline, on the low carbohydrate, and the 55% carbohydrate diet was performed by a paired Students-t test. In each case, the baseline diet was considered to be the American Diabetes Association prescription of at least 55% carbohydrate. The baseline variables entered were weight, body mass index (BMI), blood pressure, hemoglobin A_{1c} and fasting glucose. An unpaired Students-t test analysis was performed to compare the demographics between the two groups studied.

RESULTS

Table 1 describes the subject population. Of the 28 subjects, 19 were taking oral hypoglycemic agents prior to entry into the study and nine had never been treated with oral hypoglycemic agents. As shown in Table 1, there were no differences between those subjects who had not previously received oral hypoglycemic agents and those who had (except that the former were slightly heavier and had shorter duration of diabetes compared to the later).

Each of the 19 subjects taking sulfonylurea agents were able to discontinue them with significantly improved glycemia during the 25% carbohydrate diet (Table 2). Table 2 further documents that there was a significant decrease in weight, diastolic

Table 2. Diabetic Patients Previously Treated With Oral Hypoglycemic Agents (N=19)
Comparison of variables after a mean duration of 8 weeks of 25% carbohydrate diet

	Baseline ^a	After 25% CHO diet ^a	Significance
Weight (kg)	76.0±15.1	74.6±16.8	<0.001 ^b
BMI (kg/m ²)	27.9±4.8	26.5±6.1	NS
Systolic BP (mmHg)	136±11.4	131.5±12.4	NS
Diastolic BP (mmHg)	83.2±6.4	78.5±5.6	0.013 ^b
Hb A _{1c} (%)	9.9±1.9	8.1±1.0	0.002 ^b
Fasting blood glucose (mg/dl)	257.6±50.8	192±37.4	0.001 ^b

Comparison of variables after a mean of 12 weeks on a 55% carbohydrate diet

	After 55% CHO diet ^a	Significance compared to 25% carbohydrate diet
Weight (kg)	77.0±16.7	NS
BMI (kg/m ²)	31±5.8	NS
Systolic BP (mmHg)	133±14.1	NS
Diastolic BP (mmHg)	78±6.3	NS
Hb A _{1c} (%)	8.9±1.3	0.008 ^b
Fasting blood glucose (mg/dl)	183±43	NS

^a Mean±standard deviation determined with the paired Student's t-test.

^b Indicates significance less than 0.05.

NS=not significant.

blood pressure and glycemia as documented by hemoglobin A_{1c} values and fasting plasma glucose.

Similar, but less dramatic findings, occurred in the nine subjects who entered the study having been treated with diet alone (Table 3). There was a trend toward weight loss and a diastolic blood pressure decrease in this group of subjects but the results were not statistically significant. There was a significant decrease in glycemia as documented by hemoglobin A_{1c} values and fasting plasma glucose. No significant correlation was found between diet duration and blood pressure, weight or fasting blood glucose levels in either group.

Fig. 1 and 2 diagram the change in glycemic control during the three observation periods: before the low carbohydrate diet, after the low carbohydrate diet, and after at least 12 weeks of a 55% carbohydrate diet. As can be seen, in both the patients who were previously treated with sulfonylurea agents and those who came to the study on dietary treatment alone, a low carbohydrate diet significantly improved their glycemic control. Once they were placed on a 55% carbohydrate diet, their glycemic control deteriorated, as manifested by a significantly higher hemoglobin A_{1c} level in both groups.

DISCUSSION

The present study documents that introduction of a low carbohydrate diet with caloric requirements based on ideal

Table 3. Diabetic Patients Not Previously Treated with Oral Hypoglycemic Agents (N=9)
Comparison of variables after a mean duration of 8 weeks of 25% carbohydrate diet

	Baseline ^a	After 25% CHO diet ^a	Significance
Weight (kg)	81.7±20.1	80.9±20.5	NS
BMI (kg/m ²)	29.6±6.5	29.3±6.6	NS
Systolic BP (mmHg)	128.8±15.5	133.8±13.3	NS
Diastolic BP (mmHg)	80.8±5.5	78.7±6.5	NS
Hb A _{1c} (%)	9.2±1.6	7.8±1.9	0.049 ^b
Fasting blood glucose (mg/dl)	261.7±71.2	171.6±61.6	0.004 ^b

Comparison of variables after a mean duration of 12 weeks of 55% carbohydrate diet

	After 55% CHO diet ^a	Significance compared to 25% carbohydrate diet
Weight (kg)	82.0±21	NS
BMI (kg/m ²)	31±6.0	NS
Systolic BP (mmHg)	128±13.0	NS
Diastolic BP (mmHg)	78±11	NS
Hb A _{1c} (%)	9.0±1.3	NS
Fasting blood glucose (mg/dl)	231±54	0.04 ^b

^a Mean±standard deviation determined with the paired Student's t-test.

^b Indicates significance less than 0.05.

NS=not significant.

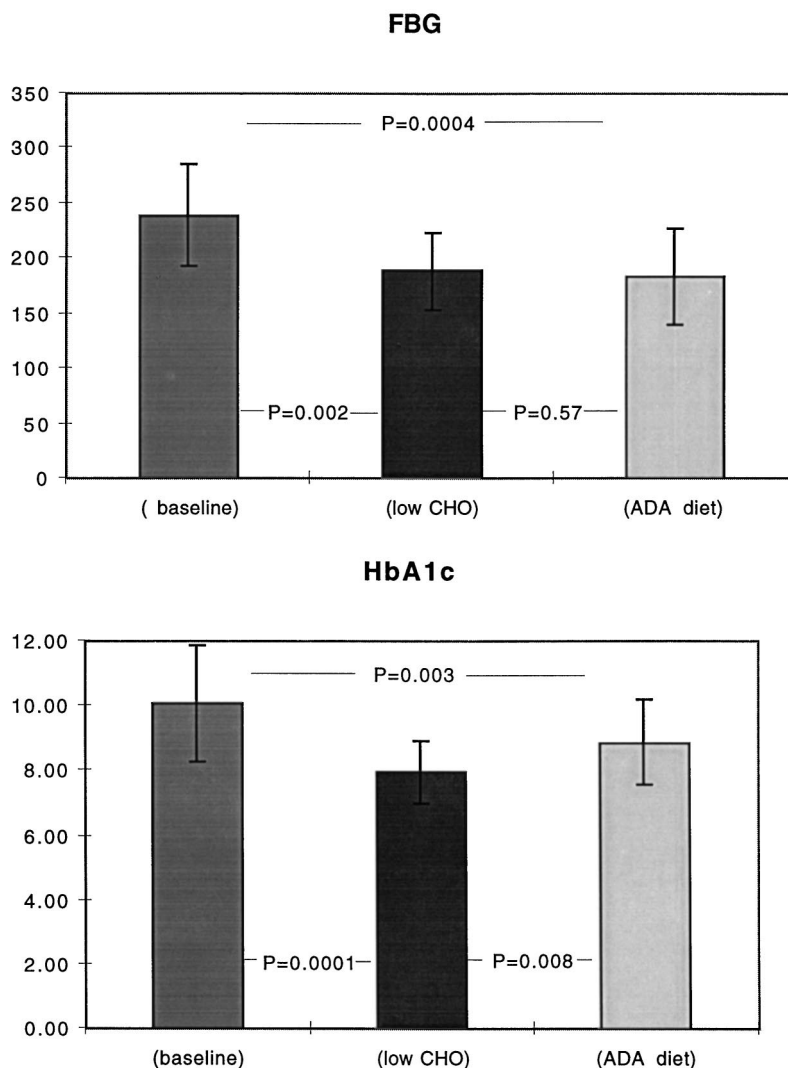


Fig. 1. Comparison of the fasting blood glucose levels and HbA_{1c} in 19 patients previously oral sulfonylurea failures treated with a mean of 8 weeks on a 25% carbohydrate diet (low CHO) and then switched to a 55% carbohydrate diet (ADA diet). Bars represent standard deviations from the mean.

body weight results in short term improvement in glycemia in type 2 diabetic subjects, who have failed either diet alone or diet plus sulfonylurea therapy. In those subjects on sulfonylurea therapy, the improved glycemia was achieved despite discontinuation of the oral hypoglycemic agent. Improved glycemia was obtained in the group of subjects who achieved significant weight loss (previously treated with oral agents), and in those who did not (previously treated with diet alone). In addition, increasing the percentage of carbohydrate in the diet, while maintaining the caloric restriction, resulted in deterioration of glucose control as manifested by a significantly increased hemoglobin A_{1c} level. It is of note that sulfonylurea therapy is commonly associated with weight gain [20]. Thus discontinuation of the oral agent may have facilitated weight loss in this group of subjects over the time course of the study.

Although the effects of a high protein diet in persons with

diabetes have been studied before in well-designed studies [21] it remains to be seen whether the short-term gain in glycemia documented in the present study can be sustained with continued dietary management, whether sustained consumption of higher protein content diets may be detrimental and lead to progressive decrease in renal function and damage over time, and an increased risk of breast and colon cancer. Nevertheless, the results of the present study emphasize the utility of a return to dietary instruction on carbohydrate content of the meal plan even in those patients who have failed oral hypoglycemic agent therapy before insulin therapy is begun. In addition, improved insulin sensitivity and thus improved glycemia may also have been related to the type of carbohydrates prescribed. The relative benefit of insulin therapy in type 2 diabetes remains controversial and the results of our study would suggest that dietary therapy may sustain remission for an interim and allow

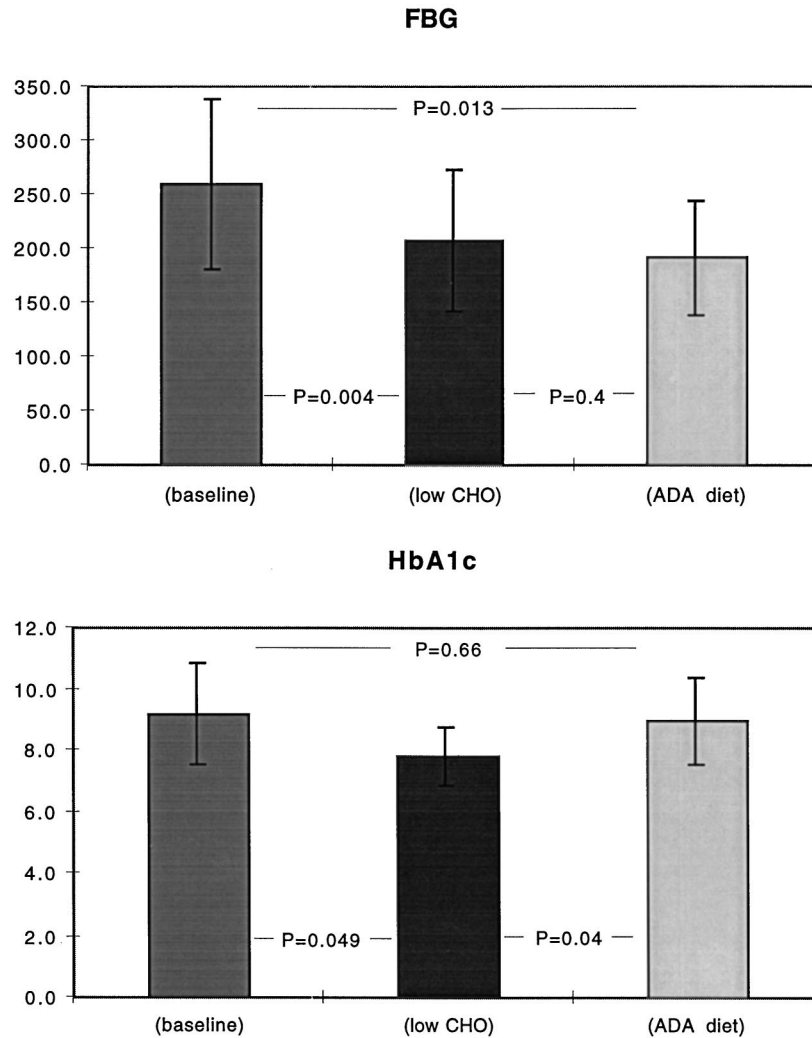


Fig. 2. Comparison of the fasting blood glucose levels and HbA_{1c} in nine patients previously diet alone failures treated with a mean of 8 weeks on a 25% carbohydrate diet (low CHO) and then switched to a 55% carbohydrate diet (ADA diet). Bars represent standard deviations from the mean.

the re-introduction of oral hypoglycemic therapy in the event that low carbohydrate diet therapy alone is not successful. The 1.6% reduction in hemoglobin A_{1c} values achieved by minimizing carbohydrates in the diet is comparable to the decrease in hemoglobin A_{1c} values seen in studies of acarbose, an alpha-glucosidase inhibitor of starch metabolism in the intestine [22]. Thus with a low carbohydrate diet, one can achieve the benefits of this form of oral hypoglycemic therapy without exposure to an additional drug.

The longer term consequences of the dietary approach evaluated here remain to be determined. In view of the positive response of glycemia seen in our subjects, further studies are warranted to determine whether similar improvements are seen in lipid levels and for what subsets of subjects with type 2 diabetic patients low carbohydrate diets might be advantageous.

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