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Diet in Patients with Non-Alcoholic Fatty Liver Disease: A Pilot Study

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Aim: The aim of this study was evaluating the role of diet in induction and management of NonAlcoholic Fatty Liver Disease (NAFLD).
Place and Duration of Study: The study was performed in Taleghani Hospital, Tehran, Iran for one year.
Methodology: Dietary intakes of 24 patients with biopsy proven NAFLD referring to Taleghani Gastroenterology Clinic (Tehran, Iran) were analyzed by a detailed food frequency questionnaire. Dietary intervention including a proper dietary intake and advice on increasing individual activities was applied for them, and the effect of it was assessed after 6 months.
Results: we did not find any significant differences between patients with NAFLD and healthy control population in the case of blood pressure, blood glucose, total cholesterol, and HDL cholesterol, but weight, height, BMI, waist, waist/hip ratio, and triglycerides, were significantly higher in patients than controls. The carbohydrate intake in patients was significantly more than controls while the protein consumption was significantly lower in patients than controls. We did not find any significant difference in the other dietary intakes. All anthropometric, biochemical, and histopathologic characteristics of the patients decreased after six months dietary intervention, however none of these differences were statistically significant.

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Conclusion: Our results indicate that dietary intake in patients with NAFLD is different from normal population, and a 6-month dietary and life-style consultation might result in improvement in clinical and para-clinical features of NAFLD.

Keywords: NAFLD; diet; NASH; nutrition; nutrients.

1. INTRODUCTION

Non-alcoholic Fatty Liver Disease (NAFLD) can be defined as significant hepatic steatosis that is not the result of alcohol, drugs or any other single identifiable cause. While patients with steatosis alone tend to have a relatively benign course, patients with NAFLD are at risk for progression to fibrosis and cirrhosis. The prevalence of this syndrome is going to be the most common liver disorder in the most countries by increasing the prevalence of obesity [1,2].

Although the exact mechanism for development of NAFLD is not known, recent studies have shown that the characteristics of the metabolic syndrome (abdominal obesity, fasting glucose, blood pressure and dyslipidaemia expressed by hypertriglyceridaemia or by lower levels of high density lipoproteins; HDL) are also high-risk categories for NAFLD [3-6]. However, the association of some dietary factors with these risk factors have been shown previously [7,8], there are limited studies evaluated the relationship between diet and NAFLD [9-11], and there is no established guideline for treatment of NAFLD [12-17].

The aim of this study was to compare dietary habits in patients with NAFLD with an age and sex matched normal population and to assess the effect of the standardized diet in management of these patients.

2. METHODS

2.1 Subjects

Twenty four patients with biopsy proven NAFLD whose diagnosis was confirmed by liver biopsy, and 780 age and sex matched patients without liver diseases were studied in the Gastroenterology Clinic of Taleghani Hospital (Tehran, Iran). The diagnosis of NAFLD was based on the established criteria described previously [18], and was proven by liver histology. Patients with other causes of liver disease including markers of chronic viral infection B and C, alcohol intake more than 20 g/day, alpha-2 antitrypsin deficiency, primary biliary cirrhosis, hemacromatosis, autoimmune hepatitis, and Wilson disease were not considered based on history, lab results, and histologic features. No patient was on medications known to cause steatohepatitis, or weight loss, and none of them had a weight loss surgery in the past year. The study was approved by Research Center for Gastroenterology and Liver Disease Ethics Committee and all patients gave their written informed consent to participate.

2.2 Assessment of Dietary Intake

Dietary intake was assessed using a 68-item semi-quantitative food frequency questionnaire (FFQ), which were administered by trained dietitians. The FFQ consisted of a list of foods with a standard serving size and participants were asked to report the frequency with which they consumed each food item during the previous year on either a daily (e.g. bread), weekly (e.g. rice or meat), or monthly (e.g. fish) basis. For standardization purposes, portion sizes were converted from household measures to grams and every food and beverage item were subsequently coded according to the protocol and analyzed for energy content and other nutrients using Nutritionist III software (Version 7.0; N-Squared Computing, Salem, OR), which was designed for Iranian food.

2.3 Assessment of Other Variables

The weight of each participant was obtained, and recorded to the nearest 0.1 kg, using a digital scale, when they were minimally clothed and not wearing shoes. Using a tape measure, the height of each participant was acquired, when they were standing in a normal position without shoes. The height and weight measurements were then used to calculate the body mass index (BMI) for each participant. To avoid placing pressure on the body, a lax tape measure was used to measure each participant's hip circumference as the widest point. Waist circumference was also measured and recorded, but it was taken from the narrowest point between the lowest rib and the iliac crest. The measurements were recorded

to the nearest 1/10th of a centimeter. Individuals' blood pressure was measured on two occasions, after each had sat for a fifteen minute period. Additional, previously validated, questionnaires were used to obtain further covariate information, such as age, and history of other disorders. Body Impedance Analysis (BIA) was used to assess body composition in patients with NAFLD. Blood samples were drawn from each subject after an overnight 12 hour fasting period for the purpose of glucose, insulin, alanin aminotransferase (ALT), aspartate aminotransferase (AST), and lipid concentration measurements. Insulin resisresistance was assessed by homeostasis model assessment of insulin resistance (HOMA-R) calculated as the product of plasma glucose (milligrams per deciliter) multiplied by serum insulin (milliunits per liter) divided by 405. Liver biopsy was performed for each patient before and after dietary intervention using modified Brunt scoring described previously [19].

2.4 Dietary Intervention

All patients with NAFLD received standardized nutritional counseling. The diet was designed according to an individual basis, body composition analysis, clinical status, and lab features of patients. The patients were divided to three groups according to their BMI. Subjects with normal BMI were educated how to consume each food group properly. Patients with over weight to obesity class III underwent a regimen with a lower calorie than they needed to loss weigh (2-4 kg/month). All of diets were based on 15-20% of calories from proteins, 25-30% from fats with emphasis on mono and poly unsaturated fats, and 50-55% from carbohydrates with emphasis on complex carbohydrates.

In the first 3 months, patients should consume only vegetarian protein and in the second 3 month they should consume either vegetarian protein or vegetarian proteins combined with meats. The dietary adjustments included increased intake of fibers such as vegetables and fruits, and advice on increasing the individual activities. Patients were monthly controlled to be motivated and continue their diet. They could easily make contact to our clinic, if they had any problem. The patients were visited every month, and their adherence to recommended diet was evaluated using a 24 hours recall. All clinical and Para clinical examination were repeated 6 months after intervention.

2.5 Statistical Analysis

All data are presented as means±standard deviation. Statistical analysis was performed using SPSS software (version 11.5; SPSS Inc, Chicago, IL). Data were analyzed using the chi-square or Fisher exact test. Quantitative variables were compared using analysis of covariance, after adjustment for height, and log transformation if normality was not present. $P< 0.05$ was considered statistically significant.

3. RESULTS

Base line Clinical and para-clinical features of patients and controls are presented in Table 1. As we matched the age and sex between patients and controls, there is no significant difference in these regards. Also, we did not find any significant differences between two groups' blood pressure, blood glucose, total cholesterol, and HDL cholesterol, but weight, height, BMI, waist, waist/hip ratio, and triglycerides, were significantly higher in patients than controls. The dietary intakes of patients and controls are compared in Table 2. The carbohydrate intake in patients was significantly more than controls while the protein consumption was significantly lower in patients than controls. We did not find any significant difference in the other dietary intakes. All anthropometric, biochemical, and histopathologic characteristics of the patients decreased after six months dietary intervention table-3, however none of these differences were statistically significant.

4. DISCUSSION

Our results showed that some metabolic syndrome characters such as central obesity, hypertriglyceridemia, and history of Diabetes type 2 are more prevalent in patients with NAFLD, which further consolidate the general consensus [20,21] indicating that NAFLD might be the hepatic feature of metabolic syndrome; however we did not find a significant difference between patients and controls in the field of the other components of metabolic syndrome. Our findings are exactly in line with Gholam et al. study [22] that has shown that hypertriglyceridemia and hyperglycemia but not other components of the metabolic syndrome are associated with NAFLD.

Unlike Cortez-Pinto et al. [9] who reported that NAFLD patients recall a diet richer in fat and

poorer in carbohydrates and protein, we found that the patients with NAFLD consume more carbohydrates, and less protein than the normal population. Toshimitsu et al. [23] also have shown that the patients with NAFLD have a more intake of carbohydrate and less intake of protein and zinc in comparison with the patients with simple steatosis, but they did not find any difference in nutrient intakes between patients and healthy controls. These different results can be due to different social and cultural behaviors in the different study groups. Also, the duration of diagnosis of disease and the physician advices in this regard might be resulted in less consumption of fat in some patients, which is a limitation in our study.

Table 1. Demographic, anthropometric, and lab characteristics of patients and controls*

Parameters	Patients (n=24)	Controls (n=780)
Age (y)	40.59±10.4	40.58±11.8
Male/Female	10/2	653/127
Weight (kg) †	88.1±12	71±13.5
Height (cm) †	170±9.8	163±7.9
BMI (kg/m^2) †	30.5±5.3	26.6±4.8
Waist (cm) †	94.66±16.2	83.26±11.8
Waist/Hip ratio†	0.98±0.1	0.86±0.08
SBP (mm Hg)	121.1±12.8	118.7±15.5
DBP (mmHg)	80±8.5	77.9±9.8
Type 2 diabetes (%)†	25%	5.3%
FBS (mg/dl)	101±22	98±12
Triglycerides (mg/dl) †	138.2±54	107.3±65
Total cholesterol (mg/dl)	204±43	201±54
HDL cholesterol (mg/dl)	48±12	53±29

*ALT, alanin aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; HOMA-R, homeostasis model assessment of insulin resistance; SBP, systolic blood pressure; *Data are presented as mean ±SD. †significant difference between patients and controls (p<0.01)*

Moreover, our data showed that a 6-month dietary and life-style consultation might result in improvement in clinical and para-clinical features of NAFLD. Limited studies are available on the efficacy of non-pharmacologic and pharmacologic interventions on liver histology in patients with NAFLD, and to our knowledge, there is no pharmacologic therapy proved to be effective for the treatment of these patients. According to recent studies, the most acceptable drug for these patients is pioglitazone. In one pilot study, Promrat et al. [24] have shown that pioglitazone can improve the histologic and biochemical feature of NAFLD in two-thirds of the patients. However, most of the patients gained weight with the average of 3.5 kg. In another study, 55 patients with NAFLD and impaired glucose tolerance were treated with a hypocaloric diet plus pioglitazone or a hypocaloric diet plus placebo. The improvement in hepatic biochemical and histologic features was more significant in those taken pioglitazone than the placebo group [25]. Despite receiving a hypocaloric diet, the patients who were treated with pioglitazone had a modest weight gain of 2.5 kg and an increase in body fat of 1.5±0.5%. Some studies have shown that gradual weight loss improves serum transaminases as well as reduces hepatic steatosis, inflammation and fibrosis on biopsy [26,27] (23-25). The weight gain, however, is the known side effect of thiazolidinediones, and the long side effects are currently unknown. Our patients had a mean weight reduction of 2.6 kg, while patients in the above mentioned studies had a mean weight gain of about 3 kg.

Table 2. Daily dietary intakes in patients and controls*

Nutrient	Patients (n=24)	Controls (n=780)
Energy (kcal)	2745±230	2543±547
Carbohydrates (g)	401±143	317±35
Fat (g)	91±32	88±34
Protein (g)	75±16	87±34
Carbohydrate (% kcal)†	58±3	50±10
fat (% kcal)	30±7	31±10
Protein (%kcal)†	11±2	14±4
Simple carbohydrate (%)	7.1±4.5	5.9±5.6
Fiber (g)	13±9	17±12
Saturated fat (g)	26±10	22±3
Monounsaturated fat (g)	31±15	21±5
Polyunsaturated fat (g)	16±5	15±9
n-6/n-3 ratio	5.4±0.5	4.1±2.5
Cholesterol (mg)	322±21	316±43
Iron (mg)	5.5±2.3	5±4.5
Zinc (mg)	1.5±0.5	1.2±0.8
Copper (mg)	9.4±1.2	8.1±2.4
Calcium (mg)	786±124	733±256
Magnesium (mg)	289±34	234±55
Vitamin A (µg)	1267±745	1433±132
Folate (µg)	302±4.5	295±15
Vitamin E (mg)	8.7±0.2	8.5±1
Vitamin C (mg)	126±13	125±67

**Data are presented as mean ±SD*
†significant difference between patients and controls (p<0.05)

Table 3. Comparison of the patients characteristics before and after dietary intervention*

Parameters	Before	After
Weight (kg)	88.1±12	85.5±11
BMI (kg/m^2)	30.5±5.3	29.6±5.5
Waist (cm)	94.66±16.2	93.5±15.3
Waist/Hip ratio	0.98±0.08	0.97±0.07
SBP (mm Hg)	121.1±12.8	120±13
DBP (mmHg)	80±8.5	78±9.5
FBS (mg/dl)	101±25	100±28
HOMA-R	4.5±2.8	3.4±3
Triglycerides (mg/dl)	138.2±54	129±62
Total cholestrol (mg/dl)	204±43	205±45
HDL cholesterol (mg/dl)	48±12	48±14
AST (IU/L)	61.9±29.3	48.4±14
ALT (IU/L) †	67.5±35	41.4±17
Body fat percent	31.9±6.6	28.1±7
Steatosis score (0-4)	2.2±1	1.5±1.2
Hepatitis score (0-9)	3.9±1.8	3.1±1.6
Fibrosis score (0-4)	1.8±1.1	1.7±1.1
Total NAFLD score (0-17)	7.9±3.1	6.3±3.1

*ALT, alanin aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; HOMA-R, homeostasis model assessment of insulin resistance; SBP, systolic blood pressure; *Data are presented as mean ±SD. †significant difference between patients and controls ($p<0.05$)*

5. CONCLUSION

In summary, our results indicate that lifestyle modification can improve all aspects of NAFLD, although the differences between before and after intervention did not reach statistical significance. This was likely secondary to the small sample size, and short duration of this pilot study. Hence, larger randomized clinical trial could be the logical next step to explore these results.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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