The Effects of Low-Carbohydrate Diet and Protein-rich Mixed Diet on Insulin Sensitivity, Basal Metabolic Rate and Metabolic Parameters in Obese Patients

Obez Hastalarda Düşük Karbonhidrat Diyeti ve Proteinden Zengin Karma Diyetin İnsülin Sensitivitesi, Bazal Metabolik Hız ve Metabolik Parametreler Üzerine Etkisi

Abstract

**Objective:** Various diet plans with varying ratios of carbohydrates, proteins, and fat ensure weight loss in obesity. The primary aim of our study was to evaluate the effects of weight loss on metabolic parameters; and the secondary aim was to compare the successes of various weight loss regimens in maintaining weight loss.

**Material and Methods:** A team of doctors comprising a dietary consultant and a psychologist developed a program that was followed throughout our study. Twenty-two patients were included in our study. Based on their preference, they were classified into two groups: low carbohydrate diet (Atkins) group and protein-rich mixed diet group.

**Results:** The mean age of the patients was 52.4±3 years, and the mean body mass index (BMI) was 36.1±1.2 kg/m². Five patients followed the Atkins diet, whereas 17 followed the protein-rich mixed diet. Compared with the baseline values, in the 3rd, 6th, and 12th months, body weight (BW), BMI, and waist circumference decreased significantly (p<0.001) in all the patients. Basal metabolic rate decreased in the third and sixth months but increased in the 12th. Fasting blood glucose, fasting insulin, HbA1c, 120-minute blood glucose level in oral glucose tolerance test, total cholesterol, low-density lipoprotein, free fatty acids, and uric acid did not change significantly (p>0.05). In the Atkins group, BMI decreased significantly in the 6th month (p=0.03) but increased in the 12th month (p=0.29). In the protein-rich mixed diet group, BMI (basal 35.1±1.5 kg/m²) decreased significantly (32.8±1.5, p<0.001) in the 6th month, and continued to decrease in the twelfth (31.5±1.2, p=0.007).**

**Conclusion:** In obesity, approximately 10% weight loss can change metabolic parameters moderately. The Atkins and protein-rich mixed diets caused similar weight loss ratios in the first six months, but a protein-rich mixed diet was more successful in terms of long-term sustainability and maintenance of weight loss.

**Keywords:** Atkins diet; diet plans; weight loss

**Anahtar kelimeler:** Atkins diyeti; diyet rejimleri; kilo verme

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Introduction

Obesity is a chronic disease considered to be a global epidemic with increasing incidence worldwide (1). It is associated with a significant increase in morbidity (including diabetes mellitus, hypertension, dyslipidemia, heart disease, stroke, sleep apnea, and cancer) and mortality (2). In weight loss, the aim is to prevent or revert the complications of obesity and increase the quality of life (3). The first step in weight loss management is the intervention of an extensive lifestyle that includes changes in diet, exercise, and behavior (4). Obesity has a multifactorial characteristic that originates from genetic, epigenetic, physiological, behavioral, sociocultural, and environmental factors, and leads to long-term imbalance between energy intake and expenditure. However, in most cases, obesity is caused by behaviors such as a sedentary lifestyle and increased calorie intake (5). To ensure weight loss in obesity treatment, all individuals need to receive consultation on diet, physical activity, behavioral changes, and weight loss goals (6). Data on the success of diet plans, which include varying ratios of dietary fat, protein, and carbohydrate, are controversial (7-10).

The primary aim of this study was to evaluate the effects of weight loss on metabolic parameters, and the secondary aim was to compare the successes of various weight loss regimens in maintaining weight loss.

Material and Methods

Patients who volunteered to participate in the weight loss program were randomly selected and included. A total of twenty-two volunteers (nineteen females and three males) were included in the study. Before the weight loss program began, the patients were asked to record their diet for three days and were provided consultation on their habits. In the weight loss program, two different dietary strategies were implemented: a protein-rich mixed diet and a low-carbohydrate Atkins diet. The patients made the choice of diet for themselves. Calorie intake was set between 1,409 kcal and 2,090 kcal, depending on the patient. The protein-rich mixed diet comprised of 33% protein, 33% fat, and 34% carbohydrate. Atkins diet is usually followed in three stages (11): Stage 1 diet includes 35% protein, 35% fat and 30% carbohydrate for one week; Stage 2 diet includes 35% protein, 35% fat and 30% carbohydrate for eight weeks; and Stage 3 diet includes 30% protein, 30% fat and 40% carbohydrate for a duration that is of the patient’s preference. The patients in the Atkins diet group did not proceed to the third stage after the second but continued with a carbohydrate percentage of 30%.

During the first six months, twenty meetings were conducted for the patients, with each meeting lasting for 2.5 h. During the first 1.5 h of the first nine meetings, group training, which included practical cooking methods, were provided to the patients by the dietary consultants. In the final hour of every meeting, a mild sports activity, which included either gymnastics or water sports, was performed. A doctor was presenting every meeting, and a psychologist was presenting at least ten meetings to provide training. In the last six months, one meeting was conducted every month in the form of 1.5 h of group training, in which dietary consultation was provided (total of six meetings).

Physical examination, basal metabolic rate (BMR) measurement (MVmax29, Sensor Medics, USA), bioimpedance analysis (AKER SRL, 50136 Flana-Italy), and blood gas analysis (ABL 505, Radiometer Kopenhag, DK-2700 Bronshoj/Denmark) were performed in the beginning and in the third, sixth and twelfth months of the study. In addition, real-time serum total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride, free fatty acids, fasting blood sugar, HbA1c, creatinine, urea, uric acid, complete blood count and C-reactive protein levels were measured. A 75 g oral glucose tolerance test (OGTT), test was performed on each patient in the beginning and in the sixth month of the study. A euglycemic clamp test was performed on thirteen patients. Biochemical analyses were performed in the central laboratories of Benjamin Franklin University Hospital in Berlin, Germany.

Euglycemic Clamp Test

It was performed on patients after ten hours of fasting while the patients were lying in a supine position. Single-arm infusions of 40
mU/m²/min human insulin (Actrapid, Novo Nordisk) and 10% dextrose were given to patients. When blood glucose levels were stable for at least two hours, blood samples were collected from the other arm. Capillary blood samples were collected at 5-minute intervals and analyzed using the glucose oxidase method. Insulin resistance was calculated according to the glucose infusion rate. The glucose level was calculated when glucose levels were stable for at least 2 h (80±10% mg/dL was considered stable). Two cannulas were inserted: one in an antecubital vein for the infusion of glucose and insulin, and the other in the opposite upper extremity radial artery or antecubital vein, which was warmed with a heating pillow to arterialize venous blood. When the glucose levels were stable, the blood glucose level was divided by the patient’s weight to calculate the M-value. Homeostatic model assessment for insulin resistance (HOMA-IR) was calculated by using the formula: fasting insulin (mIU/L)×fasting glucose (mmol/L)/22.5 (12).

**Results**

The mean age of patients was 52.4±3 years and the mean body mass index (BMI) was 36.1±1.2 kg/m². Five patients chose to follow the Atkins diet, whereas seventeen patients chose to follow the protein-rich mixed diet. Demographic data and the laboratory values measured in the patients at the beginning of the study are shown in Table 1. Of the twenty-two patients, four left the study during the first three months. Eighteen patients remained in the study for six months, and later, seven left, and eleven patients remained in the study for twelve months. During the follow-up sessions, when all the patients were evaluated, it was found that in the third, sixth and twelfth months, the patients’ body weight (BW), BMI and waist circumference values decreased significantly compared with their baseline values (p<0.001) (Table 2, Figure 1). BMR decreased in the third and sixth months but increased in the twelfth month (1,544-1,524-1,547 kcal). From the bioimpedance

| Patients | Total (n=22) | Atkins diet (n=5) | Protein-rich mixed diet (n=17) | p |
|----------|-------------|------------------|-------------------------------|---|
| Age      | 52.4±3      | 51.6±7.1         | 52.6±3.4                      | 0.26 |
| Sex      |             |                  |                               | 0.63 |
| Female, n (%) | 19 (86.4) | 4 (80)           | 15 (88.2)                     |
| Male, n (%)  | 3 (13.6)   | 1 (20)           | 2 (11.8)                      |
| BMI       | 36.1±1.3    | 39.7±2.2         | 35.1±1.50                     | <0.001 |
| Waist circumference (cm) | 115.4±2.64 | 121±2.65         | 114.1±3.12                    | 0.01 |
| Fat-free mass (kg)   | 60.45±1.55  | 63.03±2.04       | 59.7±1.90                     | <0.001 |
| BIA-Fat mass (kg)    | 39.2±2.04   | 43.2±3.61        | 38.11±2.4                     | <0.001 |
| BIA-Fat percentage (%) | 39.33±0.9  | 40.53±2.5        | 39.0±1.0                      | 0.01 |
| BMR (kcal)         | 1544.1±53.8 | 1713.8±105.6    | 1495.6±57.53                  | <0.001 |
| SBP (mmHg)         | 128.5±4.6   | 139.7±10.5       | 125.5±4.91                    | <0.001 |
| DBP (mmHg)         | 80.6±3.0    | 86.3±11.9        | 79.0±2.5                      | <0.001 |

BMI: Body mass index; BIA: Bioimpedance analysis; BMR: Basal metabolic rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.
analysis, the initial fat mass was 39.2 kg and decreased to 34.7 kg in three months (p=0.007). It was 34.2 kg in the sixth month and remained at 34.9 kg in the twelfth month (p=0.001 compared with the baseline value). Fat-free mass, which represents the muscle mass, decreased from 60.4 kg to 56.4 kg in three months (p<0.001). It was 56.9 kg in the sixth month (p<0.001) and 57.8 kg in the twelfth month (p=0.22 compared with the baseline value). An insignificant decrease was detected in the systolic and diastolic blood pressure in the sixth month compared with the initial values, and an insignificant increase was detected in the twelfth month (Table 2). Fasting blood glucose decreased from 99.83 mg/dL to 93.96 mg/dL in six months (p=0.027). At the end of the twelfth month, fasting blood glucose, fasting insulin, HbA1c, and 120-minute blood glucose level in OGTT did not change significantly compared with the baseline values. Total cholesterol, LDL, TG, free fatty acids, and uric acid also did not change significantly compared with the baseline values. HDL cholesterol increased from an initial level of 1.22 mmol/L to 1.5 mmol/L in twelve months (p=0.008). C-reactive protein and adiponectin levels did not change significantly at the end of the study compared with the beginning of the study (Table 3).

In the Atkins diet group, BW, BMI, and BMR decreased significantly in the sixth month compared with the baseline value (baseline/follow-up values: 104.83/94.6 kg, p=0.03; 39.7/35.8 kg/m², p=0.03; 1,713/1,587.5 kcal, p=0.04, respectively). In the twelfth month, BW increased to 99.4 kg (p=0.3 compared with the baseline value), and BMI increased to 38.9 kg/m² (p=0.29 compared with the baseline value). No significant changes were detected in the blood pH value throughout the diet (Table 4).

In the protein-rich mixed diet group, BW, BMI, and waist circumference values decreased significantly in the sixth month compared with the baseline values (baseline/follow-up values: 98.5/92 kg, p<0.001; 35.1/32.8 kg/m², p<0.001; 114.1/105.9 cm, p<0.001, respectively). The decrease in BW, BMI, and waist circumference values continued in the twelfth month (88.7 kg; 31.5 kg/m²; 105.3 cm, p<0.005, p=0.007, p=0.036, respectively). The basal metabolic rate decreased from the baseline value of 1,695 kcal to 1,373 kcal in the sixth month (p=0.055) and increased back to 1,516 kcal in the twelfth month (p=0.3 compared with the baseline value) (Table 5, Figure 1).
Discussion

The incidence of obesity is increasing globally, and the associated comorbidities constitute major issues in each geographical area. In 2015, 107.7 million (98.7-118.4 million) children and 603.7 million (588.2-
619.8 million) adults were obese worldwide. The overall prevalence of obesity in children and adults was 5.0% and 12.0%, respectively (1,13). Despite the great variance among the countries, data indicate that the incidence of obesity has increased in the last thirty years in most of the populations (6). Large epidemiological studies have shown the association of obesity with diabetes mellitus, hypertension, dyslipidemia, heart disease, stroke, sleep apnea, cancer development, and increased mortality (14-16). Weight loss reduces obesity-associated morbidities and mortality (17).

When the patients in our study were analyzed, although there was a weight change of approximately 9-10% (Table 2), no changes were detected in inflammatory markers such as adiponectin and CRP. Fat may ectopically accumulate subcutaneously and in internal organs (liver, heart, pancreas, skeletal muscle). Ectopic fat accumulation leads to low-grade inflammation (18). In our study, ectopic fat accumulation could not be assessed. The absence of any changes in the inflammatory data in our study may be due to the fact that in patients, weight loss occurred largely in the subcutaneous tissue. However, there were statistically significant changes in waist circumference. This finding is probably due to the low number of cases included. Moreover, in previous studies, it was suggested that the variance in adiponectin, as well as other biological markers in response to weight loss, is not unimportant, and in order to obtain more significant results, either larger cohorts should be analyzed or more marked differences in weight should be ensured (19-22). The results presented in our study were obtained from a small group of eighteen people. Thus, statistically, more significant results can be expected if a higher number of patients are included in cohort studies.

Dietary change is the most important basis of obesity prevention and treatment. A balanced, moderate-fat, low-cholesterol, starchy, low-salt, fiber-rich, and moderate calorie-deficit dietary plan should ideally include three main meals and two snacks (23). Although Atkins diet is popular in social life, it has certain drawbacks. At the beginning of the dietary regimen, weight loss is rapid due to dehydration. This can cause the risk of vitamin, dietary fiber, and mineral deficiencies. This diet may also lead to increased purine intake and, consequently, increased cholesterol levels due to high-fat and high-salt nutrition. Increasing water intake is of vital importance in this diet. By this, kidneys can eliminate the generated ketone bodies and uric acid. In addition to the increased risk of kidney and liver diseases, this diet is associated with a high risk of atherosclerosis, cardiovascular diseases, and gout development. In the Atkins diet group, throughout our study, we did not observe any changes in the laboratory values that confirmed these concerns. This is probably because the patients attended group therapies regularly and were mandated to follow the necessary preventative measures.

One of the significant outcomes of our study was that although a significant change in weight occurred in the Atkins group in the sixth month compared with the baseline value, it was found that the patients gained weight in the twelfth month, and could not maintain the significant weight loss compared with the baseline value. However, in the protein-rich mixed diet group, it was found that weight loss continued during the last six months, and in the twelfth month, significant weight loss compared with the baseline values was attained. Our study has shown that a protein-rich mixed diet is a more sustainable weight loss program than the Atkins diet. Corroborating our findings, a meta-analysis of five studies has reported that the group that preferred a low-carbohydrate diet could not maintain the weight loss that occurred in the first six months into the twelfth month (24). In order to prevent long-term cardiovascular complications of obesity, weight loss programs must be sustainable.

**Study Limitations**

In our study, the dietary preference was left to the patients in order to increase the compliance of the participants. Since the initial design of the study was in this way, the groups were not evenly distributed. In addition, the withdrawal of participants from the study during the follow-up affected this irregularity further.
Conclusion

Multidisciplinary training programs in obesity are successful in ensuring and maintaining weight loss. Despite the successful weight loss, a slight change in metabolic parameters is observed. While weight loss ensures improvement in insulin resistance in the obese with metabolic syndrome, it does not do so in the obese without metabolic syndrome. Atkins diet and protein-rich mixed diet lead to similar rates of weight loss in the first six months, but a protein-rich mixed diet is more successful in the long-term maintenance of weight loss.

Data Availability

This study has been approved by Charite University’s Medical Sciences Ethics Committee, and therefore performed in accordance with the ethical standards laid down by the 1964 Declaration of Helsinki and its later amendments.

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Informed consent

Informed consent of the participants was obtained.

Conflict of Interest

No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Suzan Akpulat, Andreas Pfeiffer; Design: Suzan Akpulat, Andreas Pfeiffer; Control/Supervision: Nazlı Gülsöy Kirnap; Data Collection and/or Processing: Suzan Akpulat; Analysis and/or Interpretation: Andreas Pfeiffer; Literature Review: Nazlı Gülsöy Kirnap; Writing the Article: Nazlı Gülsöy Kirnap, Suzan Akpulat; Critical Review: Andreas Pfeiffer; References and Fundings: Nazlı Gülsöy Kirnap; Materials: Suzan Akpulat.

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