Papel de la dieta cetogénica modificada en la pérdida de peso y los parámetros metabólicos

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Resumen

Fundamentos: La obesidad es un problema de salud generalizado que aumenta el riesgo de diversos trastornos. Este estudio tuvo como objetivo evaluar la eficacia de una dieta cetogénica modificada en la promoción de la pérdida de peso, la mejora de los trastornos metabólicos y la reducción de la resistencia a la insulina en personas obesas durante un período de cuatro meses**.**
Métodos: Se reclutaron 54 participantes obesos de entre 20 y 65 años, con un índice de masa corporal (IMC) superior a 30 kg/m². La dieta cetogénica modificada consistió en un 70% de grasas, un 20% de proteínas y un 10% de carbohidratos del gasto energético diario total. Se midieron los parámetros antropométricos, de composición corporal y metabólicos en el inicio y al final de la intervención. Los datos se analizaron utilizando pruebas t para muestras emparejadas y un modelo de regresión lineal múltiple**.**
Resultados: Se observaron diferencias significativas entre las mediciones iniciales y finales para todos los parámetros (P < 0,001). La dieta cetogénica modificada condujo a una pérdida de peso y reducciones en la masa grasa (0,32 unidades), los triglicéridos (TG) (0,21 unidades) y el Índice de Resistencia a la Insulina por el Modelo de Homeostasis (HOMA-IR) (2,94 unidades). Además, hubo un aumento modesto en el colesterol total (TC) (0,06 unidades) y en la masa muscular (0,03 unidades)**.**
Conclusiones: La dieta cetogénica modificada es eficaz para promover la pérdida de peso, mantener la masa muscular y mejorar los parámetros metabólicos. Por lo que puede considerarse una opción viable para una intervención nutricional a largo plazo.

Palabras clave: Obesidad; Dieta Cetogénica; Trastornos Metabólicos.

Role of modified Ketogenic diet on weight loss and metabolic parameters

Summary

Background: Obesity is a prevalent health concern that increases the risk of diverse disorders. Four months of prospective intervention study was conducted aimed to evaluate the effectiveness of a modified ketogenic diet in weight loss, metabolic disorders, and insulin resistance among obese persons**.**
Methods: A total sample of 54 obese persons between the ages of (20 - 65) years with body mass index > 30 kg/m2 were recruited. The modified ketogenic diet consisted of (70% fat, 20% protein, and 10% carbohydrate) of total daily energy expenditure. Anthropometric, body composition, and metabolic parameters were measured at baseline and the end of the intervention. A paired sample t-test and a multiple linear regression model were used**.**
Results: After 4 months of follow-up, the results found significant differences between initial and final measurements of all parameters (P < 0.001). Furthermore, the findings indicate that following a modified ketogenic diet will result in weight loss and a drop in fat mass of 0.32, TG 0.21, and HOMA-IR 2.94 units. Also, a modest rise in TC (0.06) and muscle mass (0.03) units**.**
Conclusions: The modified ketogenic diet can help with weight loss, maintain muscle mass, and improve metabolic parameters and be used to support long-term nutrition intervention**.**

Key words: Obesity; Ketogenic Diet; Metabolic Disorders.

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Introducción

Obesity is a growing public health problem affecting 38% of people worldwide [1] and is associated with impaired glucose uptake by adipose tissue or inefficient use of insulin, which increases the incidence of metabolic disorders such as type 2 diabetes and dyslipidemia [2].

Different strategies have been proposed for weight loss [3]. Traditional weight loss management such as a caloric restriction with a balanced diet is the most common dietary intervention, which often yields modest weight loss [4], low compliance, and weight regain as a result of the consumption of high-carbohydrate food [5]. Consequently, there is a need for alternative dietary interventions that can effectively induce weight loss and improve obesity-related disorders. The modified ketogenic diet is a high fat, moderate protein, and very low carbohydrate, stimulating physiological changes for effectively managing obesity and metabolic disorders [6]. The ketogenic diet shifts the body to use fat as an alternative energy source of carbohydrates, which lowers blood glucose levels and promotes the production of acetyl-CoA that leads to the formation of ketone bodies from the liver's mitochondria by incomplete fatty acids oxidation, such as acetoacetate, beta-hydroxybutyrate, and acetone [7]. Recent studies have suggested the beneficial effects of ketosis in weight loss, stabilizing blood glucose levels, and minimizing insulin secretion through metabolic pathways [8].

Insulin resistance is an impaired glucose uptake by adipose tissue and muscle, resulting in hyperinsulinemia. Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) is an indicator to evaluate insulin resistance [9]. Moreover, several studies reported the role of the ketogenic diet in improving insulin resistance. A controlled clinical trial study found a significant reduction of HOMA-IR in obese persons after six weeks of ketogenic diet consumption [10]. In addition, people with insulin resistance who follow a ketogenic diet for 12 weeks experience improved glycaemic control this improvement enhances insulin sensitivity, and weight loss, and decreases the use of diabetes medication [11]. On the other hand, dyslipidemia worsens diabetes management by releasing free fatty acids (FFAs) that worsen insulin sensitivity. However, several studies reported consumption of the ketogenic diet shows improved dyslipidemia and reduced diabetes complications [12]. A ketogenic diet improves low-density lipoprotein cholesterol (LDL-cholesterol), triglycerides (TG), total cholesterol (TC), and HOMA-IR [13].

Considering the growing evidence supporting the benefits of the ketogenic diet for weight loss and enhanced metabolic parameters, long-term adherence to the traditional ketogenic diet can be challenging; the modified ketogenic diet offers high healthy fats and a slightly higher protein, which offer flexibility in food choices and greater dietary adherence. Despite the potential benefits of the ketogenic diet, there are limited studies about the physiological impact of the modified ketogenic diet on weight loss and obesity-related disorders. Furthermore, this study aims to evaluate the effectiveness of a modified ketogenic diet in weight loss, metabolic disorders, and insulin resistance among obese individuals. This study seeks to provide practical insight into the feasibility and effectiveness of a modified ketogenic diet as nutritional therapeutic management. The practical insight of a modified ketogenic diet would consider modified ketogenic diet as a new management policy for obesity as well as metabolic disorders.

Material y métodos

Research design

A prospective intervention study was conducted between November 2023 and June 2024. 54 participants with a body mass index (BMI) greater than or equal to 30 kg/m² or were recruited from private nutrition and dietetic clinics over 4 months. The study included participants between 20 - 65 years, with stable weight for at least 4 months, and who are willing to adhere to the dietary regimen and attend regular follow-up visits. Persons who currently follow other dietary programs or use weight management supplements or herbs, those with a history of cardiovascular, liver, or kidney disease, pregnant and lactating women, and those with uncontrolled type 2 diabetes or type 1 diabetes were excluded from the study.

Intervention

The Total Daily Energy Expenditure (TDEE) was calculated using the Mifflin-St Jeor Equation. To achieve weight loss, 500-1000 calories was reduced from TDEE [14]. The modified ketogenic diet consisted of 70% fat, 20% protein, and 10% carbohydrate of TDEE. The daily intake of carbohydrates with a non-starchy low glycemic index was limited to 20-40 grams to induce ketosis. Moreover, 70% of the fat in the modified ketogenic diet was distributed as follows: 50% from polyunsaturated fatty acids and monounsaturated fatty acids, while 20% was saturated fatty acids.

The participants received individualized meal plan counseling at the baseline and every ten days from a qualified registered dietitian to adjust TDEE to ensure nutritional adequacy and maintain ketosis. Moreover, participants were provided with a shopping list, recipes, and guidelines when dining out. Additionally, the participants are instructed to avoid bread, pasta, sugar, milk, corn, beans, and rice. Table 1 shows the recommended food in a ketogenic diet. Adherence to the diet plan monitored through self-reported food diaries

Table 1. Recommended food allowance in the ketogenic diet.

Food items	Suggested food items
Protein	Chicken, turkey, fatty fish, eggs, beef
Vegetables	Cabbage, zucchini, cauliflower, mushrooms, okra, broccoli, spinach, celery, lettuce, garlic, bell peppers, onion, green beans, avocados, lemon
Fruits	Strawberries, raspberries
Fat	Olive oil, butter, ghee, flax seeds, chia seeds, almonds, pecans, walnuts, corn oil, sunflower oil
Dairy products	Heavy cream, full fat cheese
Others	Vinegar, herbs, bone broths

Anthropometric and body composition measurement

Participant's height and weight were recorded barefoot and wearing light clothing at enrollment and at each visit. Height was measured in centimeters (cm) to the nearest millimeter (mm) using a Seca 213 mobile stadiometer, and the mean of three measurements was obtained. The weight was measured using a calibrated bioelectrical scale (Tanita-SC-330). Bioelectrical scale generates the BMI and body composition measurement.

Metabolic parameters:

The participants were asked to fast for at least 12 hours before the blood sample was collected. A fasting blood sample was drawn by a qualified laboratory technician. Blood samples were collected in ethylenediamine tetraacetic acid (EDTA) vacutainer tubes. Lipid profiles such as TG, LDL- LDL-cholesterol, TC, and high-density lipoprotein cholesterol (HDL-cholesterol), were enzymatically analyzed using a standard commercial enzymatic kit.

The values of the lipid profile were expressed as mg/dl. Additionally, blood glucose and insulin levels were measured in mmol/L to calculate HOMA-IR, with the following formula:

HOMA-IR= Fasting glucose level (mmol/L)* Fasting insulin level (mmol/L)/22.5

Ethical consideration

The study was conducted in accordance with the principles of the Declaration of Helsinki, and was approved by the Institutional Review Board of Jerash University (9-2-6-2869). At the time of enrollment, informed consent was obtained from participants.

Statistical analysis

Statistical analyses were performed using SPSS version Version 22 (SPSS statistics for Windows V22, IBM Corp., Armonk, NY, USA). Mean and standard deviation (SD) were used for continuous variables; percentage was used for categorical variables to evaluate the baseline characteristics of the participants. To compare baseline and final intervention measurement values, paired sample t-tests were used. A multiple linear regression model was used to determine the degree and magnitude of association between variables. In the model, the dependent variable was the value of weight at the end of an intervention study, which represents the effect of the ketogenic diet. The independent variables were selective parameters body composition and metabolic parameters, which show the biggest effect on the modified ketogenic diet. The values of R^2 and F were considered to judge about the degree of correlation between variables in the model. In addition, the model was adjusted for age and sex. A p-value of <0.05 was considered statistically significant.

Table 2. Baseline characteristics of the participants

Variables	**N= (54)**
Age	46.8 ± 5.7
Sex	
Male	31 (57.4%)
Female	23 (42.6%)
Weight (kg)	96.4 ± 10.6
BMI	35.2 ± 2
30-35	23 (42.6%)
35-40	31 (57.4%)
TG (mg/dl)	225.4 ± 30
TC (mg/dl)	217 ± 26.1
HDL- cholesterol (mg/dl)	47.3 ± 7
LDL- cholesterol (mg/dl)	103.2 ± 31.3
HOMA-IR	4.1 ± 1
Fat mass (kg)	41.7 ± 4
Fat %	43 ± 3
Muscle mass (kg)	52 ± 9
Visceral fat	12.4 ±1.4
BMR	1600 ± 180

Data are presented as mean ± SD, percentage, BMI: Body mass index; TG: Triglycerides; HDL: High-density lipoprotein; TC: Total cholesterol; LDL: Low-density lipoprotein; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; BMR: Basal metabolic rate. *P*- value is considered significant at $P < 0.05$.

Table 3. Comparison between initial and final anthropometric, body composition, and metabolic markers measurement among participants

Variables	Measurement	Mean differences	Percentage of changes	P- value
Weight (kg)				
Initial	96.4 ± 10.6	9.5 ± 2.8	10%	0.000*
Final	86.9 ± 10			
BMI				
Initial	35.2 ± 2	- 3.2 ± 1.1	9.2%	0.000*
Final	31.9 ± 2			
TG (mg/dl)				
Initial	225.4 ± 29.8	- 12.4 ± 6.6	5.5%	0.000*
Final	213 ± 29.1			
TC (mg/dl)				
Initial	217 ± 26.1	- 14.3 ± 11.6	6.5%	0.000*
Final	202.8 ± 27			
HDL-cholesterol (mg/dl)				
Initial	47.3 ± 7	4.7 ± 5.5	10%	0.000*
Final	52 ± 6.7			
LDL -cholesterol				
Initial	103 ± 31.3	- 3.9 ±3.8	3.7%	0.000*
Final	99.3 ± 29.1			
HOMA-IR				
Initial	4.1 ± 1	- 1.5 ± 1.1	36.1%	0.000*
Final	2.6 ± 0.6			
Fat mass (kg)				
Initial	41.7 ± 4	- 6.8 ± 6.5	16.4%	0.000*
Final	34.8 ± 4.3			
Fat (%)				
Initial	43.2 ± 2.5	- 6.3 ± 5	14.5%	0.000*
Final	36.9 ± 5.3			
Muscle mass (kg)				
Initial	52 ± 8.7	3.7 ± 1.5	7.1%	0.000*
Final	55.7 ± 8.8			
Visceral fat				
Initial	12.5 ± 1.4	- 4.2 ± 0.6	33.6%	0.000*
Final	8.3 ± 1.4			

Data are presented as mean. BMI: Body mass index; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance. *P*- value is considered significant at $P < 0.001$

Resultados

Table 2 shows the anthropometrics characteristics, body composition, and baseline metabolic parameters of the participants. The results showed that the mean age of the participants was 46.8 ± 5.7 years and 57.4% of the participants had class II obesity, with a mean body mass index of (35.2 ± 2). In addition, the participants had a high HOMA-IR (4.1 ± 1), fat mass of 41.7 ± 4kg, and elevated visceral fat (12.4 ±1.4). The participants had borderline HDL- HDL-cholesterol (47.3 ± 7 mg/dl), TG (225.4 ± 30 mg/dl), TC (217 ± 26.1 mg/dl), and a normal range of LDL-cholesterol (103.2 ± 31.3 mg/dl).

Table 3 presents comparison between the, initial and final, anthropometric characteristics, body composition, and metabolic markers measurement of the participants. The results show significant differences between initial and final measurements of all parameters ($p < 0.05$). Moreover, the results indicate a significant weight loss and decreased BMI, visceral fat, and fat mass (10%, 9.2%, 33.6%, and 16.4%) respectively. In addition, there were significant improvements in metabolic parameters from initial measurements such as HOMA-IR (- 1.5 ± 1.1), TG (- 12.4 ± 6.6 mg/dl), TC (- 14.3 ± 11.6 mg/dl), HDL-cholesterol (4.7 ± 5.5 mg/dl), and LDL – cholesterol (- 3.9 ±3.8 mg/dl).

The results of the multiple linear regression models are presented in table 4. In the model, weight loss at the end of the intervention represented the effect of the ketogenic diet on body composition and metabolic parameters. The results of the linear regression models indicated a significant correlation between adherence to the ketogenic diet, represented by weight loss, and the participants body composition and metabolic parameters. Furthermore, the results showed that the models are reliable and could aid in evaluating the usefulness of the dependent variable (weight loss) in predicting the values of the independent variables (body composition and metabolic parameters). The results showed that adhering to a ketogenic diet led to weight loss and a decrease in fat mass, fat, visceral fat, TG, and HOMA-IR by 0.32, 0.29, 0.03, 0.21, and 2.94 units, respectively. On the other hand, adhering to the ketogenic diet led to an increase in TC, and muscle mass by 0.06, and 0.03 units, respectively.

Table 4. The correlation between the effect ketogenic diet on body composition and metabolic parameters.

Parameters	B	R square	F square	P -value
Fat mass (kg)	- 0.32	0.79	24.4	0.001*
Fat %	- 0.29			
Visceral fat	- 0.03			
Muscle mass (kg)	0.03			
TG (mg/dl)	- 0.21			
TC (mg/dl)	0.06			
HOMA-IR	- 2.94			

TG: Triglycerides; TC: Total cholesterol; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance. The model was adjusted for age and sex. *P*- value is considered significant at $P < 0.05$.

Discusión

This study explores the effect of a ketogenic diet on weight loss in obese people and many metabolic parameters such as lipid profile, and insulin resistance. The results of this study show that individuals who followed a ketogenic diet for 4-month experienced weight loss and an improvement in body composition by reducing fat mass and visceral fat and a slight increase in muscle mass.

A meta-analysis of 13 randomized controlled trials (RCTs) found that women on a ketogenic diet lost 0.9 kg with a 13 - 84% weight loss rate compared to a low-fat diet [15]. In addition,

results from 11 RCTs found that subjects on a low carbohydrate diet (less than 20% of total energy) experience significant weight reduction (-2.17 kg) compared to those on a low-fat diet [16]. Moreover, similar studies have shown [17] that low-carbohydrate diets are more effective than low-fat diets in reducing weight in obese people. The ketogenic diet is one of the strategic nutritional interventions for weight loss, as it uses fat as an energy source in the absence of carbohydrates, while simultaneously losing energy through ketosis and preserving muscle mass [18]. Furthermore, the ketone body has some effects on appetite suppressors due to higher satiety effects of fat and proteins and possible effects on the control of lipogenic hormones that increase lipolysis and reduce lipogenesis [19].

Insulin resistance is a common condition that affects people with obesity by reducing fat and muscle cell's ability to absorb glucose. Recently, a ketogenic diet has been recommended as a treatment option for type 2 diabetes because of its ability to improve insulin sensitivity and lower glycemic control [18]. The results of the study found that obese individuals with insulin resistance experience significantly lower HOMA-IR levels, which indicates an improvement in insulin sensitivity. The reduction of carbohydrate intake and consumption of low glycemic index food contribute to lower blood glucose levels, which subsequently decrease insulin demand and allows for an improvement in insulin sensitivity [20]. A meta-analysis of 18 RCT demonstrated that a low carbohydrate diet has favorable effects on diabetes conditions in terms of improving Glycated hemoglobin (HbA1c) (-0.28%), HDL–cholesterol (0.06 mmol/L), and TG (-0.24 mmol/L). Similarly, the improvement in diabetes parameters and reduced medication requirements were associated with lower blood glucose levels as a result of restricted carbohydrates [21].

The results of the study found that after 4 months of adhering to the ketogenic diet, the participants experienced a slight reduction of TG, TC, and LDL-cholesterol, and a slight increase in HDL-cholesterol. Moreover, results of linear regression show that weight loss after adhering to a ketogenic diet has minor effects on decreasing TG levels and increased TC levels. The results of the study are consistent with another study [16] that found that subjects on a low-carbohydrate diet experienced a reduction in TG (-0.26 mmol/l) and a greater increase in HDL cholesterol (0.14 mmol/l) compared to subjects on a low-fat diet. Similarly, another meta-analysis [22] showed a significantly greater reduction of TG (-14 mg/dl), a slight reduction of LDL cholesterol (3.7 mg/dl), and an increase in HDL cholesterol (3.3 mg/dl). These beneficial effects of the ketogenic diet were attributed to that dietary cholesterol and TG are the primary sources of energy. However, several studies reported conflicting results on the effect of the ketogenic diet on TG levels. A 4-week RCT found that 75% of the fat content from total energy in the ketogenic diet, TG, and LDL-cholesterol levels increased [23]. However, a high-fat diet coupled with low fiber intake increases the risk of increased LDL–cholesterol [24, 25]. The variability in the results obtained in the studies could be attributed to differences in the type of ketogenic diet, the type of low glycemic index and fat consumed, as well as the duration of the study.

Conclusion

The ketogenic diet has many health benefits, including weight reduction, improved body composition, lipid profile, and insulin resistance. However, the ketogenic diet is a short-term nutritional intervention in weight

loss and metabolic markers improvements. Further long-term RCTs are needed to explore the effect of the ketogenic diet on metabolic markers to provide more comprehensive recommendations about its effectiveness and efficiency. Moreover, the study has many limitations including self-report dietary adherence to the ketogenic food list and daily calorie intake, lack of a control group, and the short-term duration of the study.

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