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Comparison of the Effect of Ketogenic and Low-Calorie Diets on Weight Loss in Iranian Obese and Overweight Children

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ABSTRACT

Introduction: Overweight and obesity have increased in prevalence over the last two decades in many developed and developing countries, including Iran. The aim of this study was to compare the weight reduction effects of Ketogenic and low- calorie diets on overweight and obesity among Iranian children.
Methods: Seventy-six overweight or obese children aged 9-16 years recruited from the Nutritional Clinic of outpatient Ghaem Hospital in Mashhad, Iran, were randomly assigned into two groups of low-calorie diet (n=38) and Ketogenic diet (n=38). Both groups were treated for 3 months and followed up weekly. Fasting lipid profiles, blood sugar, uric acid, high-sensitivity C-reactive protein, and weight were measured. Body fat percentage was measured using bioimpedance analysis (Tanita body composition analyzer, BC-418, Japan) in each visit.
Results: Both Ketogenic and low-calorie diets reduced obesity indices, including body fat percentage, and improved lipid profiles (P<0.05). Changes in body weight and body mass index did not differ significantly between the two groups (P>0.05). However, low-calorie diet had more potential beneficial effect on body fat percentage and lipid profile than Ketogenic diet (P<0.05).
Conclusion: The results showed that Ketogenic diet did not have any remarkable effects on weight loss, compared to low-calorie diet. It seems that both diets had similar effects on weight loss in overweight and obese children. The findings revealed that low-calorie diet had more potential beneficial effect on body fat percentage and lipid profile than Ketogenic diet.

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Introduction

Childhood obesity contributes significantly to mortality and morbidity in adulthood (1) and is associated with several chronic conditions, such as hypertension (2). The prevalence of obesity and overweight has increased, especially in Middle East and North Africa, among adults and children. The incidence rate of childhood obesity in Tehran, the capital city of Iran, has been estimated as 17% over 10 years (3). The World Health Organization has reported that approximately 155 million school-aged children are obese or overweight (4), and that 1 per 3 children in the United States are not at the healthy weight, with 17.1% being obese or overweight (5).

A number of dietary interventions have been proposed for the management of overweight and obese children. Ketogenic diet consists of high-fat and high-protein, with low-carbohydrate intake. It was originally used as

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an adjunct to treatment for epilepsy to reduce seizure activity (6, 7). The Ketogenic diet induces a state of ketosis, in which there is an increase in the blood concentrations of ketone bodies (e.g., acetoacetate, B-hydroxybutyrate, and acetone), indicating that fat is being used to directly generate energy avoiding the gluconeogenesis pathway.

Dietary or adipose fat is used to produce energy under circumstances where glucose is not readily available, and during the process of β-oxidation, long-chain fatty acids are converted to the water-soluble ketone bodies. Dietary carbohydrate inhibits fatty acid oxidation, and hence ketosis is determined by the quantity of dietary carbohydrate (8, 9). Previous research has shown that a Ketogenic diet may increase high-density lipoprotein cholesterol (HDL-C) and decrease serum triglycerides, whilst exerting no effect on low-density lipoprotein cholesterol (LDL-C) over a period of 6-12 months (10).

However, there are few data regarding the effects of a Ketogenic diet on overweight and obese children. The aim of the present study was to compare the weight reduction, anthropometrical factors, and biochemical markers of Ketogenic and low-calorie diets on overweight and obesity among Iranian children.

Material and methods

Study population

Seventy-six overweight or obese children were recruited from the Nutritional Clinic of outpatient Ghaem Hospital in Mashhad, Iran. The inclusion criteria were overweight or obesity, age range of 9-16 years, and body mass index (BMI)-for-age above the 85th percentile. On the other hand, the exclusion criteria were lack of systemic and chronic diseases, secondary overweight, and use of the medications affecting appetite and weight. The parents were asked to sign the consent form, which was approved by the Ethical Committee of the Research Council of Mashhad University of Medical Sciences, Mashhad, Iran.

The eligibility of the subjects was determined by a clinical nutritionist who was also responsible for prescribing the diets. A pediatric endocrinologist also examined each participant to rule out the secondary causes of obesity. The participants were randomly assigned into two groups of low-calorie diet (n=38) and Ketogenic diet (n=38). The low-calorie diet group was prescribed a diet with 30% fewer calories than the estimated required energy intake with 55% carbohydrate, 30% fat, and 15% protein. The Ketogenic diet group was subjected to a diet high in protein with low carbohydrate and high fat.

Both groups were treated for 3 months and followed up weekly. Those on Ketogenic diet were checked weekly for the presence of urinary aceton. Six subjects in the Ketogenic diet group and three subjects in the low-calorie diet group did not attend to the clinic, and therefore failed to complete the study. Demographic data were collected using a questionnaire. All assessments were performed before and after the trial.

Blood sample collection

Blood samples were collected from each subject at 8.00 a.m. after 12 h of fasting both before and after the dietary period. The blood was centrifuged at 2,500 rpm for 15 min at room temperature to obtain serum or plasma. Hemolyzed samples were excluded from the analysis, and serum and plasma were stored at -80°C prior to analysis.

Anthropometric measurements

Body weight was measured and recorded to the nearest 100 g using a calibrated counterweight balance (Seca, Japan) and personal scales on a hard level surface, while the subjects were wearing light clothing (shoes, heavy outer garments, heavy jewelers, and keys were removed). Height was also measured to the nearest millimeter at the first visit using a portable stadiometer while the participant's head was in the Frankfurt plane. The BMI was calculated as weight (kg) divided by height (m2) (11). Furthermore, waist circumference was measured at the midpoint between the highest point of the iliac crest and the lowest part of the costal margin (11). Body fat percentage was also measured in each visit using bioimpedance analysis (Tanita body composition analyzer, BC-418, Japan) (11).

Biochemical analysis

Fasting blood sugar (FBS) and uric acid

were measured using standard methods. Fasting total cholesterol, LDL-C, HDL-C, and triglycerides were determined for each subject before and after the intervention. Serum lipid concentrations were measured by routine enzymatic methods. High-sensitivity C-reactive protein (Hs-CRP) was also estimated using a polyethylene glycol-enhanced immuneturbidimetry method by means of an Alcyon analyzer (ABBOTT, Chicago, IL, USA).

Statistical analysis

All data were analyzed using SPSS software (version 16; USA) and expressed as mean and standard deviation for normally distributed data or median and interquartile range for non-normally distributed data. Paired sample t-test was used to compare the variables between the two stages (i.e., pre- and post-intervention). P-value less than 0.05 were considered significant.

Effect of Ketogenic and low-calorie diets on obesity indices

Body weight and BMI did not differ between the Ketogenic and low-calorie diet groups at the baseline (Table 1; P>0.05). Both groups showed a decrease in body weight and BMI 3 months post-intervention (Table 2; P<0.01). The changes of BMI in both Ketogenic and low-calorie diet groups did not significantly differ (Table 3; 1.01% vs. 0.97%; P=0.81). Waist, hip, arm, and wrist circumferences did not differ significantly between the two groups at the baseline (Table 1; P>0.05). Both Ketogenic and low-calorie diet groups demonstrated a significant decrease in waist, hip, arm, and wrist circumstances after 3 months of treatment (Table 2; P<0.001). Changes of waist, hip, arm, and wrist circumstances did not significantly differ between the two groups (Tables 3; P>0.05).

Results

Table 1. Comparison of demographic data between Ketogenic diet and low caloric diet

Factors	Ketojenic (n=32)	Low-calorie (n=35)	*P value*
Weight (kg) (%)	1.56 (2.2%)	1.47 (2.12%)	0.904
Body mass index (kg/m2) (%)	1.01 (3.5%)	0.97 (3.4%)	0.83
Waist circumference (kg) (%)	0.08 (0.086%)	0.23 (0.25%)	0.350
Hip circumference (cm) (%)	1.12 (1.06%)	1.31 (1.25%)	0.826
Arm circumference (cm) (%)	-0.60 (-1.93%)	0.59 (1.91%)	0.071
Wrist circumference (cm) (%)	0.08 (0.47%)	0.23 (1.36%)	0.350
Fat percent (%)	0.92±3.33	2.67±3.33	0.011
Fat mass (kg) (%)	1.10 (4.3%)	1.96 (8.01%)	0.159
Right leg fat percent (%)	1.26±2.42	1.77±2.36	0.381
Left leg fat percent (%)	1.17±2.25	1.94±2.16	0.149
Right arm fat percent (%)	0.34±2.83	1.90±2.62	0.020
Left arm fat percent (%)	0.30±3.82	1.93±3.58	0.074
Trunk fat percent (%)	0.69±3.27	2.68±4.05	0.028
Total cholesterol (mg/dl)	3.76 (2.35%)	6.3 (4.33%)	0.65
Triglycerides (mg/dl)	5.0(4.54%)	4.0 (4.10)	0.838
FBS (mg/dl)	-6.60 (-8.46%)	10.81 (14.03%)	0.281
HDL-C (mg/dl)	1.37 (3.54%)	-4.81 (-12.88)	0.584
LDL-C (mg/dl)	-0.32 (0.33%)	3.97 (4.85%)	0.012
hs-CRP (mg/dl)	-0.28 (27%)	-0.13 (22%)	0.426
Uric acid (mg/dl)	0.97 (20%)	-0.324 (6%)	0.416

Values are expressed as mean ± SD as the data are normally distributed. Comparison between groups was assessed by parametric tests

Table 2. Comparison of effect of Ketogenic and low caloric diet on anthropometric and biochemical factors

Factors	Ketogenic (n=32)			Low calories (n=35)		
	Pre-treatment	Post-treatment	P-value	Pre-treatment	Post-treatment	P-value
Weight (kg)	68.12±16.13	66.56±15.96	<0.001	69.24±6.40	67.77±7.49	<0.001
Body mass index (kg/m2)	28.35±3.94	27.34±4.17	<0.001	27.84±2.41	26.87±2.57	<0.001
Waist circumference (cm)	88.68±4.99	85.58±7.54	0.004	90.89±7.10	89.54±7.56	<0.001
Hip circumference (cm)	104.96±9.16	103.84±8.82	<0.001	104.31±5.56	103.00±5.25	<0.001
Arm circumference (cm)	31.04±3.71	31.64±3.55	0.009	30.89±2.06	30.30±2.18	<0.001
Wrist circumference (cm)	17.00±1.10	16.92±1.29	<0.001	16.83±0.65	16.60±0.89	<0.001
Fat percent (%)	36.15±5.26	35.23±5.55	<0.001	35.32±3.07	32.65±4.42	<0.001
Fat mass (kg)	25.08±8.47	23.97±8.28	<0.001	24.44±4.04	22.48±4.82	<0.001
Right leg fat percent (%)	40.42±5.23	39.16±4.85	<0.001	39.11±4.68	37.34±4.81	<0.001
Left leg fat percent (%)	40.95±4.89	39.78±5.00	<0.001	39.70±4.15	37.76±4.73	<0.001
Right arm fat percent (%)	42.07±5.62	41.73±5.85	<0.001	41.06±4.64	39.15±5.16	<0.001
Left arm fat percent (%)	45.75±5.93	45.44±6.60	<0.001	43.84±6.10	41.91±5.71	<0.001
Trunk fat percent (%)	31.27±5.80	30.58±6.26	<0.001	30.76±4.80	28.08±4.75	<0.001
Total cholesterol (mg/dl)	159.80±31.64	156.04±32.61	0.026	145.26±43.08	139.00±29.95	0.040
Triglycerides (mg/dl)	110 (99-124)	119 (78-203)	0.589	97.50 (83-130)	94.20 (73.10-159)	0.910
FBS (mg/dl)	77.93±9.20	84.53±10.94	0.615	77.00±15.83	66.19±8.66	0.170
HDL-C (mg/dl)	38.65±8.49	37.28±9.21	0.011	37.33±7.12	42.14±8.08	0.028
LDL-C (mg/dl)	95.81±29.92	96.13±24.64	0.215	81.78±28.68	77.81±22.89	0.001
HS-CRP (mg/dl)	1.02 (0.70-2.38)	1.30 (1-78)	0.593	0.58 (0.51-0.64)	0.71 (0.59-0.75)	0.018
Uric acid (mg/dl)	4.80±0.72	3.83±0.30	0.391	4.61±1.63	4.85±1.22	<0.001

Values are expressed as mean ± SD (for normally distributed data) or median and interquartile range (for non-normally distributed data). Comparison between pretreatment and post treatment for both groups were assessed by paired *t* test for normally distributed data, or by Mann Whitney test for non-parametric data. HS-CRP stands for High Sensitivity C-Reactive Protein, FBS stands for fasting blood sugar, HDL_C stands for High Density Lipoprotein Cholesterol and LDL_C stands for Low Density Lipoprotein Cholesterol.

Table 3. Changes in anthropometric and biochemical measurements for both diets

Factors	Ketojenic (n=32)	Low-calorie (n=35)	*P value*
Weight (kg) (%)	1.56 (2.2%)	1.47 (2.12%)	0.904
Body mass index (kg/m2) (%)	1.01 (3.5%)	0.97 (3.4%)	0.83
Waist circumference (kg) (%)	0.08 (0.086%)	0.23 (0.25%)	0.350
Hip circumference (cm) (%)	1.12 (1.06%)	1.31 (1.25%)	0.826
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Left leg fat percent (%)	1.17±2.25	1.94±2.16	0.149
Right arm fat percent (%)	0.34±2.83	1.90±2.62	0.020
Left arm fat percent (%)	0.30±3.82	1.93±3.58	0.074
Trunk fat percent (%)	0.69±3.27	2.68±4.05	0.028
Total cholesterol (mg/dl)	3.76 (2.35%)	6.3 (4.33%)	0.65
Triglycerides (mg/dl)	5.0(4.54%)	4.0 (4.10)	0.838
FBS (mg/dl)	-6.60 (-8.46%)	10.81 (14.03%)	0.281
HDL-C (mg/dl)	1.37 (3.54%)	-4.81 (-12.88)	0.584
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hs-CRP (mg/dl)	-0.28 (27%)	-0.13 (22%)	0.426
Uric acid (mg/dl)	0.97 (20%)	-0.324 (6%)	0.416

Values are expressed as mean ± SD (for normally distributed data) or median and interquartile range (for non-normally distributed data). Comparisons between groups were assessed by paired *t* test for normally distributed data, or by Mann Whitney test for non-parametric data. HS-CRP stands for Highly Sensitive C-Reactive Protein**,** FBS stands for fasting blood sugar, HDL_C stands for High Density Lipoprotein Cholesterol and LDL_C stands for Low Density Lipoprotein Cholesterol.

Effect of Ketogenic and low-calorie diets on body fat percentage

Total body fat mass, as well as trunk, right and left legs, and arm fat mass did not differ between the Ketogenic and low-calorie diets at the baseline (Table 1; P>0.05). Both Ketogenic and low-calorie diet groups showed a reduction in total body, trunk, right and left legs, and arm fat mass 3 months post-intervention (Table 2; P<0.001). Changes of fat percentage in total body, right arm, and trunk were significantly higher in the children on low-calorie diet than in those on Ketogenic diet (Table 3; P<0.05).

Effect of Ketogenic and low-calorie diets on biochemical markers

Lipid profile, FBS, uric acid, and hs-CRP did not differ between the Ketogenic and low-calorie diet groups at the baseline (Table 2; P>0.05). Both Ketogenic and low-calorie diets reduced total cholesterol, triglycerides, and uric acid, and increased HDL-C (Table 2; P<0.01). The low-calorie diet group demonstrated a decrease in LDL-C (Table 2; P<0.05), which was not observed in the children on Ketogenic diet (Table 2; P>0.05). The FBS did not significantly change in neither groups after 3 months of intervention (Table 2: P>0.05). Changes of LDL-C in the low-calorie diet group was significantly higher than those in the Ketogenic diet group (Table 3; P<0.05).

Discussion

In the present study, Ketogenic and low-calorie diets reduced weight and improved lipid profile. However, Ketogenic diet did not have any remarkable effect on weight loss, compared to low-calorie diet. Furthermore, low-calorie diet had more potential beneficial effect on body fat percentage and lipid profile than Ketogenic diet.

Obesity indices and Ketogenic and low-calorie diets

Krebs et al. (2010) showed that BMI Z-scores (BMI-Z) in two groups of high-protein low-carbohydrate diet and low-fat diet reduced significantly. This reduction was significantly higher in the high-protein low-carbohydrate group, compared to that in the low-fat diet group (P=0.03). In the follow-up visit, both groups showed a significant decrease in the BMI-Z. There was no significant difference between the two types of diets in terms of BMI-Z changes (12), which is similar to the findings of the present study. In a systematic review, it was shown that low-carbohydrate diet reduced weight depending on the length of diet and amount of energy intake rather than the type of the carbohydrate used in the diet (13).

In this study, the results revealed that both diets led to the reduction of weight. The modified Ketogenic diet, consisting of a high-fat, high-protein, and low-carbohydrate diet, caused a weight reduction of at least 1.5 kg during 3 months, which was similar to that caused by low-calorie diet within the same period of time. However, in most of the studies, the Ketogenic diet in overweight and obese adults has been reported to reduce weight more than the low-calorie diets. Skov et al. showed that high-protein diet resulted in the reduction of 8.9 kg, while control diet led to 5.1 kg weight loss during 6 months. They also showed that high-protein diet resulted in the reduction of more fat, compared with control group (7.6 kg vs. 4.3 kg) (14).

Mechanism of weight reduction in a high-protein diet may be different with those of other diets. Protein inhibits energy-intake in ad libitum due to its effect on satiety (15). The difference between obese adults and children in terms of the effect of Ketogenic diet may be related to the consumption of more carbohydrate that mentioned in their diet in obese children that adults or different effect of high protein on satiety between adults and children.

Body fat percentage and Ketogenic and low-calorie diets

In the present study, low-calorie diet reduced fat percent about 2.5 times more than Ketogenic diet, and the difference in changes between Ketogenic and low-calorie diets was significant. This may be one of the disadvantages of Ketogenic diet for children. It is believed that low-carbohydrate diets, such as Atkins, Zone, and South Beach, are more probable to produce obesity and fail short of reducing weight (16). However, research showed that low-carbohydrate diets are more capable of decreasing weight for a period of 4-6 months, compared with low-fat diets, although the differences were not significant after a year (16). High-protein diets maintain or raise fat-free mass, but decrease fat mass, and also raise the metabolic profile (15).

Biochemical markers and Ketogenic and low calorie diets

A low-carbohydrate high-protein diet has a considerable effect on serum lipids; however, there are controversial results in this regard (17-20). In the current study, Ketogenic diet increased triglyceride more than low-calorie diet, but the changes between them were not significant. Furthermore, total cholesterol was reduced in low-calorie diet more than Ketogenic diet, but the changes between these diets were not significant. Westman et al. showed a reduction in total, LDL-C, and very-LDL-C following a low-carbohydrate high-protein diet. This diet was accompanied with a reduction in the percentage of small LDL particles (17).

In a similar study, an identical trend was reported regarding the amount of LDL particles both in the absence of weight loss with a Ketogenic diet or the presence of weight loss (18). However, the findings of the previous studies are in contrary with this result (19, 20). They found that a low-carbohydrate and high-protein diet did not remarkably decrease neither total cholesterol nor LDL-C concentrations after 6 months. In a study, an increase was reported in HDL-C concentration (20); however, this elevation was not observed in overweight and obese children (19). Both of the mentioned studies showed a significant decrease in triglycerides following a low-carbohydrate diet. These changes could be the result of conventional weight loss diets either alone (21) or in combination with exercise (22, 23).

In a study, a low-carbohydrate high-protein diet did not consistently decrease LDL-C level (24). In another study conducted on 24 obese men and women for 12 weeks (2 weeks of normal diet, 8 weeks of low-carbohydrate and high-protein diet, and then again 2 weeks of normal diet), uric acid, LDL-C, and free fatty acid levels increased significantly in the low-carbohydrate high-protein diet; however, HDL-C was not increased, although plasma triglyceride was decreased (25). In another study performed on 52 obese subjects for 25 days, uric acid was increased in a high-protein, high-fat, and low-carbohydrate diet, but blood sugar was decreased (26). The difference in the results of various studies regarding the effect of Ketogenic diet on lipid profile may be related to different age groups (children vs. adults), duration of weight loss (12 vs. 24 weeks), ethnicity (Asian vs. Western), and type of Ketogenic diet (Ketogenic vs. modified Ketogenic).

Disadvantage of Ketogenic diet

The most prevalent side effects of low-carbohydrate diets are constipation and headache due to the decreased consumption of vegetables, fruits, whole-grain bread, and cereals. This restriction in low-carbohydrate diets, if continues for a long time, may lead to cancer, cardiovascular diseases, general weakness, muscle cramps, halitosis, and diarrhea, compared with low-fat diet (13). Weight reduction in children has its own characteristics. Use of modified Ketogenic diet is useful for adults; however, there are some difficulties for using it in children. Some studies revealed that modified Ketogenic diet had negative effect on growth. Santoro et al. showed that children on Ketogenic diet were at a high nutritional risk (27).

The modified Ketogenic diet provides enough protein for growth and remaining healthy. However, this diet appears to have insufficient water-soluble vitamins, such as B and C, and also calcium. So, it is necessary to prescribe supplements to prevent deficiencies (28). Therefore, the use of Ketogenic diet in children for a long time is not recommended as this kind of diet has its own side effects, especially in children, and the percentage of weight reduction is not significant with low-calorie diet.

Research limitations

The major limitations of this study were the small sample size and short period of follow-up. However, this is the first trial to compare low-calorie diet with Ketogenic diet in children, and for ethical reasons, it was felt that the period of the study should not exceed 3 months.

Conclusion

Both Ketogenic and low-calorie diets reduced the indices of obesity, including body fat percentage, and improved lipid profiles. Changes in body weight and BMI did not differ significantly between the two groups. However, low-calorie diet had higher potential beneficial effects on body fat percentage and lipid profile than the Ketogenic diet. Ketogenic diet is hard for children due to the elimination of carbohydrate; furthermore, it has some disadvantages, such as the restriction of growth, headache, and constipations. Therefore, it is reasonable to use low-calorie diet rather than Ketogenic diet for weight management in children. However, these data should be reconfirmed by other studies with a larger sample size and longer follow-up period involving the evaluation of new risk factors.

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