



Comparing the Efficacy of Ketogenic Diet with Low Fat Diet for Weight Loss in Obesity Patients: Evidence-Based Case Report

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Abstract

Introduction Obesity is a nutritional disease which is still a health burden particularly in Jakarta. The main treatment for obesity is nutritional intervention. Nowadays, several dietary approaches have been developed, including ketogenic diet, which is still controversial. **Methods** Literature search had been done within 4 databases including PubMed®, Cochrane®, Google® Scholar, and Science Direct®, using keywords: obesity, ketogenic diet, low-fat diet, and weight loss. Then, Medical Sub Heading (MeSH) was used. The search resulted in two articles which were appraised according to aspects of validity, importance, and applicability **Results** A randomized-controlled trial study showed similar effect of weight loss with ketogenic diet compared to low-fat diet. On the other hand, a meta-analysis study showed ketogenic diet caused more weight loss than low-fat diet. Both studies showed an increased risk of cardiovascular disease from the ketogenic diet group, which were shown by a decrease of flow-mediated dilatation and an increase of LDL-C. **Conclusion** Ketogenic diet shows a better long-term effect for weight loss in obese patients than low-fat diet. However, ketogenic diet may increase the cardiovascular event risk significantly.

Keywords ketogenic diet, low-fat diet, obesity, weight loss

Introduction

Obesity and overweight, also known as malnutrition, are diseases in nutrition and the metabolic field. These define as conditions in which a patient has an above normal body mass index (BMI).¹ In Indonesia, BMI values are referred from the Asia-Pacific World Health Organization guidelines, with the normal range of 18.5–22.9 kg/m². Overweight and obesity are

defined as body mass index of 23–24.9 kg/m² and >25 kg/m², respectively.² Obesity is an important issue due to its high prevalence. According to *Riset Kesehatan Dasar* (Riskesdas) Indonesia in year 2013, the prevalence of obesity in Jakarta is 30% in men and 40% in women.³ In addition, obesity is a major risk factor of chronic degenerative diseases, such as diabetes mellitus, dyslipidemia, and hypertension.⁴

The etiology is mostly due to poor eating behavior, thus patient management focuses mainly in nutritional intervention. The nutritional intervention widely used is calories restriction using low-fat diet.^{5,6} However, this nutritional intervention often causes lack of obedience of the patients.⁵

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In order to overcome the problem, several nutritional interventions had been suggested using various macronutrient compositions. Among them is ketogenic diet, which defines as dietary pattern with high-fat and very-low-carbohydrates compositions for daily intake.^{7,8} The goal of ketogenic diet is to increase ketogenesis, which happens when the body is lack of adequate energy from carbohydrate, particularly the central nervous system.⁷

Ketogenic diet remains controversial in our population. It can cause weight loss however the long-term effect on body weight and the adverse effects are still unknown.⁷ In addition, the effect of weight loss from ketogenic diet compared to other diets is still controversial.^{7,8} Therefore, this paper focuses on evidence-based critical review about comparing the efficacy of ketogenic diet with low-fat diet for weight loss in obese patients.

Case Illustration

Male, 46 years old, visited clinic for health consultation. He said during exercise, there was cholesterol check-up and his cholesterol level was 252 mg/dL. The patient was concerned about his condition which could cause health complications in the future. He has family history of cardiovascular disease: his older brother had heart attack 3 months ago and his father had stroke. The patient also complained about his excessive body weight. Anthropometric measurement showed body height of 158 cm and body weight of 82 kg. Thus, the BMI is 32.4 kg/m² (grade II obesity). Other physical examinations showed normal results. Therefore, he was suggested to have a lifestyle change (especially in his dietary pattern). He heard from his friends that ketogenic diet could reduce weight faster than other diets. Therefore, patient came to clinic to consult the doctor about ketogenic diet or the appropriate dietary pattern for his health.

“In obese patients, is ketogenic diet intervention better than low-fat diet for weight loss?” Table 1 shows clinical questions formula.

Table 1. Clinical questions formula

Patient/ Problem (P)	Intervention (I)	Comparison (C)	Outcome (O)
Obese patients	Ketogenic diet	Low-fat diet	Weight loss
Clinical Question Type	Treatment		
Study Design	Randomized-controlled trials (RCTs) or meta-analysis or systematic review of RCTs		

Methods

Literature search had been done within 4 databases: PubMed®, Cochrane®, Google® Scholar, and Science Direct® by using the keywords obesity, ketogenic diet, low-fat diet, and weight loss. Afterwards, Medical Sub Heading (MeSH) was used. Table 2 shows the strategies for articles search.

The total number of articles found based on keywords was 168 articles. Inclusion criteria for title selection and abstract were researches in patients with overweight or obesity; with randomized controlled trials (RCTs), meta-analysis or systematic review of RCTs as study designs; and available in free English full-text. Ten articles in which titles and abstracts matched with the inclusion criteria were found. Then, duplication equality screening was done, which resulted in remaining 4 articles. Reviews were performed on the 4 full-text articles. Among them, two articles were relevant to the clinical questions. One of them was an individual RCT while the other was a meta-analysis of RCTs. Figure 1 shows flow chart of the method used for article searches and selections.

Critical reviews were performed on selected articles using the criterias from Oxford Center for Evidence Based Medicine 2011 including the aspects of validity, importance, and applicability.

Table 2. The strategies for article search

No	Database	Keywords	Findings	Selected
1.	PubMed®	Ketogenic Diet [MeSH] OR Diet, Carbohydrate-restricted [MeSH] AND Diet, Fat-Restricted [MeSH] AND Obesity [MeSH] OR Overweight [MeSH] AND Weight Loss [MeSH]	79	6
2.	Cochrane®	Ketogenic Diet [MeSH] OR Diet, Carbohydrate-restricted [MeSH] AND Diet, Fat-Restricted [MeSH] AND Obesity [MeSH] OR Overweight [MeSH] AND Weight Loss [MeSH]	52	4
3.	Google® Scholar	Ketogenic Diet [MeSH] OR Diet, Carbohydrate-restricted [MeSH] AND Diet, Fat-Restricted [MeSH] AND Obesity [MeSH] OR Overweight [MeSH] AND Weight Loss [MeSH]	17	0
4.	Science Direct®	Ketogenic Diet [MeSH] OR Diet, Carbohydrate-restricted [MeSH] AND Diet, Fat-Restricted [MeSH] AND Obesity [MeSH] OR Overweight [MeSH] AND Weight Loss [MeSH]	20	0

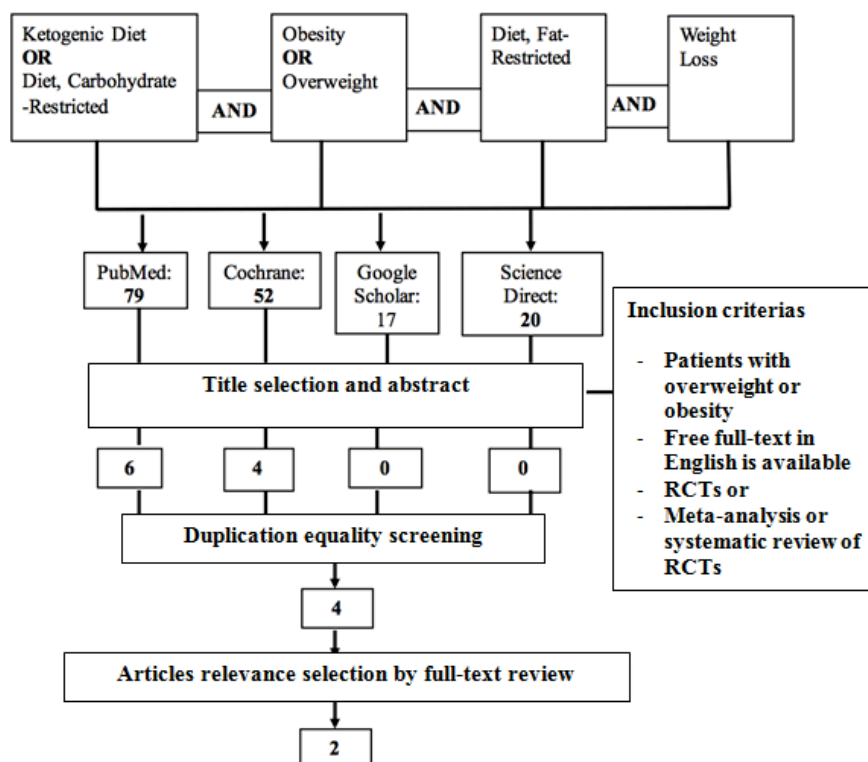


Figure 1. Flow chart of the methods used for article search and selection

Results

Validity

Table 3 shows the critical appraisal on the validity of the study by Wycherley TP et al.⁹

Table 3. Critical appraisal on the validity of study

Parameter of validity	Wycherley TP et al (2010) ⁹
Title	Long-term effects of weight loss with a very-low-carbohydrate and low-fat diet on vascular function in overweight and obese patients
Subjects	The total study subjects were 118 patients, consisted of 57 patient with low carbohydrate high fat diet (61%) and 61 patients receiving low fat diet with equally calculated calories. At the end of the study, only 49 patients finished the whole study, i.e subjects in the intervention group and 23 in the control group.
Randomization	Yes, randomization was done on patients who received both ketogenic and low-fat diets.
Randomization blinding (allocation concealment)	Yes, blinding technique was used by the investigators in this study, but could not be applied to the study subjects.
Initial characteristics of the subjects/ objects	Yes, both groups of patients have similar demographic characteristics in terms of age, sex, body mass index, blood pressure and cardiovascular risk profile.
Equal treatment	Yes, both groups were equally treated.
Adequate follow up	Yes, both groups underwent a follow-up and nutritional consultation in week-8 and every month afterwards. Data was obtained in the beginning of the study and after 52 weeks.
Intention-to-treat analyses	No, data analysis in this study utilized a per-protocol analysis
Level of Evidence	2 (Individual RCT)

Table 4 shows critical appraisal on the validity of Bueno NB et al¹⁰ study.

Table 4. Critical appraisal on the validity aspect of *meta-analysis*

Parameter Validity	Bueno NB, et al (2013) ¹⁰
Title	Very-low-carbohydrate ketogenic diet vs low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials
PICO (Patient, intervention, comparison, outcome)	PICO used during searching strategy was as follows: P: patients with BMI >27.5 kg/m ² ; I: ketogenic diet; C: low-fat diet; O: weight loss during the last 12 months
Literature searching	Articles were searched through MEDLINE, CENTRAL, Science Direct, Scopus, LILACS, SciELO and ClinicalTrials.gov using key words: ketogenic diet, weight loss, and cardiovascular risk factors.
Include all relevant studies	Yes, all relevant studies were included; studies which met the PICO criteria and RCTs were included in the analyses.
Validity assessment on each study	Yes, validity assessment was done on each study
Result consistency in each study	Yes, the results were consistent on each study
Level of Evidence	1 (a meta-analysis from RCTs)

Importance

Assessment of the study importance was not done using the 2 x 2 table since the outcomes were numerical variables. Therefore, the results of each study were assessed based on the primary and secondary outcomes, if available. Table 5 shows the critical appraisal of the importance of each study.

Table 5. Critical appraisal of the importance aspect of each study

Study	Results
Wycherley TP, <i>et al</i> (2010) ⁹	Weight loss was observed during the study period (week-0 to week-52), i.e. a reduction of 14.9 ± 2.1 kg in the ketogenic diet group and 11.5 ± 1.5 kg in the low-fat diet. The difference of weight loss was not significant between both groups ($p=0.20$). Meanwhile, BMI reduction was 5.3 ± 0.7 kg/m ² in the ketogenic diet group and 3.9 ± 0.5 kg/m ² in the low-fat diet group ($p=0.14$). The secondary outcome was the brachial artery flow-mediated dilatation (FMD), which was significantly different between both groups. The FMD reduction was $2.1 \pm 0.6\%$ in the ketogenic diet group and $0.3 \pm 0.6\%$ in the low-fat diet group ($p=0.045$). This showed a higher risk of endothelial damage in the ketogenic diet group.
Bueno NB, <i>et al</i> (2013) ¹⁰	13 studies were included in the meta-analysis; 9 studies were done in 12 months and the other 4 studies were completed in 24 months. Based on this meta-analysis, weight loss was significantly higher in the ketogenic diet group with weighted mean difference (WMD) of -0.91 (95%CI: $-1.65, -0.17$) kg, $p=0.02$; $I^2 = 0\%$, $p=0.47$. The result was consistent across all subgroup analyses, except for the subgroups with 24 months of follow-up. The secondary outcome was low density lipoprotein cholesterol (LDL-C) levels. Among 12 studies, which included a total of 1255 patients, a significantly greater increase of LDL-C levels was observed in the ketogenic diet compared to low-fat diet group (WMD 0.12 ; 95% CI: $0.04, 0.2$ mmol/L, $p=0.002$; $I^2 = 0\%$, $p=0.7$).

Applicability

Table 6 shows critical appraisal on the applicability of both studies.

Table 6. Critical appraisal on the applicability of both studies

Parameter of Applicability	Wycherley TP, <i>et al</i> (2010) ⁹	Bueno NB, <i>et al</i> (2013) ¹⁰
Resemblance of the study subjects with the case	Subjects were males or females, age 24-64 years old, with BMI of 26-43 kg/m ² (Asian Pacific criteria of obesity). Each subject also had at least one risk factor of metabolic syndrome, no history of organ dysfunction or malignancy, was not pregnant and had no smoking habit. This study was relevant to the case illustration.	Studies included in the meta-analysis had inclusion criteria that corresponded with PICO. However, the characteristics of the study subjects were not further detailed.
Agreement to the value and preference in the community	Doubtful. Since ketogenic diet might not be appropriate for Indonesian's culture, therefore adjustment for ketogenic diet is needed with Indonesian's local food availability.	
Feasibility of the therapy in the setting of daily clinical practice	Probably. Professional consultation is required before undergoing ketogenic diet, especially with comorbid diseases.	

A summary of the results of critically appraised RCT and meta-analysis is given in Table 7.

Table 7. Summary of results from both studies

Author	End-point	Result	Conclusion
Wycherley TP, <i>et al</i> (2010) ⁹	Subject's weight loss, calculated from the beginning of study (week 0) to week 52. In addition, the cardiovascular risk was also counted.	Weight loss in subjects receiving ketogenic diet vs low-fat diets were 14.9 ± 2.1 kg vs 11.5 ± 1.5 kg, respectively ($p=0.20$). Additionally, the FMD reduction was $2.1 \pm 0.6\%$ vs. $0.3 \pm 0.6\%$, respectively ($p=0.045$).	Body weight reduction was higher in the ketogenic diet group yet not statistically significant. However, FMD reduction was significantly higher in the ketogenic diet group, which suggested higher cardiovascular risk.
Bueno NB, <i>et al</i> (2013) ¹⁰	Body weight changes and indicator of cardiovascular risk among various RCTs involving ketogenic diet intervention.	From all of the 13 studies included, weight loss was significantly higher in subjects assigned to ketogenic diet compared to low-fat diet group (WMD -0.91 (95% CI 1.65–0.17) kg, $p=0.02$, $I^2 = 0\%$). In addition, there was also an increased LDL-C levels in 12 studies (WMD 0.12; 95% CI: 0.04–0.2; $p=0.002$; $I^2 = 0\%$).	There was a significantly greater weight loss in the ketogenic diet group. The results also showed homogeneity. Secondary outcome assessment showed a homogenous result, i.e. significantly higher increased of LDL-C levels in the ketogenic diet group.

Discussion

After critically assessed the study by Wycherley TP *et al*,⁹ a potential drawback was observed in the validity aspect of the study due to high number of drop out cases, i.e. 69 drop outs of the 118 subjects. Consequently, the analysis could only be done per-protocol. However, since it was difficult to lower the drop out number in this kind of study, we decided to continue critical appraisal for the importance and applicability aspects. In the importance aspect, the results showed that body weight reduction was greater in the ketogenic diet group compared to the low-fat diet group. However, statistical analysis failed to reach significance and thereby making it inapplicable for generalization to wider populations.

Regarding the applicability, the study result is applicable to patients with similar condition. However, it should be noted that there was a secondary outcome showing that subjects treated with ketogenic diet experience significantly greater FMD reduction ($2.1\% \pm 0.6\%$ vs. $0.3 \pm 0.6\%$)

implying a greater risk of cardiovascular event. It has been documented that 1% FMD reduction can increase the risk of cardiovascular event to 13%. Therefore, based on the results of this study, ketogenic diet treatment for 12 months can increase the risk of cardiovascular event by approximately 26%.⁹

Critical appraisal done to the meta-analysis by Bueno NB, *et al*¹⁰ showed a good validity assessment in terms of PICO strategy, study validity and consistency of the results. In the importance aspect, a significant result was shown by the higher reduction of body weight in the ketogenic diet group (WMD -0.91 kg; 95% CI: -1.65, -0.17; $p=0.02$) with good homogeneity, as shown by the $I^2 = 0\%$. Assessment on the applicability aspect also found that the result from this meta-analysis could be applied to the case. On the other hand, the secondary outcome showed higher LDL-C levels in the ketogenic diet group (WMD 0.12; 95% CI: 0.04, 0.2; $p=0.002$; $I^2=0\%$), indicating a statistical significance and homogenous results.¹⁰

Based on the critical assessment of both studies, ketogenic diet showed a long-term benefit on weight loss, which is better or similar to the low-fat diet. In support of this finding, a review by Paoli *et al*¹² concluded that ketogenic diet had a weight loss effect and was effective in a short period of time to induce weight loss. The mechanisms by which ketogenic diet may reduce body weight include a reduction in appetite by reducing insulin production and by affecting body metabolism that maintain muscle mass and reducing much of the fat mass.^{6,11,12}

On the other hand, the secondary outcome suggested that ketogenic diet might increase the risk of cardiovascular event. This finding was supported by the reduction of FMD values in the trial by Wycherley *et al*⁹ and increased LDL-C levels in the meta-analysis by Bueno *et al*. Increased LDL-C levels by ketogenic diet is associated with the high consumption of saturated fat. A study by Chiu *et al*¹³ stated that high consumption of high saturated fat would increase LDL-C levels and the risk of cardiovascular disease. In term of FMD reduction by ketogenic diet, another study by Schwingshackl and Hoffmann¹⁴ has shown a consistent finding. Moreover, a study by Jonavoskli *et al*¹⁵ also stated that a low-carbohydrate diet of <5% might reduce FMD. However, a short-term trial by Volek *et al*¹⁶ showed an contrasting result; they found that low-carbohydrate diet was better in maintaining the FMD. Therefore, further studies are needed to address this issue.

Based on these two critically appraised articles, it can be concluded that ketogenic diet intervention showed a good efficacy in weight loss, which include the short-term (≤ 3 months) or long-term (12 to 24 months) effects. However, aside from the desirable body weight loss, ketogenic diet poses a substantially increased risk of cardiovascular event. Therefore, ketogenic diet cannot be recommended as a choice of weight-loss therapy for patients with high risk of cardiovascular disease. Further studies are needed to evaluate the effect and long-term safety of ketogenic diet on cardiovascular risk.

Conflict of Interest

Authors declared no conflict of interest regarding this study.

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