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A VLC diet with gradual transition to Mediterranean low glycemic foods as a treatment of obesity – a pilot study

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Abstract.
BACKGROUND: Improved approaches to treat obesity are urgently needed, especially those feasible for the primary health care system. Such treatments should preferably reduce body weight by altering the long term habitual dietary and lifestyle pattern. In this work we studied the weight reducing effect of using the ketogenic, low calorie Eurodiet approach for 7 months.
METHODS: Forty-four patients with a baseline BMI of 34.8 were recruited to participate in a 7 month Eurodiet treatment program at Dr. Fedon Lindberg's Clinic in Oslo, Norway. Mean participant age was 50 years and final study group consisted of 8 men and 24 women. Primary outcome was weight loss. Body weight, body composition and blood variables were measured at baseline and after 7 months. The Eurodiet method is a four phase method, and is initiated with a ketogenic very low calorie diet based on Eurodiet products and selected vegetables. Food intake is then gradually increased until the patient has established a Mediterranean inspired, low glycemic load diet.
RESULTS: Thirty-two patients completed the 7 month treatment. Average weight loss was 14.7 kg ($p < 0.01$) or 14.2% of baseline weight. Bioimpedance analysis (BIA) showed a mean loss of 2.8 kg fat free mass. The treatment resulted in statistically significant improvement in the risk profile for diabetes and cardiovascular diseases. Fasting serum glucose was reduced by 0.4 mmol/L, insulin by 31.2 pmol/L, total cholesterol by 0.3 mmol/L, LDL-cholesterol by 0.3 mmol/L, and fasting triglycerides by 0.7 mmol/L, and HDL-cholesterol was increased by 0.2 mmol/L.
CONCLUSIONS: The Eurodiet treatment method of obesity appeared effective over 7 months, and was accompanied by an improved risk profile for diabetes and CVD. The long term effects are not documented and such documentation should be investigated.

Keywords: Obesity, VLC, VLCD, diet, ketogenic, mediterranean, weight loss, glycemic load

1. Background

According to the Norwegian health directorate the prevalence of obesity has increased greatly during the last two decades. The number of Norwegians characterized as obese in studies from 2000–2003 averaged 11–29% for men and 9–38% for women albeit with large geographical variations [1]. During the last 15 years, average weight for men and women aged 40–45 has increased by 5,0 and 5,8 kg [2].

The rising number of people with BMI $\geq$40 poses a large challenge for the health care system which offers mainly bariatric surgery and some lifestyle alternatives as treatment. Because the number of people in line for surgery is increasing [3], and because not all obese subjects are suitable for or interested in surgery, effective non-surgical treatment alternatives are urgently needed. In The Norwegian Directorate of Health's priority guidelines for morbid obesity from 2009, it is stated that people with BMI $\geq$40 or $\geq$35 with additional risk factors have a right to treatment

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in the public health system. However, several treatment methods exist and many are not thoroughly documented, which makes it difficult for both health workers and patients to make sensible choices. Thus the need for documenting the different existing strategies is extensive.

Dietary treatment of obesity using very low calorie diets (VLCD) has been shown to be effective and offering quick reductions in risk factors for both diabetes and cardiovascular disease (CVD) [3–5]. VLCD's can also be ketogenic, if the level of carbohydrates is low enough. A ketogenic diet reduces insulin levels, thereby increasing lipolysis of endogenous fat. This causes an increased production of ketone bodies, which may in large part replace glucose as a fuel source, thereby limiting the need for dietary glucose and glucose derived from gluconeogenesis. Studies of ketogenic diets have shown very promising results compared to fat and energy restricted diets [6] and greater improvement of the metabolic syndrome [7].

However, a VLC diet is so energy restricted that normal foods must eventually be reintroduced. But this leaves open the question of what kind of foods are reintroduced, a question of great importance because the kind of foods that are reintroduced is likely an essential factor in weight maintenance. Going back to one's regular diet will usually cause lost weight to come back [8]. Weight lost using traditional weight loss solutions are also too often regained, and long term success is therefore small [9]. In a recent study from Sweden a VLC diet with reintroduction of "normal food" resulted in 11.5 kg weight loss after one year in a group with baseline BMI of 34 [10]. These results show the effectiveness of a VLC diet, but leaves open the question of whether results could have been improved through manipulating the form of the reintroduced diet.

Thus, both the need for feasible weight loss treatment alternatives to surgery and the need to further improve VLC diets so they may perhaps become those alternatives, form the background for this pilot study. The primary goal was an attempt to evaluate the short term effect of the Eurodiet treatment method for weight reduction, thereby possibly providing a basis for longer trials involving the same treatment principles.

2. Methods

The study examined a 7 month Eurodiet Weight Coach course. This treatment was divided into 4 phases of which the first two were a ketogenic VLCD-period lasting 1-2 months. In these periods the patients consumed Eurodiet meal replacement products and vegetables and the dietary goal was 500–800 kcal/day of which 80–100 grams was protein and a maximum of 50 grams was carbohydrate. A subgroup of patients performed daily testing for urinary ketones using urinary ketone reagent strips, to ensure that the initial phases were ketogenic. After the initial ketogenic phase the patients gradually introduced low glycemic load foods with an ultimate goal of establishing a diet following the low glycemic load Mediterranean eating pattern. The treatment period included 4 group counseling sessions (8–12 people per group) and 3 individual counseling sessions. Each patient had a maximum of 7 sessions (3 individual and 4 group sessions). Sessions were conducted by specially trained health personnel at Dr. Fedon Lindberg's clinic in Oslo.

Patients were also recommended to increase the level of physical activity and were given standard dietary supplements (omega 3 and 6, magnesium, potassium, vitamin C and vitamin E) and extra supplements where levels were considered low following initial blood testing. The Eurodiet method is thus a treatment that is adapted to the individual need, but is in general based on a standardized dietary regime.

Because of the substantial change in diet made by the participants, and the use of fortified meal replacements, several blood variables related to nutritional status such as vitamins and minerals, were measured in addition to factors related to general health, as these factors relate to the general safety of the treatment.

Fasting blood samples were taken at baseline, at the initiation of each new phase, and after the end of treatment. In the following we only present baseline and end of treatment results. All blood samples were taken and analyzed at the Fürst Medical Laboratory. At the last consultation at the clinic, patients were given a requisition for blood sampling, but they were themselves responsible for having their blood sampled. Unfortunately, four patients did not get this last blood sampling done. For these participants, the results from the second last sampling were used (taken 20–40 days prior to the end of treatment), and a carry forward analysis was used.

At both individual and group meetings participants were weighed and body composition measures were taken on a Tanita BIA weight (Model BC-420).

2.1. Final study group

Mean age of participants was 50 years (range 23–74 years). Inclusion criteria were: BMI >30 or BMI >27, with at least one risk factor for CVD/metabolic syndrome. Following exclusion criteria were used:

- Under 18 years of age
- Medicinal treatment of thyroid related disorders
- Pregnancy or planned pregnancy
- Weight loss inducing medications such as orlistat or sibutramine
- Cardiac or cerebral infarction during the last 6 months
- Heart arrhythmia
- Clinically proven liver or heart failure
- Psychosis
- Disordered eating pattern (bulimia nervosa or anorexia nervosa)
- Addictions (alcohol or drug)
- Type I diabetes
- Catabolic conditions:
  - Infectious or inflammatory diseases
  - Cushing's disease
  - Hyperthyroidism
  - Cancer
  - Corticosteroid treatments

44 patients were included of which 12 dropped out and 32 completed. Reasons for drop-out are given in Table 1. The final study sample consisted of 8 men and 24 women. Because of issues with logistics, not all participants had all blood variables analyzed. The number of participants included in each blood sample variable is given in Table 3.

At baseline one patient did not provide blood in a fasted state. Blood variables from this patient are therefore excluded, but the anthropometric results are included. We also have reason to believe that two patients had a measurement error on the baseline BIA measurement, as data showed a loss of fat free mass exceeding 10 kg during the first 4 weeks. This was significantly (more than 2 SD) different from the other patients. In these two patients the second BIA measurement during the treatment is used (approximately after 8 weeks treatment) as baseline. We performed analysis of anthropometric variables with and without these two patients included, and found that the treatment effect on average body composition measures was not significantly different from the results excluding the two patients.

At baseline the most common comorbidities were high blood pressure ($n = 6$), high cholesterol ($n = 4$) and previous heart disease ($n = 4$). All patients were on regular medication for these conditions. No other comorbidities that are part of the metabolic syndrome were existent and no cases of diabetes, but one patient were on blood glucose lowering medication. No participants increased their medication dose during the study.

Table 1
Drop out

Nr. of participants	Reason for drop out
4	No reason given
4	Lack motivation
1	Mycoplasma infection and chronic fatigue syndrome
1	Pregnancy
2	Divorce/separation

2.2. Statistics

Data were analyzed using SPSS for windows v.17.0. Values are given as mean ± SD. Student *t*-test was used to measure treatment effect. Pearson correlation coefficient was used to determine correlations between variables.

2.3. Ethics

Informed consent was signed by all participants. The study is registered in clinicaltrials.gov (NCT01235208) and reported to the Norwegian ethical committee although an approval was not necessary as this is data collected from an established treatment.

3. Results

Changes in anthropometric variables are given in Table 2. Weight loss averaged 14.7 kg ($p < 0.01$) or 14.2% of baseline body weight. The loss ranged from 7.6 kg to 24.2 kg (6,3%–23,8%). Fat free mass was reduced by 2.8 kg ($p < 0.01$). There appeared to be no correlation between fat mass loss and fat free mass loss. Two patients achieved a weight loss greater than 20%, 14 patients achieved weight loss greater than 15%, 27 patients achieved a weight loss greater than 10% of body weight and the last five patients all lost more than 5% body weight.

Serum glucose was reduced from 5.6 mmol/L to 5.1 mmol/L ($p < 0.01$) and glycated hemoglobin was reduced from 5.7 to 5.4 mmol/L ($p < 0.01$) (Table 3). Several common risk factors for CVD were significantly improved ($p < 0.01$). Total serum cholesterol was reduced by 0.3 mmol/L, HDL-cholesterol increased by 0.2 mmol/L, LDL-cholesterol was reduced by 0.3 mmol/L and serum fasting triglycerides were reduced by 0.7 mmol/L).

As insulin plays a central role in fat storage, we examined if there were any correlations between anthropometric variables and measures of insulin and blood glucose. At baseline there was a significant positive correlation between fasting serum insulin and body weight ($r = 0.420$, $p = 0.03$), fasting serum c-peptide and body weight ($r = 0.588$), $p = 0.001$), and between fasting serum glucose and body weight ($r = 0.501$, $p = 0.009$). Change in weight and level of fasting C-peptide also correlated significantly ($r = 429, p < 0.05, n = 26$), and there was a significant positive correlation between change in body weight and change in fasting insulin ($r = 0.391$, $p = 0.048$, $n = 26$).

Linear regression analysis with control for age and sex showed a positive correlation between weight loss and reduction in c-peptide ($p = 0.02$), and borderline significance ($p = 0.059$) between weight loss and fasting insulin reduction (Table 4). The association between body weight change and change in fasting insulin and C-peptide was little affected by adjusting for age and sex. When adjusting for age and sex there was a significant positive association between change in fat mass and change in insulin level ($t = 3.6$, $p = 0{,}002$, $n = 28$) and change in fasting C-peptide level ($t = 2.5$, $p = 0.020$, $n = 28$). These results are not shown in Table 4.

An intent to treat analysis, including the 12 dropouts with last measurement carried forward (Table 5), showed a mean weight loss of 12.5 kg (105,3 kg – 92,8 kg). Only four of these patients managed to have two measurements

Table 2
Anthropometric results ($n = 32$) given as mean (with SD in parenthesis)

	Baseline	7 months	Change	Significance
Age	49.5 (13.2)			
Height (cm)	172.5 (8.9)			
Weight (kg)	103.9 (19.0)	89.2 (17.5)	−14.7 (4.9)	$p < 0.01$
Fat percentage	41.7 (8.0)	35.3 (8.7)	−6.4 (2.9)	$p < 0.01$
Fat mass (kg)	43.3 (11.1)	31.3 (9.9)	−11.9 (4.3)	$p < 0.01$
Fat free mass (kg)	60.6 (14.9)	57.8 (14.9)	−2.8 (2.3)	$p < 0.01$
Total body water (kg)	43.2 (10.9)	40.8 (9.9)	−2.4 (2.0)	$p < 0.01$
BMI (kg/m^2)	34.8 (5.0)	29.8 (4.2)	−5.0 (1.8)	$p < 0.01$

Table 3
Results fasting blood sampling. Number of patients is given in parenthesis. Results are mean ± SD

Variable (*n*)	Baseline	7 months	Change	Significance
Glucose, mmol/L (26)	5.6 (1.0)	5.1 (0.5)	−0.4 (0.7)	$p<0.01$
HbA1c, % (28)	5.7 (0.4)	5.4 (0.3)	−0.3 (0.7)	$p<0.01$
Insulin, pmol/L (26)	113.3 (95.0)	82.2 (61.7)	−31.2 (57.3)	$p=0.01$
C-peptide, pmol/L (28)	708 (376)	626 (331)	−81.8 (333)	$p=0.20$
Total cholesterol, mmol/L (28)	5.4 (0.9)	5.1 (0.8)	−0.3 (1.0)	$p=0.11$
HDL, mmol/L (28)	1.3 (0.3)	1.5 (0.3)	0.2 (0.3)	$p<0.01$
LDL, mmol/L (28)	3.5 (0.9)	3.3 (0.8)	−0.3 (0.7)	$p=0.06$
Triglycerides, mmol/L (22)	1.7 (0.8)	1.0 (0.5)	−0.7 (0.8)	$p<0.01$
Lp(a), mg/L (25)	207 (236)	220 (258)	12 (52)	$p=0.23$
Homocystein, μmol/L (19)	10.0 (3.2)	10.1 (3.0)	0.1(2.3)	$p=0.84$
MicroCRP, mg/L (18)	4.1 (3.1)	2.7 (2.9)	−1.4 (1.9)	$p<0.01$
TSH, mU/L (23)	2.1 (0.9)	1.8 (1.0)	−0.3 (0.9)	$p<0.01$
Uric acid, μmol/L (26)	351 (80)	310 (76)	−41 (66)	$p<0.01$
Vit B12, pmol/L (27)	360 (259)	429 (277)	70 (212)	$p=0.10$
Vit D3, nmol/L (26)	61.8 (22.3)	73.2 (16.8)	11.4 (27)	$p=0.04$
Hemoglobin, g/dl (19)	14.2 (0.9)	13.9 (0.7)	−0.3 (0.6)	$p=0.02$
ALAT, U/L (23)	36.7 (22.8)	24.3 (9.5)	−12.3 (19.7)	$p<0.01$
Creatinine, μmol/L (27)	66.6 (14.7)	65.7 (11.5)	−0.9 (14.1)	$p=0.02$
Ferritin, μg/L (25)	111.4 (84.8)	113.9 (70.1)	2.6 (50.1)	$p=0.80$
Folate, nmol/L (23)	17.2 (11.0)	21.0 (10.1)	3.8 (10.7)	$p=0.12$
Potassium, mmol/L (27)	4.3 (0.2)	4.2 (0.3)	−0.07 (0.2)	$p=0.10$
Magnesium, mmol/L (26)	0.81 (0.07)	0.82 (0.08)	0.01 (0.06)	$p=0.29$
Sodium, mmol/L (28)	141.5 (1.8)	140.9 (2.0)	−0.6 (1.8)	$p<0.01$
Selenium, μmol/L (21)	1.1 (0.2)	1.1 (0.1)	0.0 (0.1)	$p=0.26$
Zinc, μmol/L (22)	13.3 (1.8)	12.8 (1.9)	−0.5 (2.3)	$p=0.36$

Table 4
Linear regression analysis with change in body weight as dependent variable, and change in insulin, c-peptide and glucose as independent variables

Variable	Model 1				Model 2			
	B (SE)	Beta	t-value	*P*	B (SE)	Beta	t-value	*P*
Delta C-peptid	0.006 (0.003)	0.429	2.421	0.023	0.007 (0.003)	0.469	2.561	0.017
Delta Insulin	0.032 (0.016)	0.391	2.081	0.048	0.032 (0.016)	0.392	1.990	0.059
Delta Glucose	0.789 (1.343)	0.119	0.588	0.562	0.672 (1.387)	0.101	0.484	0.633

Model 2 is adjusted for age and sex.

of blood variables. Accordingly, there is not sufficient data to evaluate the change in blood variables in the patients who dropped out.

There were no noted side effects or complications that could be tied to the treatment in the study participants.

4. Discussion

Compared to the results of similar trials using VLC diets, the Eurodiet method appear highly effective in the short term. Hemmingson and coworkers achieved an 11.5 kg weight loss after one year in a group with baseline BMI of

Table 5
Intent to treat. Anthropometric results ($n = 44$) given as mean (with SD in parenthesis)

	Baseline	7 months	Change	Significance
Age	49.7 (13.7)			
Height (cm)	172.7 (9.1)			
Weight (kg)	105.3 (18.9)	92.8 (18.5)	−12.5 (6.3)	$p < 0.01$
Fat percentage	41.5 (7.8)	36.3 (8.6)	−5.2 (3.4)	$p < 0.01$
Fat mass (kg)	43.6 (11.3)	33.6 (10.7)	−10.0 (5.5)	$p < 0.01$
Fat free mass (kg)	61.7 (14.7)	59.2 (14.8)	−2.6 (2.1)	$p < 0.01$
Total body water (kg)	44.3 (10.1)	42.1 (10.3)	−2.2 (1.9)	$p < 0.01$
BMI (kg/m^2)	35.2 (5.0)	31.0 (4.9)	−4.2 (2.3)	$p < 0.01$

34 [10]. When only the completers were considered weight loss averaged 13.8 kg. We found little variation in the loss of lean body mass, suggesting that some loss of LBM is expected regardless of fat loss. Change in fat free mass was under 20% of total weight loss, including the common loss of water observed with carbohydrate restriction. Thus, loss of lean body mass should be considered low. However, the Tanita BC-420 has to our knowledge not been validated in small sample sizes such as in this study and the large variation in the measures in a two of the patients suggest caution in the interpretation of the body composition results.

In a recently published trial, bariatric surgery was compared to a traditional weight loss regime focusing on reduced caloric intake and increased energy expenditure [11]. Gastric bypass produced a weight loss of 30% of initial weight while the lifestyle alternative led to an 8% weight loss. From these results, surgery clearly appears the more attractive option, if one takes only or primarily the degree of weight loss into account. But because surgery implies higher risk of complications and many morbidly obese individuals do not wish to opt for bariatric surgery, there is a need for lifestyle weight loss alternatives. These alternatives do not have to be as effective as surgery to be considered feasible alternatives, but an average 8% weight loss may be considered an unattractive alternative for those who are very obese. The 14.2% average weight loss with the Eurodiet method seems a more attractive strategy. It should be considered though that the average BMI in our study (34.8 kg/m^2) was somewhat lower than that of the lifestyle (43.3 kg/m^2) and surgery (46.7 kg/m^2) arms of the Hofso study.

Changes in several factors related to nutritional status were observed (Table 3). None of these factors suggest a lack of specific nutrients or negative health effects related to inadequate nutrient intakes.

The Eurodiet method is based on dietary induced ketosis in the two starting phases. The results observed in the present study are in agreement with results from previous studies of carbohydrate restriction and low glycemic index/load diets which usually show a greater weight loss than alternatives [12]. Data also indicate that ketogenic diets cause greater satiety than low fat diets [13–15], and this seems to be an advantage when weight loss is desired. The large initial weight loss with carbohydrate restriction may also be an important motivational factor. Despite the fact that carbohydrate restriction is an effective weight loss method in the short term, it is difficult to say how long severe restriction should be used. The Eurodiet method shows that dietary ketosis from carbohydrate restriction can be used as an effective tool during the initial phase of a weight loss method.

The Eurodiet method implies that an effective weight loss strategy should focus on reduction in insulin levels by restricting carbohydrates and focusing on the glycemic index/load of foods. In support of this hypothesis baseline weight, total weight loss and fat mass reduction were all inversely correlated with fasting insulin and C-peptide. On the other hand, we did not find a significant correlation between change in insulin and change in fat mass. In spite of this there was a strong positive correlation between total weight loss and change in fat mass ($r = 0{,}883$, $p < 0{,}01$). We can offer no good explanation for this. The reason for a stronger correlation between weight loss and C-peptide than between weight loss and insulin, might be that insulin is metabolized faster than C-peptide and this might explain the higher coefficient of variation for insulin (80%) compared to C-peptide (50%). In the examined treatment fasting insulin level was reduced by 30.3pmol/L (27%) between the first and second blood sampling approximately four weeks after baseline.

In accordance with other studies [16] we found a significant negative correlation between vitamin-D and body weight, and between vitamin-D and insulin level. Vitamin-D level is commonly low in both obese patients as well as in CVD patients and this has prompted supplementation of vitamin-D in treatments [17]. In the Eurodiet method vitamin-D supplements are recommended where the serum level is found to be low and this may thus have contributed to the positive correlation between vitamin-D and weight loss.

Considering the goal of finding lifestyle based treatment alternatives to bariatric surgery, VLC diets seems an interesting option, provided that the weight loss can be maintained long term. Because long term weight maintenance following VLC diets is poor [18] we need to consider how we follow up the VLC diets. A low glycemic load option as the Eurodiet approach is here shown effective during 7 months and we now strive to test the long term effects of this strategy.

The reason for focusing on glycemic load in the reintroduced diet is that both weight and risk factors for diabetes and cardiovascular disease are closely linked to the actions of glucose and insulin. It is thus likely that the combination of overweight and lifestyle diseases appear in individuals particularly sensitive to the harmful effects of high glucose and insulin levels. In order to maintain as much as possible of the beneficial effects of the VLC diet a low glycemic load diet has therefore been chosen.

In our opinion, the results of this pilot study seem promising, but a larger controlled long term trial is needed to properly evaluate the effects of the treatment.

5. Limitations

Dropout rate in this study was 27%, which is a common finding in similar studies [18, 19]. When regarding this dropout rate one should consider that this is a treatment paid for by the patients and that financial reasons thus may affect drop-out rate. Lack of a control group means we cannot determine changes not affected by treatment and one should consider differences in study groups when comparing these results with the results of other studies. As the Eurodiet method is a complex lifestyle method we cannot determine which part of the treatment produced the observed results, or which part of the treatment had the greatest effect.

6. Conclusion

Compared to available studies of obesity treatments focusing on dietary and lifestyle intervention, the Eurodiet method of combining a VLC diet with a low glycemic load Mediterranean diet, appears effective in reducing body weight, and improving the risk profile for diabetes and CVD. Despite the fact that the treatment caused a significant weight loss at 7 months we do not know to what extent weight loss is sustained in the course of time.

Competing interests

This study was funded by Eurodiet Scandinavia. The study was conducted by PJ and ATH who do not have any financial or other interests concerning the outcomes of the investigation. FAL is part owner of Eurodiet Scandinavia.

Authors' contributions

All three authors conceived and designed the study. PJ carried out all subject recruitment and data collection, was responsible for data analysis and assisted with manuscript preparation. ATH contributed with data analysis and manuscript preparation. FAL contributed with manuscript preparation. All authors read and approved the final manuscript.

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