



Long-term effects of a very low calorie diet (Nutrilett®) in obesity treatment. A prospective, randomized, comparison between VLCD and a hypocaloric diet+behavior modification and their combination

KR Rytting^{1,2}, H Flaten³ and S Rössner²

¹MEDDOC, Research Centre, Venlighedsvej 6, DK-2970 Hørsholm, Denmark; ²Obesity Unit, Norrbacka, Karolinska Hospital, S-171 76 Stockholm, Sweden and ³Nycomed Pharma AS, PO Box 4284, Torshov, N-0401 Oslo 4, Norway

OBJECTIVES. To compare weight loss on a balanced hypocaloric diet to that of a Very Low Calorie Diet (VLCD) after two months of treatment and to further compare 26 months of weight maintenance and safety with or without VLCD assistance in obese patients.

DESIGN. Prospective, randomized, controlled intervention trial, initially with two and later with three parallel groups.

SETTING. Swedish University out-patient obesity clinic.

SUBJECTS. Eighty-one obese patients of both gender with a BMI ≥ 30 kg/m² from the waiting list participated in a structured weight reduction + weight maintenance programme.

INTERVENTION. Twenty-seven patients (group A) were randomized to a balanced diet of 6720 kJ/d (1600 kcal/d) during the whole treatment period. The other patients ($n=54$) were randomized to VLCD (Nutrilett®) 1764 kJ/d (420 kcal/d) diet during the first two months. The VLCD treated patients were rerandomized after the initial treatment to the well balanced hypocaloric diet (6720 kJ/d) with (group C) or without (group B) 1 MJ of VLCD to be taken during the evening.

MAIN OUTCOME MEASURES. During the first two-month period, the mean body weight loss in the VLCD group was 18.9 ± 7.1 kg compared to 7.2 ± 4.8 kg in the diet treated group, with a similar relative fat loss assessed by bioimpedance of 68% and 76% respectively. The maintained weight loss in all groups after 28 months of treatment was 10.9 ± 10.2 kg in the 52% who completed the programme. Weight losses and drop-out rates were similar in all three groups.

CONCLUSIONS. Twenty-four months weight maintenance and drop out rates are independent of whether the initial treatment commences with VLCD or a hypocaloric diet. One MJ nutrition powder taken freely does not affect 24 months weight maintenance on a hypocaloric (6.7 MJ/d) diet.

Keywords: body weight; diet; fat-free-mass; night eating; treatment compliance; VLCD; weight changes.

Introduction

It has been hypothesized that reduction of body weight obtained with a balanced low calorie diet soon leads to a plateauing due to a reduction in fat-free-mass (FFM).¹ It has also been hypothesized that VLCD treatment leads to a higher post-treatment body weight compared to the pre-treatment body weight due to a change in body composition.² The body composition of the post-obese patient with a lower FFM and subsequently lower metabolic rate may however be determining for weight fluctuations later.³

The short-term effects of VLCD have been substantially documented,⁴ and results of adequately

designed long-term trials of VLCD treatment combined with behaviour modification have also been published.^{5,6} Night eating as described by Stunkard⁷ is a prominent manifestation in our patients. Some studies indicate that protein *per se* has a satiating effect.^{8,9} We therefore decided to include a VLCD preparation as a component of our basic long-term behaviour modification programme in an attempt to prevent uncontrolled overeating, especially in the evening and to improve long-term compliance.

Methods

Subjects

Obese patients (BMI ≥ 30 kg/m²) from the waiting list of the obesity unit at Karolinska Hospital were invited to participate in the trial. Only patients, who were able

to complete a visual analogue scale (VAS) concerning hunger feelings at three o'clock daily during a two week run-in period were included.

Eighty-one patients (44 females, 37 males) were included in the trial. The patients were between 21 and 64 y of age and had a stable body weight (fluctuations ≤ 3 kg) within the last two months before commencing the treatment. Excluded were: Patients with known history of renal, cardiac, cerebrovascular, gastrointestinal ulcer, or gallbladder diseases. Patients suffering from IDDM, gout and porphyria. Patients with psychiatric disturbances (depression, schizophrenia and behaviour disorders such as alcoholism and drug abuse). Treatment with the following drugs: antihypertensives, antidepressants, anorectics and lithium, oral contraceptives and estrogen substitution therapy (the two latter only if this treatment was instituted less than six months before the start of the VLCD period). Pregnancy, lactation, vegetarian diet and lack of informed consent were also exclusion criteria.

Patients were instructed to maintain the same physical activity and smoking habits throughout the whole trial period. Physical activity and smoking were controlled by simple check lists at each visit.

Design

Body weight, blood pressure (systolic and diastolic) and heart rate were measured and side-effects of the treatment were assessed by interview every week during the first month, then every second week during the following month, monthly during the next seven months and finally every seventh week during the rest of the observation period. The patients were weighed at the same time in the morning on a scale (Seca delta model 707), which was calibrated regularly. Waist-hip ratio, sagittal diameter and fat percentage using a standard single frequency tetrapolar (50 kHz) bioelectrical impedance instrument (TVI-10, Danninger Medical, Columbus, Ohio, USA) were evaluated regularly during the treatment period. A 12-lead resting ECG was taken initially, after six months and at the end of the trial.

Laboratory variables

Serum-electrolytes (s-calcium, s-potassium and s-sodium), blood-glucose, fasting s-lipids (cholesterol and triglycerides) and urine tests (protein, ketones and glucose) using stix were performed initially, after three and seven months and at the end of the trial. All laboratory tests were performed using the routines at the Karolinska Hospital. During the first three weeks the patients were followed by daily phone contact and monitoring of ketone bodies in the morning urine.

Treatment

Patients were initially randomized into two groups. Twenty-seven patients (group A) were prescribed a

hypocaloric diet (6720 kJ/d) using different recipes together with behaviour modification during the whole treatment period.¹⁰ The average energy content of the hypocaloric diet was approximately protein 75 g, fat 60 g and carbohydrate 180 g. The remaining patients (groups B and C) were prescribed a VLCD treatment consisting of five sachets Nutrillett® (1764 kJ/d) as sole source of nourishment during the first two months. After a one week transition period, with gradually increased intake of normal food, this VLCD group was rerandomized into group B, receiving the same diet as group A for the rest of the treatment period, and group C prescribed also the same total energy intake as group A but with 1 MJ/d provided as three sachets of Nutrillett/d. The VLCD were taken to prevent loss of food intake control, in practice often in the evening. The powder was dissolved in a glass of water (approximately 250 ml) and ingested. The energy content in each sachet was 12.3 g protein, 1.2 g fat and 6.1 g carbohydrate.

The patients were encouraged to drink as much water or non-caloric beverage as they were able to, at least 2.5 l daily. A capsule containing the recommended daily intake of vitamins, minerals and essential fatty acids was also ingested each day by the patients in the VLCD period and when needed a dietary fibre supplement, Fiberform®, was allowed in order to avoid constipation.

By routine, patients were seen by a specially trained nurse with medical expertise always immediately available whenever clinical problems arose. Eating habits and dietary compliance were checked by interviews initially and after 2, 6, 14 and 26 months of treatment by a dietitian who instructed the patients in regular group sessions during the transition period and intermittently during the maintenance period. The diet was basically the same throughout the long-term treatment. The programme was free of charge for all patients.

Statistical analysis

Quantitative data were summarised using number of observations, mean, standard deviation, minimum and maximum values. Qualitative data were summarised by using frequency tables. Analysis of variance (ANOVA) at different time was used to analyse efficacy data such as weight reduction, fat and FFM. The following effects were included in the model: treatment, sex and treatment * sex. Subgroup analyses were made for the patients completing the 12 months and the 26 months follow-up respectively. *P*-values below 0.05 were considered statistically significant. The statistical analysis was performed using SAS 6.10 under OS/2 WARP.

Ethics

The protocol was approved by the Ethics Committee at the Karolinska Hospital, Sweden.

Results

Subjects

The anthropometric and clinical data are given in Table 1. Four patients in the VLCD groups discontinued the treatment prematurely during the first two months: Two because of side-effects of the VLCD preparation, one due to epileptic seizure not related to the treatment, and one moved abroad. Furthermore 39 patients (22 females, 17 males) discontinued the treatment before the two year follow-up.

Body weight and composition

Pre-treatment mean body weight for the patients randomized to group A was 116.2 ± 21.0 kg compared to 113.2 ± 17.7 for the other patients B + C (NS). After the first two-month treatment period the mean body weight for the VLCD patients (94 ± 13.9 kg) was significantly lower compared with group A (109.0 ± 18.9 kg) ($P < 0.0001$). The mean body weight in group A at the end of the programme was 110.7 ± 17.4 kg and in the groups B and C 107.3 ± 15.1 kg and 107.5 ± 16.9 respectively (NS). The weight changes during the treatment programme are summarized in Figure 1. The weight reduction in percent of initial body weight for the completers at the end of the 26-month period was 7, 10 and 9.5% in the groups A, B and C respectively.

The fat percentage of the weight reduction after two months of treatment was 76 and 68% and at the end of the programme it was 71, 66 and 57% in groups A, B and C respectively. Pre-treatment waist circumference in group A was 114 ± 21 cm compared to 116 ± 19.4 cm in the VLCD group. After 26 months the reduction in percent in the completers of the three groups were 5, 7 and 8% respectively.

Hunger feeling

Overall no changes in hunger feelings were noted during the treatment period.

Table 1 Anthropometric and clinical data of the 81 patients

Variable	Units	Group A (N=27)	Group B+C (N=54)	P values A vs B+C
Female/male		14/13	30/23	
Age	y	39.5 ± 10	44.0 ± 10	NS
BMI	kg/m ²	37.6 ± 5.7	37.7 ± 3.9	NS
BW	kg	116.2 ± 20.8	113.2 ± 17.6	NS
SAD*	cm	30.5 ± 3.5	31.6 ± 3.3	NS
WHR**		0.87 ± 0.09	0.88 ± 0.07	NS
SBP	mmHg	131.6 ± 14.5	138.5 ± 18.6	NS
DBP	mmHg	84.3 ± 8.9	85.8 ± 10.4	NS
Fat	%	45.0 ± 5.2	46.5 ± 5.0	NS
s-Chol	mmol/l	5.8 ± 1.0	5.6 ± 1.0	NS
s-HDL	mmol/l	1.1 ± 0.3	1.1 ± 0.2	NS
s-TG	mmol/l	2.0 ± 1.6	2.0 ± 0.9	NS

Figures are given as mean \pm s.d. and NS = $P \geq 0.05$.

*SAD = Sagittal abdominal diameter.

**WHR = Waist-hip ratio.

Blood pressure

Changes in the systolic blood pressure are given in Figure 2a and b. The average systolic blood pressure decreased by 5, 9 and 8 mm Hg during the first two-month period in the groups A, B and C respectively. The systolic blood pressure increased again after the 26-month period close to pre-treatment values. The reduction in diastolic blood pressure followed the same pattern as the systolic blood pressure.

Heart rate and ECG

Heart rate changed little during the whole treatment programme. During the treatment period minor ECG variations were observed in three patients. These ECG changes did not warrant withdrawal.

Blood and urine chemistry

Mean s-electrolytes (sodium, potassium and calcium) did not change during the treatment (Table 2). The post-treatment values of the lipid parameters within, or between the three groups were not significantly changed compared to pre-treatment values. The daily urine ketone body measurements in the morning urine during the initial VLCD period ranged between 4 and 16 mmol/l.

Compliance

Fifty-two percent of all patients completed the whole 26 month programme. Sixteen (59%) completed the treatment in group A vs 11 (41%) and 15 (56%) in groups B and C respectively (NS).

Side-effects

The most frequent complaints were headache, dizziness, fatigue, muscular weakness, gastrointestinal problems and nausea. After the two-month treatment period 1 patient in group A, 10 in group B and 9 in group C complained of partial transient alopecia. Hair growth began within a few weeks of the subsequent diet treatment period.

Discussion

The overall results of this study demonstrate that after two years the mean values of body weight in the completers were between 7–10% below the respective pre-treatment values. The design of the study made it possible to achieve adherence by 53% of the patients during 26 months, in spite of limited staff resources. This figure is higher than reported in most recently published studies.^{11,12} Based upon our previous experiences⁵ with proper patient selection, the results from this study further support the concept that a VLCD programme to a great extent can safely be run by a trained nurse with only limited involvement of a physician. The short-term results obtained in our trial

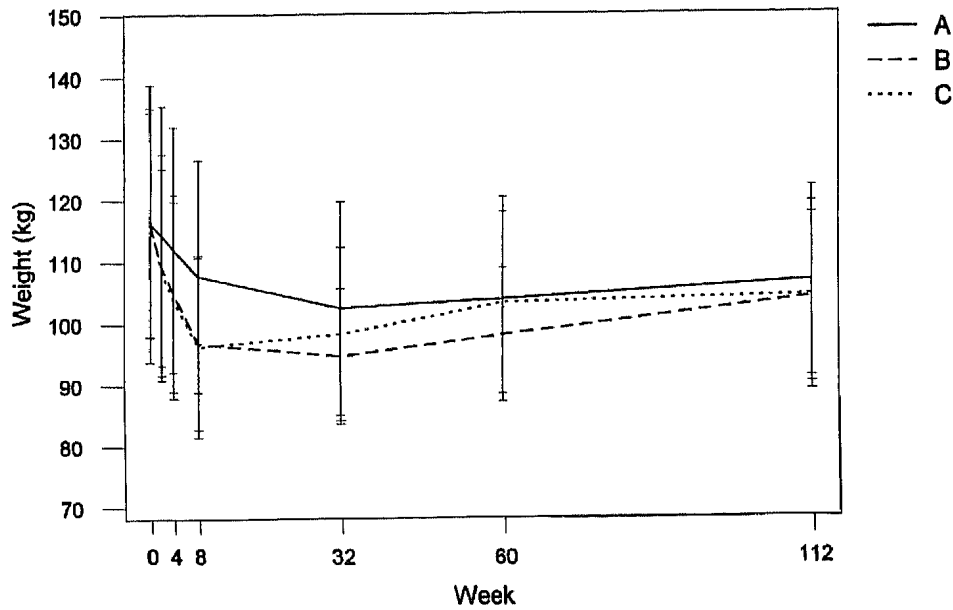


Figure 1 Weight changes during treatment (mean ± s.d.).

with a weight loss of 15% in the VLCD groups compared to 6% in the hypocaloric group are similar to the results of most published reports with similar patient selection and study design.^{13,14} The average weight changes in the three groups showed the expected u-curve with a statistically significant weight loss only in the VLCD groups up to half a year after initiation. In the VLCD groups, the most pronounced weight increase was seen in group C. The reduction in FFM at the of the 26 month treatment period was 3% in group A, vs 4% and 5% in the groups B and C respectively, showing that FFM could be preserved to a high degree. It has been postulated that subjects using VLCD are more liable to weight cycling and thereby at an increased morbidity risk but this has recently been disputed.¹⁵ Our two-year weight loss result did not demonstrate an increase in morbidity risk judged by the investigated metabolic parameters. The fact that drug treated hypertension was an exclusion criterion may explain why blood pressures remained unchanged by therapy.

Conclusions

Several obese patients have problems controlling overeating during the late afternoon and evening.⁷ It may be hypothesized that a protein rich VLCD could prevent evening hyperphagia during the weight maintenance period. Free use of 1 MJ/d had however no influence on body weight in our study. It is possible that instructions for future use of single VLCD sachets must be tailored individually and much more in detail than intended with this study.

Acknowledgements

We thank research nurse Lena Mannström for dedicated and meticulous expert work in connection with performing this trial, and for never failing motivating the patients. Inga Lena Andersson RD provided excellent dietetic support. Nycomed Pharma AS, Oslo, Norway supported this project and Tricum

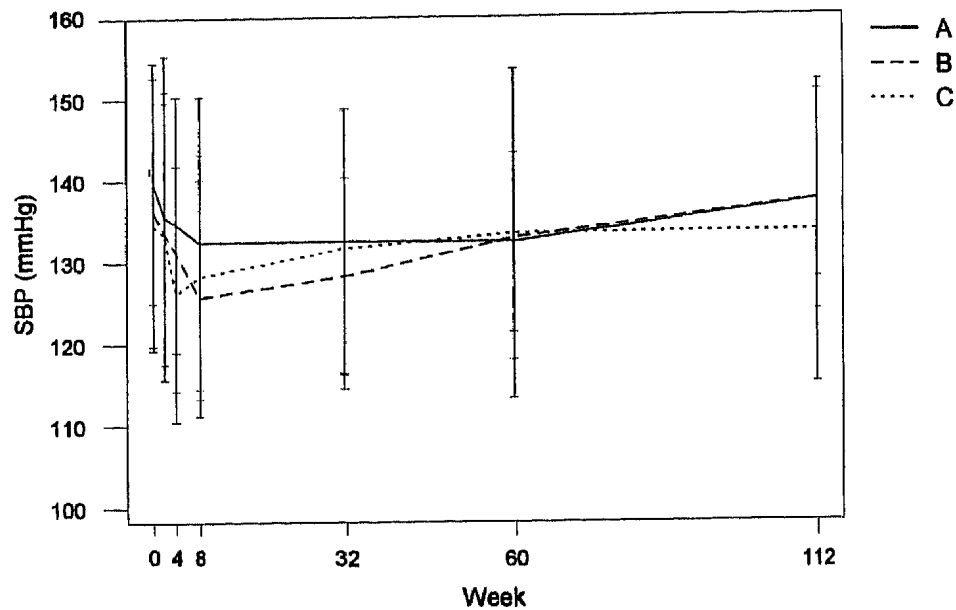
Table 2 Changes in serum-lipids and blood-glucose (mmol/l) during maintenance treatment (mean ± s.d.)

Variable	Group*	Month 0	Month 8	Month 12	Month 26	P (26-0)
s-Chol.	A	5.7 ± 1.3	5.4 ± 1.3	5.3 ± 1.4	5.7 ± 1.5	NS
	B	5.4 ± 1.1	5.1 ± 1.1	5.4 ± 1.2	5.2 ± 1.1	NS
	C	5.9 ± 1.1	5.5 ± 1.2	5.7 ± 1.0	5.5 ± 1.0	NS
s-TG	A	2.2 ± 1.4	1.6 ± 0.9	1.6 ± 0.7	1.8 ± 1.3	NS
	B	1.8 ± 0.9	1.3 ± 0.5	1.3 ± 0.7	1.2 ± 0.5	NS
	C	2.4 ± 1.6	1.5 ± 1.0	1.6 ± 0.6	1.8 ± 0.7	NS
B-glucose	A	5.7 ± 1.6	4.9 ± 0.5	5.1 ± 0.9	5.4 ± 1.9	NS
	B	5.2 ± 0.9	4.7 ± 0.4	5.0 ± 0.5	5.0 ± 0.6	NS
	C	5.6 ± 1.1	5.0 ± 0.7	5.2 ± 0.5	5.0 ± 0.9	NS

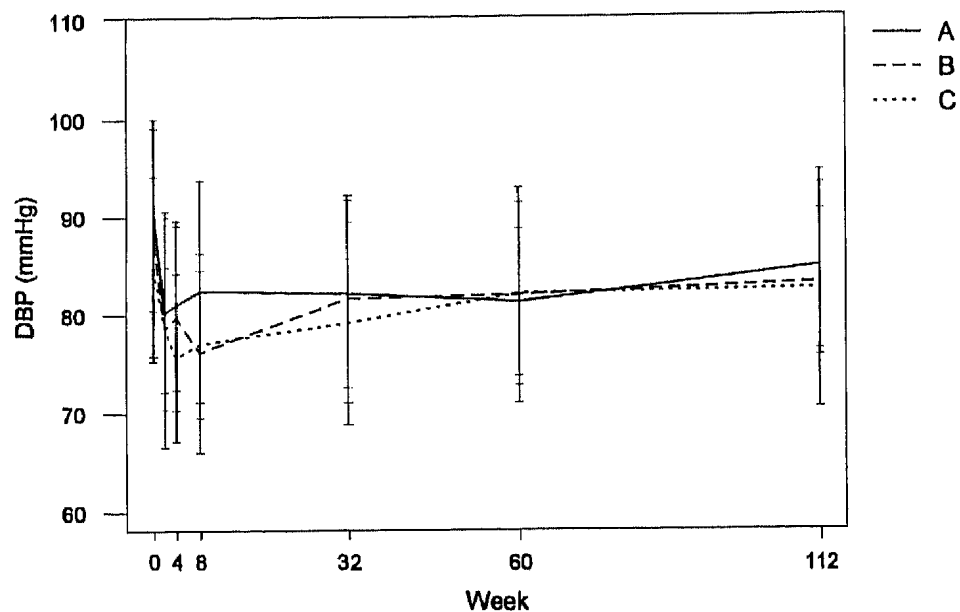
*Group A = 6720 kJ/d, balanced diet.

*Group B = 1764 kJ/d for two months followed by 6720 kJ/d, balanced diet.

*Group C = 1764 kJ/d for two months followed by 6720 kJ/d, of which 1 MJ kJ/d is provided by VLCD sachets.



(a)



(b)

Figure 2a and b Changes in systolic and diastolic BP during treatment (mean \pm s.d.); *Group A = 6720 kJ/d, balanced diet; *Group B = 1764 kJ/d for two months followed by 6720 kJ/d, balanced diet; *Group C = 1764 kJ/d for two months followed by 6720 kJ/d, of which 1 MJ kcal/d is provided by VLCD sachets.

AB, Höganäs, Sweden generously provided the dietary fibre supplement.

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