Review Article

State of the science: VLED (Very Low Energy Diet) for obesity

Elizabeth Delbridge BSc (Hons) MND, MPH and Joseph Proietto MB BS FRACP PhD

University of Melbourne, Department of Medicine(AH/NH), Repatriation Hospital, Heidelberg, Victoria 3081, Australia

It is often stated, “the faster you lose weight, the faster it is regained”. A review of existing literature does not support such a statement - indeed if anything the reverse is true. The origins of this erroneous view are the misconceptions that weight regain is a simple matter of bad dietary and social habits and that it takes time to change these, that physiological adaptations to rapid weight loss are different to those of gradual weight loss and that weight regain is simply due to a return to old habits. Indeed there are many advantages to rapid weight loss achieved with the use of a modern very low energy diet, including the fact that rapid weight loss is a motivating factor, that the mild ketosis that occurs not only suppresses hunger, but also slows protein loss and that adherence is easier with a structured dietary regime. VLEDs are dietary preparations that provide all nutritional requirements together with between 1845 and 3280 KJ (450 and 800 Kcal) per day. An individual takes this meal replacement three times daily as a substitute for breakfast, lunch and dinner. In addition, a bowl of non-starchy vegetables once daily provides some fibre and helps to satisfy the social aspect of eating. A teaspoon of oil on the vegetables contracts the gall bladder to minimise the risk of gall stone formation. Since weight loss, at whatever rate, results in physiological adaptations leading to weight regain, careful attention must be paid to the period after the VLED regime is completed. Lifestyle modification, diet and exercise are instituted optimally with behaviour modification. If, despite the subject’s best efforts, weight regain occurs, an appetite suppressant is advisable to help control the drive to eat.

Key Words: weight loss, obesity, leptin, hunger, very low energy diet, VLED, pharmacotherapy.

Introduction

It is often said that rapid weight loss using Very Low Energy Diets (VLEDs) is inadvisable because “the faster you lose the weight the faster it is regained”. The reason given for this popular view is that the VLED does not promote the necessary lifestyle changes required to maintain weight loss in the longer term. Such a view has at its basis several assumptions that can be challenged: 1) overweight is only the result of self-chosen lifestyle; 2) the physiological adaptations that occur following weight loss are different from those that follow slow gradual loss; 3) all weight regain is due to simple return to old habits.

Is there evidence that rapidly achieved weight loss is regained faster than weight that is lost slowly?

Very low energy diets are effective in achieving large and rapid weight losses in a short period of time. The process of using VLEDs will be explained in more detail later in the paper. In his review of the literature on VLEDs and sustained weight loss, Saris suggested that not many conclusions can be drawn from randomised controlled trials using VLEDs because of the difficulty in comparing studies that differ in design, treatment modalities, length of initial treatment, and follow-up activities. He reported a large variation in weight regain following a VLED. Percentage of initial weight loss ranged from -7% to 122% after 1 year, to 26% to 121% after 5 years.

A review of the literature conducted in 2000 by the National Health and Medical Research Council of Australia as part of its evidence-based guidelines for the management of obesity, compared long-term weight loss with different diet therapies (Table 1). Within the limitations suggested by Saris, this review demonstrated that 2 years after initiation of weight loss therapy, weight loss maintenance using a VLED is no worse and possibly better than other diet therapies. Mustajoki and Pekkarinen compared weight loss outcomes achieved in randomized trials with a minimum of 30 patients who were followed up for 1 year or more. The VLED period varied from 8-16 weeks in duration and the non-VLED approach was a 1200kcal/day balanced diet. The results achieved are shown in Table 2. These results caused the authors to conclude that: “There is no evidence that VLED programmes lead to worse long-term results or are associated with more untoward effects than programmes with low calorie or other dietary approaches”.

Correspondence address: Professor Joseph Proietto, Dept of Medicine, Repatriation Hospital, 300 Waterdale Rd Heidelberg 3081, Victoria, Australia Tel: +61 3 9496 2250; Fax: +61 3 9497 4554 j.proietto@unimelb.edu.au Accepted 30 June 2006
Whereas the above analyses of the literature found that the long-term weight of people who followed a VLED is no worse than people who followed low energy diets, another review found that followers of VLEDs lose significantly more weight initially and maintain significantly greater weight losses than followers of low energy, balanced diets. Toubro and Astrup randomized obese patients to a VLED or a conventional low calorie diet and counselled them to lose 13.6 and 13.8 kg respectively. The VLED group took 8 weeks to achieve the target weight loss whereas the conventional group took 17 weeks. After 1 year, the VLED group was maintaining an extra 2.4 kg loss compared to the conventional group. After 2 years the difference was 3.0 kg extra. Although the differences were not significant, the study did show that a large and rapid weight loss did not result in poor maintenance of the loss compared to a conventional diet.

So there appears to be little evidence that “the faster you lose weight the quicker you regain it” yet the anecdote is often touted in the lay-press and by health practitioners. Is there any evidence supporting the basic assumptions underlying this common misconception?

### Obesity is the result of a self-chosen lifestyle

There is no doubt that the aetiology of obesity involves both environmental and genetic influences. The recent increase in the prevalence of overweight and obesity is clearly due to the continuous availability of high-energy foods, together with a major reduction in the obligatory need for physical activity that has characterised man’s existence until very recent times. However not everyone becomes obese when placed in an obesogenic environment. Thus a genetic predisposition is required for the environment to produce obesity. Studies on monozygotic and dizygotic twin pairs either reared together or reared apart suggest that ~70% of the influence on body weight is genetic while ~30% is environmental. The dominance of genetic influences has been confirmed with adoption studies in which it was shown that adoptees resemble their biological parents in body size and have very little resemblance to their adopted parents. Some of the genes that could predispose to obesity have been identified but there are likely to be many more as yet undiscovered.

### Do physiological adaptations differ depending on rate of weight loss?

There is little evidence in support of this proposition and more research is required, however the little available evidence does not suggest a difference. The effects of a low energy versus a very low energy diet on metabolic rate and body composition were studied in Zucker rats. Although the rate of weight loss was twice as fast in the VLED group, daily energy expenditure and resting metabolic rate was depressed equally in the two groups. Coxon and colleagues compared fat free mass and resting metabolic rate change between two groups of women with different rates of weight loss (1.1 kg/week vs 1.9 kg/week over 8 weeks). They showed that there was an equivalent FFM/Wt loss (0.42 and 0.44) in the two groups and the RMR/FFM ratio remained the same in the two groups. Finally it has been shown that there are no differences in the adaptive changes in urea kinetics in response to either different rate or extent of weight loss.

### Is weight regain simply a return to old habits?

Following weight loss, an individual experiences physical and physiological benefits including increased energy levels, improved mobility, better sleeping patterns and reduced blood pressure. There are also psychological benefits from weight loss such as improved self-esteem. Although these benefits are all favourable, for most people they are not enough to outweigh the strong biological processes driving weight regain. There is strong support from animal and human studies that weight regain is driven by physiological processes that are likely to be genetically determined.

Studies in obese-prone rats that have become obese have shown that when weight loss occurs, resting metabolic rate is suppressed beyond what would be expected for the reduction in weight. These rats also exhibit enhanced metabolic efficiency that is evident during a period of weight maintenance when energy intake is controlled. When control over energy intake is removed, these rats experience very rapid and high weight regain. These findings have been replicated in human studies, but it is unclear if the metabolic efficiency persists during weight maintenance and is responsible for almost inevitable weight regain.

Leptin levels and substrate oxidation following weight loss are also likely to play important roles in weight regain. A comparison of age and BMI-matched post obese male and female subjects with never-obese subjects found that plasma leptin levels were lower but respiratory quotient (RQ) was higher in post-obese subjects. A higher RQ indicates a low level of fat oxidation, which
predicts body weight gain. It has been suggested that lep-
tin may have a stimulating effect on fat oxidation in obese
subjects.\textsuperscript{15}

It is well documented that leptin levels decrease
following weight loss. Interestingly, in surgery-induced
weight loss, 1-year post surgery serum leptin is decreased
beyond expected values based on body composition, a
factor that may favour weight regain after surgically
induced weight loss.\textsuperscript{16}

The National Weight Control Registry (NWCR) is a
prospective investigation of long-term successful weight
loss maintenance. The aim of the registry is to identify
characteristics of individuals who have successfully main-
tained a 13.6kg weight loss for 5.8 years. Over 5000
individuals are on the registry. They periodically com-
plete questionnaires and surveys that assess behavioural
and psychological characteristics and the methods em-
ployed to maintain their weight loss. The registry re-
searchers have identified that successful weight mainte-
nance is associated with following a moderate fat diet and
doing a high level of physical activity.\textsuperscript{17} However, people
on the registry are a unique, self-selected group of people.
The overwhelming evidence is that most people cannot
maintain weight loss despite initially being highly moti-
vated.

What is a VLED?
A Very Low Energy Diet (VLED), also known as a Very
Low Calorie Diet (VLCD) is defined as a total diet
replacement which provides between 1845 and 3280 KJ
(450 and 800 Kcal) per day. VLEDs are generally taken
as a commercial formulation of liquid or powder that
serves as the sole source of nutrition. VLEDs contain car-
bohydrate, fat and protein and are fortified with the
recommended daily allowances of essential nutritional
requirements. Treatment frequency and duration varies
depending on the product chosen and the degree of obe-
sity in the individual being treated, but the usual length of
treatment is 8-16 weeks.

VLEDs are generally not the first choice of treatment
for obesity. They tend to be reserved for use in individu-
als who have failed with more conservative methods of
weight loss. The purpose of VLED use is to achieve “a
large weight loss whilst preserving vital lean body
mass".\textsuperscript{18} VLEDs have been shown to be very effective in
the treatment of obesity with an immediate weight loss of
1.0-1.5 kg per week that is predominantly fat mass. They
are typically prescribed for the “morbidly obese or for
patients in whom rapid weight loss is medically ne-
cessary”.\textsuperscript{19} They provide a constructive alternative to other,
more conservative approaches to weight loss in the treat-
ment of obesity.

Advantages of using VLED
There are several advantages of using a VLED approach
to weight loss in obese subjects:
1. Rapid weight loss is a motivating factor.
2. VLED results in diuresis which improves patients
   feeling of wellness early in the treatment.
3. VLED is low in carbohydrate and the patients
   become mildly ketotic and mild ketosis results in
   reduced hunger
4. Ketosis slows the rate of muscle loss
5. The convenience of VLEDs in the form of meal
   replacements has been found to assist with accepta-
   bility and compliance.\textsuperscript{20} Paradoxically, restricting
   choice of food items available for consumption to a
   small number (eg a milkshake, bar, soup or mousse)
   improves adherence compared to a low-fat, ad-
   libitum style diet.

Side effects
Modern VLEDs are accepted as being safe with only mi-
nor, inconvenient side effects. Side effects include halo-
tosis, headache, poor tolerance to the cold, hair loss, irrit-
ability and postural dizziness. Individuals taking VLEDs
may also complain of constipation as the preparations
generally do not contain sufficient fibre. A further side
effect of increased prevalence of gallstone formation has
also been reported during VLED use\textsuperscript{21}, but this is on a
background of obesity being an independent risk factor
for cholelithiasis.

How should VLEDs be used?
When commencing a VLED several issues need to be
addressed:

Contraindications to VLED
1. Pregnancy or advanced age
2. History of severe psychological disturbance, alco-
holism or drug abuse.
3. Presence of porphyria, recent myocardial infarct
   or unstable angina, severe renal or liver failure. In
   addition, care should be taken in patients with dia-
abetes treated with insulin or sulphonylureas as hypo-
glycaemia may occur without a reduction in medi-
cation.

Setting realistic targets
Severely obese subjects cannot maintain a low energy diet
for an extended length of time. Modest weight reduction
has measurable health benefits and has a better chance of
being maintained in the longer term. Targets should be
set following consultation with the patient. Patients need
explanation on why it best to set modest targets. A
reasonable initial target is a 10% weight loss.\textsuperscript{22}

Exercise
Exercise should be both formal (i.e. walking a set time
each day) and incorporated into daily living (i.e. increased
activity such as using stairs instead of lifts, parking the
car a little further away from the entrance to the super-
market, getting up to change the TV channel etc).
Patients should aim for the equivalent of at least one hour of
walking per day, more if possible. Other forms of exercise
such as swimming, exercise bikes etc. may also be
appropriate, keeping in mind the patients age and health
status.

Commencing a patient on a VLED
When it is decided to commence a patient on the VLED
regimen the patient is given written instructions and told
of the general strategy. The importance of achieving mild
ketosis to suppress hunger should be emphasised and the
patients should be encouraged to avoid carbohydrate
supplementation of the VLED plus vegetables when hungry. Advise them to have lean meat or fish in the first week prior to the onset of ketosis.

**Follow-up**

Once commenced on a VLED the patient should be followed up on a fortnightly basis in the clinic for check-ups, advice and encouragement. Blood tests should be repeated mid way through the VLED phase. At the end of the VLED phase, the patient should be commenced on the maintenance program (see below).

**Blood tests on VLED**

Careful supervision of patients on VLED is important because of the potential for serious consequences while on these diets. There have been very few electrolyte imbalances using the modern VLEDs.

Baseline blood tests:

- Biochemistry - Electrolytes/ Creatinine, liver function tests, fasting glucose, Cholesterol/Triglycerides/HDL, Uric Acid, Haematology - Full Blood count, Iron studies

Follow-up blood tests:

- Electrolytes should be checked half way through the VLED regime or earlier if required by the patient’s condition (e.g patients with renal impairment)

**How long should a patient continue on the VLED?**

Usually patients continue on VLED for 12 weeks. However, this period is variable and depends on the patient’s ability to tolerate the VLED. It is not necessary for patients to reach the goal weight with one period of VLED use. They may have repeated periods of use separated by periods of weight maintenance. In very large people who are doing well on the VLED it is appropriate to continue the VLED for longer. However it is advisable to perform blood tests for electrolytes, full blood count to exclude deficiency anaemia, uric acid, magnesium and calcium. If all tests are normal the patient can continue on the VLED but from then on these investigations should be done regularly at 1-2 monthly intervals.

**Finishing VLED**

The patient is weaned off a VLED over a period of two months. Before finishing the VLED (i.e. stopping 3 VLED meals a day) the patient should be reviewed to repeat baseline measurements and be given relevant dietary information. The patient then has 2 VLED meals and one specified meal of food a day for 4 weeks, followed by 4 weeks of 1 VLED meal and 2 specified meals of food a day. After two months, the patient should be following a standard low fat reduced carbohydrate diet.

At the start of the weaning off period the patient is referred to the dietitian for commencement of the lifestyle change program. This involves using the low fat reduced carbohydrate diet, instruction on lifestyle changes in a group program, the use of pedometers to encourage walking and movement and if necessary one-to-one consultation with the dietitian.

Once off a VLED it may be that a patient does not lose further weight. It is sufficient and an acceptable clinical goal for the patient to simply maintain the weight loss.

Patients are followed closely initially at monthly intervals. If the weight loss is maintained, the lifestyle regime is continued and gradually the interval between visits is increased to three monthly. If the weight is starting to rise again and/or the patient reports difficulty with controlling food intake, consideration should be to initiate drug therapy to assist with weight loss maintenance.

**Drugs**

**When to prescribe drugs**

It is becoming increasingly clear that severe obesity is a chronic, largely incurable condition that has a biological basis. As mentioned previously, an important physiological adaptation that occurs after weight loss is a profound reduction in leptin levels. This has been shown to lead to increased feelings of hunger. As such, it is legitimate to consider long-term chronic treatment for the condition. The problem with chronic treatment however is that the long term safety of some of the currently available drugs has not been proven.

**Drugs available**

**Noradrenergic agonists**

Phentermine (Duromine), Diethylpropion (Tenuate Dospan)

These centrally acting adrenergic agonists have been in use for many years. They work by reducing food intake and possibly stimulating energy expenditure. They have side effects and their long-term safety has not been tested. When given to patients taking Fenfluramine, phentermine caused cardiac valvular abnormalities in some patients. Since no long term studies have been conducted with these agents it is inadvisable to use them continuously for more than 3 months hence they are not suitable for assistance with short term maintenance of weight loss.

**Sibutramine (Reductil®)**

Sibutramine is a tertiary amine whose secondary and primary amine metabolites inhibit both serotonin and noradrenaline re-uptake. Originally developed as an antidepressant, it was soon noted in clinical trials that it was more active in causing weight loss than in relieving depression. Because of its dual action, sibutramine acts like the combination of phentermine (an adrenergic agonist) and fenfluramine or dexfenfluramine (serotonin agonists). Animal studies have shown that activating both adrenergic and serotoninergic neurones has a more powerful effect to reduce food intake than each agent alone. Controlled studies have shown that sibutramine produces dose related weight loss with optimal doses of 10-15 mg per day. Weight loss with sibutramine is better than with placebo, an effect that is maintained for at least 12 months.

**Topiramate (Topamax®)**

Topiramate is an anti-epileptic drug currently available for difficult to control epilepsy. It was found that the drug has a powerful effect to suppress appetite and a common side-effect is weight loss. A trial program to assess the use of topiramate in the management of obesity was undertaken proving its efficacy, however, development for this indication is not proceeding at this point. Effective dose seems to be between 25 and 100mg per
day. Side effects include depression, difficulty concentrating, closed angle glaucoma (rare) and parasthesiae (common). This can be considered for use “off label” in the management of severely obese patients in whom sibutramine is contraindicated (e.g. arrhythmia or pulmonary hypertension).\(^{28}\)

**Conclusion**

The available evidence suggests that treatment with a VLED does not lead to worse long-term results than other dietary approaches. In fact, some studies suggest that individuals maintain more weight loss when the weight loss is achieved using a VLED compared to a low energy diet. VLED is most effective when combined with behavioural change, active follow-up and pharmacotherapy to suppress the drive to eat if required.

**References**

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Review Article

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Elizabeth Delbridge BSc (Hons) MND, MPH and Joseph Proietto MB BS FRACP PhD

University of Melbourne, Department of Medicine(AH/NH), Repatriation Hospital, Heidelberg, Victoria 3081, Australia

常聽說：「瘦得愈快，復胖愈快」。然而查證現有的文獻並不支持這個論，難道真的是凡事相反的才對。這個錯誤的觀念源起於對於復胖的誤解，認為復胖只是因不好的飲食及社交習慣，並且要改變這些習慣需要花時間。然而急速的減重在生理上的適應作用是不同於漸進的減重，因此復胖單純因為積習未改所致。事實上利用現代化的極低能量攝取減肥法來達到快速減重有許多好處，能快速減重是一種動機，而輕微的酮酸中毒不僅可以抑制飢餓，還同時減緩蛋白質的流失，而且遵從從也比整套的飲食療法容易。VLEDs能提供所有營養需求，但只包含及每天1845-3280千焦(450-800大卡)熱量。一個人可以每天食用3次的代餐來代替三餐。另外，每天一碗非澱粉類蔬菜可提供一些纖維來幫助滿足對飲食的社會期望。一茶匙的油加在蔬菜上可降低膽結石的危險性。不論體重以何種速度降低，生理適應作用都會導復胖，所以VLED的減肥方式完成之後仍需花費一段時間小心的注意。改變生活習慣，飲食及運動是被視為是最理想的行為改變。如果已經盡了最大的努力後，但是復胖還是發生，那麼建議可以使用食慾抑制劑來幫助控制吃的欲望。

關鍵詞：減重、肥胖、瘦體素、飢餓、極低熱量飲食、藥物療法