A controlled comparison of three very-low-calorie diets: effects on weight, body composition, and symptoms

Gary D Foster, Thomas A Wadden, Francis J Peterson, Kathleen A Letizia, Susan J Bartlett, and Alicia M Conill

ABSTRACT To determine the optimal energy intake of very-low-calorie diets (VLCDs), 76 obese women were randomly assigned, in a double-blind fashion, to one of three liquid-formula diets: 1758 kJ/d (420 kcal/d), 2763 kJ/d (660 kcal/d), or 3349 kJ/d (800 kcal/d). Weight, body composition, symptoms, mood, and acceptability of the diet were assessed throughout the 6-mo study. There were no significant differences in weight losses or changes in body composition among the three dietary conditions at the end of treatment, nor were there significant differences among conditions in acceptability of the diet, symptoms, or mood. These results suggest that there is no clinical advantage to using VLCDs that provide < 3349 kJ/d (800 kcal/d). Am J Clin Nutr 1992;55:811-7.

KEY WORDS Very-low-calorie diets, symptoms, weight loss, body composition, psychological functioning

Introduction

It is estimated that 12-15 million people worldwide have used very-low-calorie diets (VLCDs) during the past decade (1). These diets are extremely popular among patients because they produce rapid weight losses that are facilitated by the narrowing of food choices. The diets are recommended only for people ≥ 30% overweight who receive appropriate medical supervision and a multidisciplinary program of lifestyle change (2). Early concerns about the adverse health effects of these diets have been allayed by studies that document their safety and efficacy when used appropriately (3-8).

Despite the widespread use of these diets, little research has been conducted to ascertain the optimal energy intake of VLCDs. The energy level of these diets varies across studies ranging from an ultralow intake of 334 kJ/d (80 kcal/d) (9) to a variety of levels between 921 kJ/d (220 kcal/d) and 3349 kJ/d (800 kcal/d) (8, 10-13). Weight range reflects, in part, the varying definition of what constitutes a VLCD in European and other nations. Advisory committees recommend 1381 kJ/d (330 kcal/d) in Denmark and Spain, 1632 kJ/d (390 kcal/d) in France, 3001 kJ/d (717 kcal/d) in Germany, and 3767 kJ/d (900 kcal/d) in Switzerland (14). In the United Kingdom the Committee on Medical Aspects of Food Policy (COMA) report (15) recommends that a VLCD provide a minimum of 1674 kJ/d (400 kcal/d) with 40 g protein for women and 2093 kJ/d (500 kcal/d) with 50 g protein for men. No such governmental recommenda

dation exists in the United States, but an expert panel defined VLCDs as providing < 3349 kJ/d (800 kcal/d) (16), although most VLCDs provide 1674-3349 kJ/d with 45-100 g protein (2).

One potential advantage of lower energy intake is increased weight loss. The additional caloric deficit associated with a 1674-vs a 3349-kJ/d regimen, for example, is 11720 kJ/wk (2800 kcal/wk), resulting in an additional loss of ≈ 1.5 kg/mo or 6 kg over 4 mo. This theoretical advantage may be misleading, however, because it assumes that changes in energy expenditure and fat-free mass (FFM) remain constant during different levels of caloric restriction. In a clinical series, Vertes (17) showed that the weight loss resulting from a 1758-kJ/d (420 kcal/d) diet was not significantly different from that of a 3349-kJ/d (800 kcal/d) diet in subjects who consumed the diets for 4-14 wk. Kanders et al. (18) showed similar results in testing the same diets, but those who consumed the 3349-kJ/d diet were overrepresented by males and heavier subjects.

Lower energy formulations may also be associated with less hunger, as suggested by studies comparing 2093-kJ/d (500-kcal/d) with 5023-kJ/d (1200-kcal/d) diets (19, 20). Conversely, lower intakes may be associated with increased symptoms, making adherence more difficult. The purpose of this study was to compare the effects of three VLCDs—ranging from 1758 to 3349 kJ/d (420 to 800 kcal/d)—on weight, body composition, psychological functioning, and symptoms, with the ultimate goal of identifying an optimal intake level.

Methods

Subjects

Subjects were 76 women, recruited from physician referrals and newspaper advertisements, who participated in a clinical

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An 812kcal/d diet (200kcal/d) was prescribed to each subject. All participants were prescribed a VLCD diet (1200kcal/d) balanced diet for a 1-wk adaptation period, after which they remained on one of three liquid-formula VLCDs for 12 wk (Sandoz Nutrition Co, Minneapolis). The three diets were prepared by mixing one packet of powdered formula with 240mL noncaloric beverage to be consumed five times each day. The packets contained no nutritional information so that the subjects and the practitioners were blinded to the dietary condition. The packets were identified by number and distributed by research assistants who were not involved in the clinical care of subjects.

The 1758-kj/d (420-kcal/d) diet provided 70g protein, 30g carbohydrate (CHO), and 2g fat daily. The 2763-kj/d (660-kcal/d) diet provided 90g protein, 30g CHO, and 20g fat daily. The 3349-kj/d (800-kcal/d) diet provided 70g protein, 100g CHO, and 13g fat daily. All three diets provided a minimum of 100% of the recommended dietary allowance (RDA) for established vitamins and minerals (23).

During the next 6 wks (weeks 14–19) conventional foods were gradually reintroduced and the amount of formula was reduced so that by week 19 all subjects consumed a 4186-kj/d (1000-kcal/d) diet composed solely of conventional foods. At week 8, subjects were prescribed a modest exercise program that consisted of walking two to three times a week for 10 min at 40–60% of estimated maximum heart rate (24). By the end of treatment, this prescription was increased to three or four times per week for 30 min at 60–70% of estimated maximum heart rate.

Dependent measures

Weight and body composition. Weight was measured weekly on a balance-beam scale to the nearest 0.1 kg. Body composition was assessed by densitometry (25) at baseline and at week 21 (2 wk after refeeding had been completed) with an apparatus previously described (26). Measurements were repeated six or more times (on each occasion) until three readings within 25g were obtained. Body density was derived from the formula of Brozek et al (27), and fat was determined by using Siri’s formula (28). Fat-free mass was defined as body weight minus body fat. Residual lung volume was measured on each occasion by the oxygen-dilution technique (29).

Acceptability, symptoms, and mood. Subjects rated the acceptability of the diets (ie, degree of hunger, preoccupation with food and eating; and liking, convenience, and disruptiveness of the diet) by using a set of five 100-mm bipolar visual-analog scales (19, 20). These ratings were obtained on days 2, 4, and 6 of each week and were averaged to obtain a weekly rating. To assess the relationship between hunger and ketosis during the VLCD, serum acetone concentrations were measured by headspace gas chromatography at baseline and at week 9 in 27 subjects selected at random across the three conditions (30, 31). There were 10, 9, and 8 subjects in the 1758-, 2763-, and 3349-kj/d conditions, respectively. The number of subjects was limited because of the high cost of the assay.

Once a week subjects reported, by using four-point scales, the degree to which they experienced a variety of symptoms (0, not at all; 1, slight amount; 2, moderate amount; 3, great amount). Symptoms included difficulty with concentration, constipation, diarrhea, dizziness, dry skin, fatigue, feeling cold, food cravings, hair loss, headache, sadness, tension, vomiting and nausea, and weakness.

Mood was assessed weekly by the Beck Depression Inventory (BDI) (32). The BDI is a 21-item self-report inventory in which higher scores indicate higher levels of dysphoria.

All acceptability, symptom, and mood data were analyzed after 1 week of the 5023 kj/d diet, monthly during the VLCDs (weeks 5, 9, and 13), after 2 and 6 wk of refeeding (weeks 15 and 19), and at the end of treatment (week 24).

Statistical analyses

Changes in the dependent measures were analyzed by a multiple analysis of variance (MANOVA) with a repeated-measures design (SPSS PC+, SPSS, Inc, Chicago). Univariate F tests were performed in cases in which the MANOVA was statistically significant. Of the 76 original subjects, eight were excluded from the analyses. Three subjects developed hypothyroidism within 2 mo of completing treatment, three were prescribed antidepressant medication, and two were prescribed progesterone. The remaining 68 subjects averaged (±SE) 40.6 ± 1.1 y, 102.3
TABLE 2
Weight loss during treatment*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Week of treatment</th>
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<tr>
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<td>5</td>
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<tr>
<td>All (n = 68)</td>
<td>8.3 ± 0.3</td>
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<tr>
<td>1758 kJ/d (n = 21)</td>
<td>8.9 ± 0.4</td>
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<td>2763 kJ/d (n = 23)</td>
<td>8.7 ± 0.5</td>
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<td>3349 kJ/d (n = 24)</td>
<td>7.2 ± 0.2†</td>
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* ± SE.
† Significantly different from the 1758- and 2763-kJ/d conditions, P < 0.05.

± 2.0 kg, and 164.1 ± 0.8 cm, with a body mass index (BMI, in kg/m²) of 37.6 ± 0.6. Seven of the 68 (12%) subjects discontinued treatment. The subjects were evenly distributed across conditions (two, two, and three subjects in the 1758-, 2763-, and 3349-kJ/d conditions, respectively). Five subjects discontinued the study during the VLCD, one during refeeding, and one at week 22. Data for these subjects were included until the time of attrition.

Results

Subjects in the three conditions lost an average of 17.8 ± 0.6 kg after 12 wk of the VLCD (week 13). Weight losses for the 1758-, 2763-, and 3349-kJ/d conditions were 18.2, 18.5, and 16.6 kg, respectively. Differences among conditions were not statistically significant at this or at any other time during the VLCD except at week 5. Subjects in the 3349-kJ/d condition lost significantly less weight than did those in the other two conditions at week 5. Subjects in the three conditions lost an average of 20.6 ± 0.8 kg at the end of the refeeding period (week 19) and 20.7 ± 1.0 kg at the end of treatment (week 24). Weight losses of the three conditions did not differ significantly at either period (Table 2 and Fig 1).

Subjects in the three conditions lost an average of 3.1 ± 0.4 kg FFM at week 21 (2 wk after refeeding). There were no significant differences among conditions in changes in FFM, with reductions of 3.2 ± 0.7, 3.3 ± 0.7, and 2.9 ± 0.6 kg for subjects in the 1758-, 2763-, and 3349-kJ/d conditions, respectively. Fat comprised 85.4 ± 3.7%, 86.1 ± 2.6%, and 88.2 ± 2.9% of the weight loss in each of the three conditions, respectively. Baseline BMI, baseline FFM, weight loss, and dietary condition were entered into a stepwise multiple regression to examine the factors associated with changes in FFM. Among these variables, weight loss was the single best predictor of the change in FFM, accounting for 42% of the variance. Adding baseline BMI to weight loss accounted for an additional 4% of the variance. Thus, subjects who lost the most weight lost the most FFM; degree of caloric restriction was not associated with the change in FFM.

Subjects in the three conditions reported significant decreases in hunger while consuming VLCDs as compared with their baseline ad libitum diet (Table 3 and Fig 2). The reduction in hunger persisted during the refeeding period (week 15) and at the end of treatment (week 24), despite subjects consuming substantially fewer calories than at baseline. There were no significant differences among the three conditions in changes in hunger.

No serum acetone was detected in any subject at baseline. Serum acetone concentrations for the 1758-, 2763-, and 3349-kJ/d conditions at week 9 were 413.8 ± 120.7, 344.8 ± 120.7, and 75.9 ± 51.7 μmol/L, respectively. The difference between the 1758 kJ/d and 3349 kJ/d conditions was statistically significant (P < 0.05). No relationship was found (r = −0.18, P = 0.4) between hunger and serum acetone concentrations at week 9, as determined by collapsing across conditions (n = 27).

Subjects reported that they enjoyed the VLCD significantly less than their baseline diet of conventional foods, perhaps contributing to their decreased hunger. They also rated the VLCD as more disruptive than their baseline diet during the last 2 months of consumption and during the first 2 wk of refeeding (Fig 2). Preoccupation with food and eating did not change significantly during the study except for a small decrease after 2 mo of the VLCD. There were no significant differences among the three conditions in changes in any of these variables.

Subjects in all three conditions showed statistically significant increases from baseline during the VLCD (weeks 5, 9, and 13).
in constipation ($P < 0.004$), dry skin ($P < 0.0001$), dizziness ($P < 0.003$), cold intolerance ($P < 0.0001$), and hair loss ($P < 0.03$). Changes in cold intolerance, hair loss, and dry skin persisted during the refeeding period and at the end of treatment. Although these changes were statistically significant, no absolute values exceeded 1 (slight amount) on the four-point scale. For example, hair loss increased from 0.02 at baseline to 0.82 at the end of treatment, whereas cold intolerance increased from 0.12 to 0.75 during the same time (Fig 3). Moreover, only 5 of the 14 symptoms examined showed significant increases during the VLCD. There were no significant differences among the three conditions in changes in any of these variables.

The mean depression score at baseline for subjects in the three conditions was $8.3 \pm 0.9$, a clinically nonsignificant score. Nevertheless, scores fell to $2.1 \pm 0.5$ at the end of treatment ($P < 0.0001$) (Table 3). There were no significant differences among the three conditions in changes in mood.

**Discussion**

This study confirms previous findings of large weight losses occurring with VLCDs (8, 33–38). Subjects reduced their body

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**TABLE 3**

Acceptability and mood ratings during treatment for all subjects*  

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>1</th>
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<th>9</th>
<th>13</th>
<th>15</th>
<th>24</th>
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<tr>
<td><strong>Acceptability</strong></td>
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<td>Hunger</td>
<td>45.5 ± 2.8</td>
<td>32.7 ± 2.9</td>
<td>31.4 ± 2.9</td>
<td>31.4 ± 3.3</td>
<td>33.1 ± 3.5</td>
<td>30.8 ± 3.9</td>
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<td>Preoccupation</td>
<td>47.8 ± 2.5</td>
<td>46.7 ± 2.6</td>
<td>45.3 ± 3.1</td>
<td>39.7 ± 2.7</td>
<td>42.2 ± 3.2</td>
<td>36.0 ± 4.2</td>
<td>36.0 ± 4.2</td>
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<td>Enjoyment</td>
<td>62.2 ± 2.3</td>
<td>66.1 ± 2.6</td>
<td>53.7 ± 3.6</td>
<td>50.5 ± 3.5</td>
<td>46.7 ± 3.9</td>
<td>59.7 ± 3.9</td>
<td>69.8 ± 4.1</td>
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<td>(0.05)</td>
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<td>Convenience</td>
<td>72.3 ± 2.8</td>
<td>68.2 ± 2.7</td>
<td>75.2 ± 3.2</td>
<td>70.1 ± 3.2</td>
<td>74.0 ± 3.3</td>
<td>64.4 ± 3.4</td>
<td>68.4 ± 3.8</td>
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<td>(0.003)</td>
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<tr>
<td>Disruption</td>
<td>21.4 ± 2.6</td>
<td>22.3 ± 2.7</td>
<td>29.4 ± 3.3</td>
<td>32.9 ± 3.7</td>
<td>31.7 ± 4.1</td>
<td>31.5 ± 4.5</td>
<td>21.0 ± 3.7</td>
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<tr>
<td>Mood, BDI†</td>
<td>8.3 ± 0.9</td>
<td>7.3 ± 0.9</td>
<td>4.3 ± 0.8</td>
<td>3.7 ± 0.8</td>
<td>3.4 ± 0.8</td>
<td>4.3 ± 0.9</td>
<td>2.1 ± 0.5</td>
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<td>(0.0001)</td>
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* X ± SE. n = 68. P values representing a difference from baseline are given in parentheses.
† Beck Depression Inventory.
weight by ≈20% during 6 mo of treatment. Moreover, these significant weight losses were accomplished with relatively small reductions in FFM. Because ≈25–30% of the excess weight in markedly obese people is composed of FFM (39, 40), it might be expected that 25% of weight loss would consist of lean tissue. Only 14% of the weight loss of subjects in the current study consisted of FFM. We (26, 41) and others (42) previously reported that weight loss by a VLCD consisted of 17–25% FFM. The disparity among these findings is probably due to the small sample sizes (n < 15) of the earlier studies. A comparable study of 69 patients found that ≈23% of weight loss consisted of FFM (43). This study, however, assessed FFM while subjects were still consuming the VLCD, and the diet contained only 50 g protein/d.

The study’s most important finding is that there were no significant differences in weight losses or changes in body composition among subjects who consumed diets providing 1758–3349 kJ/d (420–800 kcal/d). Subjects who consumed the 3349-kJ/d diet lost less weight at all times during the VLCD, but the difference was not statistically significant except after the first month, and at no time was the difference clinically significant. This randomized trial, which followed a structured protocol, confirms findings from earlier uncontrolled studies in which patients consumed diets for variable lengths of time (17, 18). Both Vertes (17) and Kanders et al (18) found no significant difference in weight losses between liquid diets providing either 1758 or 3349 kJ/d. Ohno et al (44) found a similar lack of difference when comparing 1005- and 1758-kJ/d (240- and 420-kcal/d) diets.

The difference in energy intake between the 1758 kJ/d and 3349 kJ/d diets is 1591 kJ/d (380 kcal/d), or 133644 kJ (31920 kcal) over 3 mo. Assuming that the energy equivalent of 1 kg of fat is 32232 kJ (7700 kcal), the predicted difference in weight loss between the two conditions, based on energy intake alone, would be 4.1 kg. The actual difference between the two diets after 3 mo was 1.6 kg.

It is possible that the difference between the predicted and observed weight losses between the conditions is attributable to inadequate adherence among subjects in the 1758 kJ/d condition. However, we have no data indicating poorer adherence in these subjects, and the absence of differences among conditions in the acceptability of the diets suggests that any nonadherence would have been randomly distributed. The discrepancy between actual and predicted weight loss was probably attributable, in part, to the variability of subjects’ caloric deficits. As Yang and Van Itallie (45) suggested, prescribing a fixed energy intake for a group of patients will create variable caloric deficits and weight losses. Given a fixed energy level, the degree of caloric deficit will be directly related to daily total energy expenditure. Thus, the predicted difference of 4.1 kg assumes that subjects in the three conditions had equivalent energy expenditures. The largest component of daily total energy expenditure, RMR, was not statistically different among conditions at baseline. The RMR of subjects in the 1758-kJ/d condition, however, was an average of 293 kJ/d (70 kcal/d) less than that of the 3349 kJ/d subjects, amounting to 24578 kJ (0.8 kg) over 3 mo. Thus, subjects in the former condition would be expected to lose 0.8 kg less than those in the latter condition on the basis of their initial RMR alone.

In addition to the variability in RMR, the nonresting components of daily energy expenditure (thermic effect of food and the energy cost of physical activity) are also known to vary markedly among people (46). Other factors such as lipoprotein lipase activity, fuel utilization during weight loss, and magnitude of the labile glycogen component also may help explain the differences between observed weight loss and that predicted based on energy intake alone. Regardless of the reason for the difference, the important finding is that diets providing 1758 kJ/d do not produce significantly greater weight losses than those providing 3349 kJ/d when both are used in standard clinical practice.

We had anticipated that the 2763-kJ/d diet, because of its provision of 90 g protein/d, would be associated with better preservation of FFM than would the two other diets, which provided 70 g protein/d. This hypothesis was not confirmed. Denitometry, however, is not sensitive to discrete changes in FFM (eg, visceral proteins) and only assesses gross changes in body composition. Other techniques, such as magnetic resonance imaging (47), may be better able to detect regional differences. Weight loss and, to a lesser degree, initial BMI were most closely related to the loss of FFM. Greater weight losses and initial BMIs were associated with the largest reductions in FFM. It may be that, given a minimum of 70 g protein/d, changes in FFM are determined more by the magnitude of the weight losses than by the amount of dietary protein.

All three diets were rated as very acceptable by subjects. Hunger during the VLCD was significantly less than that associated with ad libitum eating at baseline, as we previously showed (19, 20). Contrary to our previous findings, however, hunger remained lower even after subjects resumed consumption of conventional foods. Differences in the form of the diet (liquid diet vs lean meat, fish, and fowl) as well as the longer length of the VLCD in this study (12 vs 8 wk) may explain the differences between these and earlier findings. The lack of significant differences among the three VLCDs in hunger suggests that once energy intake is limited to 3349 kJ/d, there is no further reduction in hunger with additional reductions in energy intake. There was no relation between serum acetone concentrations and hunger during the VLCD, confirming Rosen et al’s (48) finding that ketosis is not responsible for the reported anorexia. It is possible, however, that the ketosis experienced by all groups (≥ 76 μmol/L) exceeded a threshold level necessary for hunger reduction. Thus, exceeding the threshold may be more important than the absolute concentration of ketosis.

Two negative ratings—disruption of normal social eating and thinking about food (and wanting to eat)—increased after 2 mo of the VLCD. These data are consistent with the suggestion that there is a fatiguing effect after 8 wk of a VLCD, making adherence more difficult (49). Further research is needed to determine the optimal length of a VLCD. Subjects in all three conditions showed significant improvements in mood, confirming the positive psychological benefits of behavioral weight-loss programs (50, 51).

Subjects reported minimal physical symptoms. During the VLCD there were increases in dry skin, constipation, dizziness, cold intolerance, and hair loss. No mean score exceeded 1 (slight amount). These findings are consistent with those from other studies (19, 20). Moreover, increases were not observed in 10 of 14 variables examined, including those often reported to occur...
with the consumption of VLCDs: diarrhea, headache, nausea, fatigue, weakness, and difficulty with concentration.

There may be a limited role for VLCDs providing < 3349 kJ/d (800 kcal/d) for the control of certain medical conditions, particularly diabetes (38). Other than these potential disease-specific interventions, this study suggests that there is no advantage to using VLCDs providing < 3349 kJ/d in terms of weight loss, body composition, symptoms, acceptability of the diet, or mood. Additional studies are needed to determine whether the significant weight losses associated with VLCDs may be due to their narrowing of food choices, which may improve adherence, rather than to their extremely low energy intakes.

References