Revisión
Long-term efficacy of high-protein diets: a systematic review

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Abstract
The rationale for the use of high-protein diets is that they offer a higher level of satiety for a longer period of time when compared with carbohydrates or fats; this diminishes calorie consumption in the long-run. The purpose of this review was to assess the efficacy of long-term randomized clinical trials. We used Pubmed, EBSCO and SCIELO to conduct our searches. Inclusion criteria were: randomized clinical trials conducted in adults, with an intervention/follow-up of at least 24 weeks, stating the specific amount of energy protein (in percentages) in the diet; with a control group with either a conventional energy restricted diet or a high-fat/high-carbohydrate diet, also the studies should provide at least body weight or body mass index (BMI) at the beginning and at the end of the intervention. A total of 481 studies were found. Eight studies met the inclusion criteria. Weight loss difference in those with the highest weight loss with the high-protein diet ranged from 3.7 kg in a six month trial to 1.2 kg in a 17 month trial. The average weight loss of the eight studies in the high-protein diet was 6.3 kg and in the standard diet was 5.0 kg. Although half of the studies showed a higher weight loss with a high-protein diet, three out of four studies with the longest intervention show no statistical difference in weight loss. In this systematic review it was observed that the long-term effect of high-protein diets is neither consistent nor conclusive.

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Introduction

There is a debate regarding the macronutrient composition of diets for weight loss. High-protein diets have been used as far as 2000 years ago by Greek bodybuilders who had a diet that consisted mainly of meats and scarce vegetables. Diets promoting high protein have recently regained popularity along with modifications regarding fats and other issues.

The rationale for the use of high-protein diets is that they offer a higher level of satiety for a longer period of time when compared with carbohydrates or fats; this diminishes calorie consumption in the long-run. Weigle et al. reported a higher satiety perception in a high-protein diet than in a high fat diet, similar results have been reported elsewhere. Since the utilization of lipids as a fuel source is the main basis of this diet, the release of ketone bodies has been used as an indicator of the catabolization process. This had led to believe that an undesirable increment of total cholesterol and LDL-cholesterol would be the result of high protein diets. However, there have been studies which show that biological markers like cholesterol, LDL-cholesterol remain the same with either a high-protein diet or a conventional diet. Most studies evaluating high-protein diets usually have an intervention and follow-up period of 12 or less weeks. Since weight loss must be a long-term strategy to reduce the health implications of obesity, including the reduction of morbidity and mortality and the augmentation of quality of life, the purpose of this review was to assess the efficacy of long-term randomized clinical trials, with an intervention and/or follow-up equal or higher than 24 weeks.

Methods

We used Pubmed, EBSCO and SCIELO to conduct our searches with the following keywords: “high-protein” and “weight loss” and “Atkins diet” and “weight loss”. Limits added were: Humans, Clinical Trial, English and Spanish. Criteria for the inclusion of the studies were randomized clinical trials conducted in adult population with an intervention or follow-up of at least 24 weeks, stating the specific amount of energy from macronutrients or the absolute amount of the protein (in grams) in the diet; with a control group with either a conventional energy restricted diet or a high fat/high carbohydrate diet. In addition, the studies included should provide at least the measurement of weight or body mass index (BMI) at the beginning and at the end of the intervention. A total of 481 studies were found. Eight studies met the inclusion criteria (fig. 1).

Data extracted from RCTs:

We extracted the following from each study: gender, BMI, age, co-morbidities, population size, types of diets, daily macronutrient intakes (shown as percentages), and duration of each study. We also included retention rate at the end of the study, net weight loss and when available, the statistical difference between groups, intention to treat analysis, and statistical power (table I).

Results

In table I the characteristics of all studies are shown. The numbers of participants ranged from 50 to 119; age ranged from 18 to 70 years; BMI ranged from 25 to 43 kg/m²; contribution of protein to high-protein diets was from 25% to 40%; contribution of carbohydrates to the high-protein diets was from 5 to 45%; length of intervention was from 6 to 24 months; retention rate was from 34% in the longest trial (24 months) to 92% in a six month trial. Only one study had an intention to treat analysis, and five reported statistical power. Three out of four studies with the longest intervention...
show no statistical difference in weight loss. One out of four studies showed significantly more weight loss in the high monounsaturated fat diet group than in the high-protein diet group.\(^{18}\) Weight loss difference in those with the highest weight loss with the high-protein diet ranged from 3.7 kg in a six month trial\(^{22}\) to 1.2 kg in a 17 month trial.\(^{24}\) The average weight loss of the eight studies in the high-protein diet was 6.3 kg and in the standard diet was 5.0 kg\(^{17-24}\) However, in one study\(^{18}\) conducted during 12 months, a 9.4 kg weight loss was observed with the standard diet, which is higher than the weight loss observed with the high-protein diet in the other seven.\(^{17-19,21-24}\)

### Discussion

In this systematic review it was observed that the long-term effect of high-protein diets is neither consistent nor conclusive. Although more than half of the studies\(^{16,20-22,24}\) showed a higher weight loss with a high-protein diet, three out of four studies with the longest intervention\(^{17,23}\) show no statistical difference in weight loss. Weight loss difference in those with the highest weight loss in the high-protein diet range from 3.7 kg in a six month trial\(^{16}\) to 1.2 kg in a 17 month trial.\(^{24}\) Additionally, the non-statistical difference observed in the majority of the studies conducted for more than 12 months, suggested a diminishing trend of weight loss with the length of intervention.\(^{17,23}\)

However, one study\(^{14}\) that showed a higher weight loss reduction in the high monounsaturated fat diet group than the high-protein diet group, at the beginning of the study the former were statistically heavier than the latter, and the retention rate was only 52%. Thus, indicating a lower quality of the study. Likewise, the three studies with no significant difference had a lower retention rate.\(^{17,19,23}\)

The higher weight loss observed with the standard diet\(^{18}\) compared with the HPD in the same study, and the weight loss observed with the high-protein diet in the rest of the studies,\(^{17-19,21-24}\) indicates that when a standard diet is well designed, conducted and supervised a higher weight loss might be observed.

No side effects of the high-protein diet were reported in any of the studies analyzed, which is consistent with the conclusions made by Crowe.\(^{21}\) However, there were no evaluations on the potential adverse effects over mineral and vitamin contents of the diets, since HPD may result in restricted intakes of fiber, fruits, and vegetables. In addition, there are also several safety concerns regarding a constant state of lipolysis: higher LDL’s and cholesterol. This also needs further research in the long-term.\(^{8-14}\)

There are several limitations to this systematic review. Foremost is the small number of randomized studies available with an intervention time greater than 12 months. Five studies with an intervention greater than 12 months and no study with a follow-up greater than 24 months was found.\(^{15,23,24}\)

### Table I

<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th>Population</th>
<th>Diets (Calories from Nutrients)</th>
<th>LI (months)</th>
<th>Ret (%)</th>
<th>Body Weight (kg)</th>
<th>&lt;p between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skov et al. 1999</td>
<td>65</td>
<td>Adults: 18-56 y BMI: 25-34 kg/m²</td>
<td>HPD (25% Prot, 30% fat, 45% CHO)</td>
<td>6</td>
<td>92</td>
<td>HPD: -8.7</td>
<td>0.0002</td>
</tr>
<tr>
<td>Due et al. 2004</td>
<td>50</td>
<td>Adults: 19-55 y BMI: 26-34 kg/m²</td>
<td>HPD (25% Prot) SD (12% Prot)</td>
<td>24</td>
<td>34</td>
<td>HPD: -6.4</td>
<td>NS</td>
</tr>
<tr>
<td>Brinkworth et al. 2004(^4)</td>
<td>66</td>
<td>Adults with type 2 diabetes BMI: 27-40 kg/m²</td>
<td>HPD (30% Prot, 30% fat, 40% CHO) SD (15% Prot, 30% fat, 55% CHO)</td>
<td>15</td>
<td>58</td>
<td>HPD: -3.7</td>
<td>NS</td>
</tr>
<tr>
<td>Brinkworth et al. 2004(^4)</td>
<td>58</td>
<td>Hyperinsulinemic adults: 20-65 y BMI: 27-43 kg/m²</td>
<td>HPD (30% Prot, 30% fat, 40% CHO) HFD (15% Prot, 70% fat, 55% CHO)</td>
<td>17</td>
<td>74</td>
<td>HPD: -4.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>McAuley et al. 2005</td>
<td>96</td>
<td>Women: 30-70 y BMI: &gt; 27 kg/m²</td>
<td>HPD (30% Prot, 30% fat, 40% CHO) HFD (15% Prot, 30% fat, 55% CHO)</td>
<td>12</td>
<td>82</td>
<td>HPD: -6.6</td>
<td>0.027</td>
</tr>
<tr>
<td>Keogh et al. 2007</td>
<td>73</td>
<td>Hyperinsulinemic adults: 20-65 y BMI: 27-40 kg/m²</td>
<td>HPD (40% Prot, 30% fat, 30% CHO) HMF (20% Prot, 30% fat, 30% CHO)</td>
<td>13</td>
<td>52</td>
<td>HPD: -5.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Clifton et al. 2008</td>
<td>119</td>
<td>Women 20-65 y BMI: 27-40 kg/m²</td>
<td>HPD (34% Prot, 20% fat, 46% CHO) HC (17% Prot, 20% fat, 46% CHO)</td>
<td>15</td>
<td>66</td>
<td>HPD: -4.6</td>
<td>NS</td>
</tr>
<tr>
<td>Brinkworth et al. 2009</td>
<td>118</td>
<td>Adults: 18-65 y BMI: &gt; 29 kg/m²</td>
<td>HPD (35% Prot, 61% fat, 4% CHO) SD (24% Prot, 30% fat, 46% CHO)</td>
<td>12</td>
<td>88</td>
<td>HPD: -11.3</td>
<td>0.03</td>
</tr>
</tbody>
</table>

LI: Length of Time of intervention; BMI = body mass index; CHO = Carbohydrate; Prot = Protein; HPD = High-protein diet; HC = High CHO diet; SD = standard diet; HFD = high fat diet; HMF = high monounsaturated fat diet; FM = fat mass; NA = not available; NS = not significant.
In conclusion, the results observed from this review, show no conclusive better long term effect of the high-protein diet compared to a standard, high monounsaturated or high-carbohydrate diet. Therefore, the results warrant more long-term studies including statistical power, intention to treat analysis and high retention rates.

References