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Effects of a high protein diet on body weight and comorbidities associated with obesity

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Abstract

Red meat intake has been frequently associated with the development of coronary artery disease and type 2 diabetes but vegetable protein has been associated with protection from these diseases. Whether this is related to the protein per se or to the increased polyunsaturated fat or higher fibre levels associated with more vegetarian diets is not clear.

High protein diets are associated with greater satiety and in some studies are associated with greater weight loss compared with high carbohydrate diets especially in an ad libitum design. These diets also lower plasma triglyceride and blood pressure and sometimes spare lean mass. There appear to be no harmful effects of high protein diets on bone density or renal function in weight loss studies.

Key words: Dietary protein: heart disease: type 2 diabetes: weight loss: satiety

Introduction

The first literature on high protein weight loss diets that were not liquid, very low calorie diets appeared in 1994. Since then there has been an explosion of interest in high protein diets, prompted by the books on the Atkins diet, although scientific reports on the efficacy of this diet did not appear till much later. High protein weight loss diets have been described in the popular literature since the 1890's.

This contribution focuses predominantly on studies that have a duration of twelve months or longer and examines the effects of high protein diets on glycaemic control, hypertension and hyperlipidaemia. There are many issues that complicate the interpretation of the results, including whether the protein replaces carbohydrate or fat (this may be one of the most critical issues), whether the carbohydrate level is low or very low, thus inducing ketosis, whether the protein is animal or vegetable in origin and whether the absolute level of protein is increased (rather than just the percentage of energy from protein) compared to the usual weight stable diet.

Epidemiology

Body Weight and Heart Disease.

There is a limited amount of epidemiological data relating dietary protein intake to body weight, type 2 diabetes and cardiovascular disease. In a recent publication from 5 of the countries in the European Prospective Investigation into Cancer and Nutrition (EPIC) study a higher intake of protein from red and processed meat and chicken, rather than fish or dairy was associated with a greater body weight gain over 6·5 years, especially in women. There were no associations with plant protein. Whether the gain was due to fat or muscle was not clear but there was no clear association with changes in waist circumference suggesting that central fat was not increasing[1].The mechanism of the association was not clear but it did not appear to operate via glycaemic load changes[2]. Similar changes were seen in all 10 countries in the EPIC-Panacea study[3]. Red meat but not protein in general appears to be associated with heart disease in some data sets. In the Nurses Health Study, over a 26 year follow up, red meat, both fresh and processed and high fat dairy were associated with an increased risk of coronary heart disease (CHD) while poultry, nuts and fish were associated with a lower risk. Swapping a serve of nuts, low fat dairy, poultry or fish leads to 13–30 % lower risk of CHD[4]. In the Health Professionals Follow-Up Study neither total protein or animal or vegetable protein were associated with CHD. However if the subjects were free of hypertension, hypercholesterolaemia, and diabetes at baseline (very post hoc and not a pre specified analysis), the relative risk (RR) of CHD was 1·21 (P for trend=0·02) for total protein, 1·25 (P for trend=0·02) for animal protein, and 0·93 (P for trend=0·65) for vegetable protein[5].

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Type 2 diabetes

As with heart disease there has been some degree of association reported for a variety of red meats and an increased risk of type 2 diabetes. In only one study (the MASALA study), a small study of Indians in San Francisco, was the intake of total protein associated with an increased risk of type 2 diabetes (70 % increase in risk in the highest intake group)[6]. In the IRAS study red meat, eggs, cheese and cottage cheese were associated with an increased risk of type 2 diabetes[7]. Both of these studies were small with only 144 and 880 participants, respectively. In the Whitehall study burgers and sausages increased the risk of type 2 DM[8] as did total red and processed meat and hot dogs and bacon in the Nurses health Study with risk ratios varying from 1·26 to 1·73[9]. Murakami showed that heme iron intake was a predictor of type 2 DM in a meta analysis of 15 cohort studies[10]. A recent meta analysis of 12 cohort studies showed a modest increase in risk of type 2 DM with red meat and processed meat with RRs of 1·21 to 1·41 from highest to lowest intake categories, but there was considerable heterogeneity[11]. These findings contrast with the association of a high glycaemic load diet with about a 50 % increase in the risk of type 2 DM in US Nurses[12]. In this group the low glycaemic load diet contained about 5 % more protein and about 15 % more fat. In a further analysis of the Nurses data Halton 2008[13] showed that a low carbohydrate diet based on vegetable protein and vegetable fat were protective with an 18 % reduction in the risk of type 2 DM comparing extreme deciles while animal protein and animal fat was not protective.

In contrast in the EPIC-Potsdam cohort, substituting 5 % of energy as protein for carbohydrate reduced the risk of type 2 DM by 23 %[14] while in the Attica study total protein was unrelated to fasting glucose and insulin, but red meat was associated with increased levels of both glucose and insulin[15].

Overview of the epidemiological literature

Although red meat appears to be associated with both heart disease and type 2 diabetes in virtually all studies consumers of a large amount of red meat tend to be more obese, smoke more and exercise less so they are clearly a special group. Even though all studies are adjusted for these confounders it is possible there are unmeasured behavioural confounders that account for the relationship observed that persist after adjustment for saturated fat. There does not appear to be a good biological explanation for the association.

Interventions with high protein weight loss diets

The major problem with interpreting all of the weight loss studies is that weight loss per se has the most powerful effect on the comorbidities which leaves little room to see an effect of macronutrients.

Body weight and CVD risk markers

Only the most important large and long term studies will be discussed in detail.

The largest test of a high protein diet was performed in the USA in a 4 centre trial[16] In the study 811 participants were randomly assigned for 2 years to one of 4 possible diets: 20 % of energy as fat, 15 % as protein, and 65 % as carbohydrate (average protein); 20 % 25 %, and 55 % (high protein); 40 %, 15 %, and 45 % (high fat, average protein); 40 %, 25 %, and 35 % (high fat, high protein). The design was a 2 by 2 factorial and each diet was prescribed with a 750 kcal deficit based on calculated resting energy expenditure and activity level. At 6 months an average of 6 kg weight loss (7 %) occurred which when compared with other trials was relatively low. Subjects began to regain weight after 12 months and by 2 years weight loss was between 3–4 kg with no statistically significant differences between groups. At two years, on intention-to-treat analysis, weight loss was 3·0 and 3·6 kg in the 15 % and 25 % protein groups, respectively. In the completers (645 out of 811) it was 3·6 and 4·5 kg (P=0·11). In the 20 % fat and 40 % fat groups it was 3·3 kg for both and in the contrast of the 65 % vs 35 % carbohydrate groups it was 2·9 and 3·4 kg, respectively. Weight loss was 0·2 kg per support session attended.

Compliance to a high protein diet increased weight loss from 3 kg to 8 kg as the protein intake increased from 15 % to 25 % (Fig. 1). The number of sessions attended also increased from 42 % to 59 % and the authors attributed the increased weight loss to attending the counselling sessions (0·2 kg per session attended over the 2 years) but an equally valid interpretation is that the volunteers who liked the diet were much more compliant to it and because of this attended more sessions. Unfortunately there was no multivariate analysis incorporating both these factors. However in the average protein group an increase in the number of sessions attended was not associated with more weight loss, possibly because the target protein of 14·5 % was achieved compared with an achieved level of 24 % in the group who attended fewer sessions, suggesting that the higher protein diet *per se* was beneficial. Urinary nitrogen measures showed that the difference in protein intake was 10 g at 6 months and 5 g at 2 years rather than the 20 g target (which in itself was relatively modest) so compliance to the prescribed diet was relatively poor in this study although there was only a 20 % dropout rate over the 2 years which is far fewer than might be expected. Based on HDL cholesterol changes differences in carbohydrate intake were only 6 % rather than the expected 30 % difference.

All diets reduced cardiovascular risk factors for cardiovascular disease and diabetes at 2 years. The low fat and high carbohydrate diets reduced LDL cholesterol more than the high fat diets and low carbohydrate diets 5–6 % vs 1 %. Triglyceride was lowered by 12–17 % and there was no statistically significant greater effects in the low carbohydrate diet groups. This was almost certainly a result of small differences in achieved carbohydrate intake.

The main outcome from this study was that it was impossible to maintain significant macronutrient differences long term. What little differences were achieved had no effect.

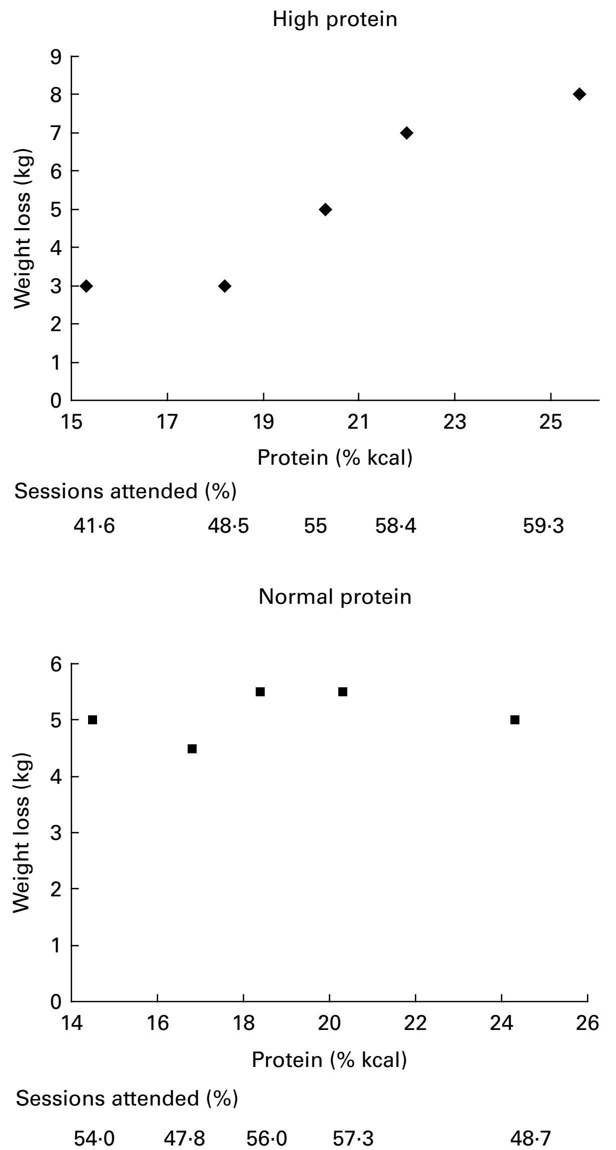

Fig. 1. Weight loss as a function of compliance and protein intake (redrawn from 16).

In the DIRECT 2 year weight loss study, 322 moderately obese participants (mean BMI 31, 86 % men) were randomized to one of three groups: low-fat, Mediterranean, or low-carbohydrate diets[17,18]; 84·6 % completed the study. In the intention-to-treat analysis, weight loss was 2·9 ± 4·2 kg for the low-fat diet, 4·4 ± 6·0 kg for Mediterranean, and 4·7 ± 6·5 kg for low-carbohydrate (diet-group × time $P<0{\cdot}001$). Weight loss among the 272 participants who completed the two-year intervention was 3·3 ± 4·1 kg, 4·6 ± 6·0 kg, and 5·5 ± 7·0 kg, respectively. Men lost more weight on the low-carbohydrate diet, but women lost more weight on the Mediterranean diet (P for group×sex $< 0{\cdot}001$) suggesting that dietary preference may have a role to play in successful weight loss.

Overall compliance at 2 years was 90 % in the low-fat, 85 % in the Mediterranean, and 78 % in the low-carbohydrate diet groups (P=·042 between groups). Dropout rates differed between the diets, 9·6 % for the low fat group, 14·7 % for the Mediterranean and 22 % for the low-carbohydrate group (P=·04 between the diet groups). In a multivariate model, significant independent predictors of dropping-out were: higher baseline BMI (OR = 1·11) and lower weight loss at 6 months (OR = 1·20). Greater weight loss achieved at month 6 was the main predictor associated with success in weight loss (>5 %) over 2 years (OR = 1·5) suggesting that in the short-term a more restrictive diet may be the best option. In those who achieved a >5 % weight loss at 2 years (42 % of the group) weight loss at 6 months was 9·3 kg while the failures (<5 % weight loss) only achieved a weight loss of 3·2 kg at this time point. Self-reported complete adherence score to diet was greater on a low-carbohydrate diet ($P<0{\cdot}05$ compared to low-fat) until month 6, but dropped overall from 81 % at month 1 to 57 % at month 24. This suggests that the low carbohydrate, high protein diet is best used for no more than 6–12 months with a change to another dietary pattern for long term weight maintenance. Although the % protein increased in the Atkins diet by 3·1 % of energy, absolute protein intake decreased by 7–20 g/day. As this was a workplace feeding study in the Negev desert its general applicability may be limited as it was much easier in this setting to maintain macronutrient differences but again the absolute differences achieved in weight outcomes were not large.

Foster *et al.*[19] compared a low carbohydrate diet to a low fat diet over 2 years. Weight loss was approximately 11 kg (11 %) at 1 year and 7 kg (7 %) at 2 years. There were no differences in weight, body composition, or bone mineral density between the groups at any time point. The number of participants commencing the study was 307 and 32 % dropped out in the low fat group and 42 % in the low carbohydrate group.

Long term follow up of the *ad libitum* 6 month Astrup study[20].

In this Danish study 65 healthy, overweight and obese subjects were placed on either a high carbohydrate (HC 58 % carbohydrate, protein 12 %) or a high protein (HP 45 % carbohydrate, 25 % protein) diet (6) with no guidance on energy intake and all food was provided by self-selection in a study shop. Weight loss after six months was 5·1 kg in the HC group and 8·9 kg in the HP group ($P<0{\cdot}001$), and fat loss was 4·3 kg and 7·6 kg, respectively ($P<0{\cdot}0001$), whereas no changes occurred in the control group. More subjects lost >10 kg in the HP group (35 %) than in the HC group (9 %)[20]. Similar results were seen in this group at 1 and 2 years, with more participants in the HP group (17 %) having lost >10 kg than in the HC ($P<0{\cdot}09$). At 24 months, both groups tended to maintain their 12 months weight loss, but more than 50 % were lost to follow-up[21].

Dansinger *et al.*[22] compared Atkins (low carbohydrate), Zone (high protein), Weight Watchers (calorie controlled) and Ornish (low fat), in 160 participants with fairly poor results at 12 months with no group exceeding a 3 kg average weight loss. Changes in TC/HDL ratio, insulin and CRP were directly related to the amount of weight lost and did not differ by diet type.

Similar diets were tested in 311 pre-menopausal women for 1 year[23] Between 35–50 % of all subjects had dropped out by 12 months. Mean 12-month weight loss was: Atkins, 4·7 kg, Zone, 1·6 kg, LEARN (a calorie controlled behavioural program), 2·6 kg and Ornish, 2·2 kg. Weight loss was not statistically significantly different among the Zone, LEARN, and Ornish groups but Atkins was different to the Zone diet only ($P<0·05$) suggesting that either satisfaction with the Atkins diet or more restricted food carbohydrate choices are important during weight loss[24]. Adherence to the diet was not predicted by age, BMI or education level[25].

Foster *et al.*[25] randomised subjects to either low-carbohydrate (high protein) or low-calorie, high-carbohydrate, low-fat diets. A difference in weight loss was seen at 6 months but not 12 months which was very similar to the results of Samaha *et al.*[26,27]. Brehm *et al.*[28] and Yancy *et al.*[29] showed better results at 6 months on a high protein low carbohydrate diet but did not extend the studies to 12 months.

McAuley *et al.*[30,31] contrasted 3 different diets of varying fat and protein levels. The high fat diet produced rises in LDL cholesterol in 20 % of the group despite the weight loss.

Overall in these 12–24 month studies there was little benefit from a high protein diet either with a moderate or a high carbohydrate diet even when compliance to the diet was achieved. There were few differences in cardiovascular risk factors.

In a meta-analysis by Nordmann *et al.*[32] five trials of the Atkins diet with a total of 447 individuals followed up for at least 6 months with intention-to-treat analysis were evaluated. After 6 months, individuals assigned to low-carbohydrate diets lost more weight than those on low-fat diets (weighted mean difference (WMD, −3·3 kg). This difference was no longer obvious after 12 months. Triglyceride levels and HDL-cholesterol values changed more favourably in individuals on low-carbohydrate diets after 6 months but total and LDL-cholesterol values changed more favourably on a low-fat diet. There were no differences in blood pressure between diets.

Thus a high protein, low carbohydrate high fat diet does not enhance weight loss but has adverse effects on the most important lipid species-LDL cholesterol.

Krieger *et al.*[33] examined 87 short term studies (some controlled and some ad libitum) finding that protein intakes of >1·05 g/kg body weight were associated with 0·6 kg better retention of lean mass and in studies greater than 12 weeks in duration this increased to 1·2 kg. In studies with a carbohydrate intake of <35–41 % there was a 2 kg greater loss of fat mass, but this was accompanied by a 0·7 kg greater loss of lean mass. In studies of 12 weeks or more this increased to 5·6 kg and 1·7 kg respectively.

Although lean mass my be better preserved on high protein diets the physiological significance of this finding is not clear as there are no benefits of a high protein diet on glucose levels.

In a study from our group at CSIRO of overweight and obese women ($n = 100$) those with high serum TG (>1·5 mmol/L, $n = 50$) lost more fat mass with the high protein than with the high carbohydrate diet (6·4 and 3·4 kg, respectively; $P=0·035$)[34]. In a 12 month follow-up of this study women who reported eating more than 90 g/day of protein were 3 kg lighter than women eating less than this amount. Protein intake was confirmed by urinary urea:creatinine ratio[35]. In a pooled analysis of data from 3 studies in overweight non diabetic subjects ($n = 215$) subgroup analysis showed that subjects with serum TG > 1·7 mmol/L lost more total fat (high protein diet 6·17 ± 0·50; standard protein diet 4·52 ± 0·52, $P=0·012$) and abdominal fat (high protein diet 1·92 ± 0·17; standard protein diet 1·23 ± 0·19, $P=0·005$) when on a high protein diet[36].

We have completed a large 12 month, energy controlled test of an Atkins style weight loss diet compared with a high carbohydrate weight loss diet particularly focused on vascular measures[37,38]. Sixty-nine participants (59 %) completed the trial: 33 in the LC group and 36 in the LF group. Both groups lost similar amounts of weight (LC: 14·5 ± 1·7 kg; LF: 11·5 ± 1·2 kg; $P=0·14$, time × diet) and body fat (LC: 11·3 ± 1·5 kg; LF: 9·4 ± 1·2 kg; P = 0·30). Blood pressure, fasting glucose, insulin, insulin resistance, and C-reactive protein decreased independently of diet composition. Compared with the LF group, the LC group had greater decreases in triglycerides (0·36 ± 0·15 mmol/L; 95 % CI: 0·67, −0·05 mmol/L; $P=0·011$), increases in HDL cholesterol (0·23 ± 0·09 mmol/L; 95 % CI: 0·06, 0·40 mmol/L; $P=0·018$) and LDL cholesterol (0·6 ± 0·2 mmol/L; 95 % CI: 0·2, 1·0 mmol/L; P = 0·001), and a greater but nonsignificant increase in apolipoprotein B (0·08 ± 0·04 g/L; 95 % CI: −0·004, 0·171 g/L; $P=0·17$. There was a significant time × diet effect for flow mediated dilatation (FMD) ($P=0·045$); FMD decreased in LC (5·7 ± 0·7 % to 3·7 ± 0·5 %) but remained unchanged in LF (5·9 ± 0·5 % to 5·5 ± 0·7 %). Pulse wave velocity improved in both groups with no diet effect ($P=0·80$). Thus the high saturated fat, high protein diet produced excellent weight loss but produced adverse effects on LDL cholesterol which reduced FMD.

Layman *et al.*[39] in a 12 month study in 130 obese adults found that a high protein diet reduced fat mass more than a high carbohydrate diet although overall weight loss was the same. The protein diet had sustained favourable effects on serum triglyceride, HDL cholesterol (HDL-C), and TAG:HDL-C compared with the high carbohydrate diet at 4 and 12 mo ($P<0·01$).

In high protein diets that are low in fat and moderate in carbohydrate some benefits are seen in terms of body composition, HDL and TG without adverse effects on LDL cholesterol.

Weight maintenance studies

High protein diets have been tested by several groups following weight loss with a very low calorie diet. Several groups have examined this question and produced conflicting answers. A recent large study (548 participants) from Europe by Larsen *et al.*[40] of diet composition in weight maintenance for 6 months showed that a modest increase in protein led to a 0·93 kg weight difference compared with normal protein and a modest reduction in glycaemic index led to a 0·95 kg weight difference compared with a high glycaemic index diet and these two strategies were additive and also produce fewer

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drop outs (26 % versus 37 %). This study has also shown that advising people to increase their protein intake is relatively ineffective in both achieving an increase in protein and enhancing weight maintenance, whereas providing high protein foods (as was done in 2 centres only out of the 8 centres in the study) is effective as has been previously shown. The reverse was shown with GI: providing low GI foods was ineffective relative to high GI foods, while asking people to choose low GI foods enhanced dietary compliance. This finding suggests the GI of foods *per se* has no impact on weight maintenance which differs from the authors' conclusions. However others have shown that high protein produces no benefit in weight maintenance at 12 months after an 8 week very low calorie weight loss phase[40] although only 47 % of subjects completed the study. We have shown that a higher protein diet (>88 g/d) is worth about 3·1 kg extra body weight loss at 12 months compared with a lower protein diet[35].

Lejeune *et al.*[42] found that a 20 % increase in protein intake (through an unmatched supplement) during weight maintenance after a 4 week weight loss period reduced weight regain by 50 % over the subsequent 3 months. Claessens *et al.*[43] found a similar effect using a matched casein supplement over 12 weeks of weight maintenance which was worth 2·2 kg of fat. Layman *et al.*[39] found that a weight loss diet that had double the amount of protein (1·6 g/kg vs 0·8 g/kg) led to better body composition at both 4 months and 12 months, especially in those participants who lost more than 10 % of their body weight over this period.

There appears to be some evidence that a high protein diet helps maintain weight loss especially in people who have had good initial weight loss.

Type 2 Diabetes and glucose control with high protein, low carbohydrate diets

Short term weight stable studies conducted by Nuttall and Gannon[44–48] over the last few years have demonstrated very impressive reductions in HbA1c with a reduction in carbohydrate of 25 % energy with replacement with fat and protein (15 % to 30 %). These reductions were of the order of a 35 % fall in area under the glucose curve and a 25 % fall in Hba1c over 10 weeks. These studies used a very small number of participants (6–12) and all food was provided. Similarly a 14 day inpatient study of a low carbohydrate diet in 10 obese patients with type 2 DM. led to a fall in Hba1c from 7·3 to 6·8 %. Energy intake decreased from 3111 to 2164 kcal/d and insulin sensitivity improved by 75 %, with triglyceride falling by 75 %[49].

In a meta analysis of 19 trials which exchanged carbohydrate with fat with a median carbohydrate reduction of 18 %, Kodama *et al.*[50] found much smaller effects than Nuttall and Gannon with 2 hour glucose 10 % higher with the higher carbohydrate diet and fasting and 2 hour insulin 8–13 % higher. As expected fasting triglyceride was 13 % higher and HDL 6 % lower with the high carbohydrate diet. In the 306 participants HbA1c, fasting glucose and LDL were not different probably because the trials were all of short duration (10 days to 6 weeks) although Nuttal and Gannon have shown significant effects on Hba1c even in 5 weeks. Whether the exchange of carbohydrate with both protein and fat that their design uses is a significant factor is not clear. Another meta analysis from Kirk *et al.*[51] which included the Nuttall and Gannon studies in its 263 participants from US and Canadian studies showed that HbA1c, fasting glucose and triglyceride were lower on a low carbohydrate diet which often included a higher protein level (in 7 studies). The longest study was 6 months duration and the rest were 1–16 weeks long.

However with free living volunteers purchasing and cooking their own food for many months the reality is quite different. In a New Zealand 6 month study with 93 participants on oral hypoglycaemics and or insulin a lower carbohydrate diet reduced weight by 1·3 kg and HbA1c by 0·4 % compared with a control group. Saturated fat fell by 2 % and protein increased by 1·6 %[52]. Ten patients from the intervention group had a reduction in medication compared with two in the control group while there were ten more patients in the control group compared with the intervention group with an increase in medications so the true difference from the intervention in HbA1c would be greater. Nevertheless the weight loss is disappointing despite 7 individual counselling sessions and a group session as well as phone support.

A recent 12 month weight loss study from Baker IDI Australia which included 98 people with type 2 diabetes compared a high protein diet with a high carbohydrate diet[53]. Weight loss at 12 months was small, 2–3 kg, with small changes in HbA1c of −0·2 − ·3 % with no differences between diets. Although reported energy intake dropped by about 25 % from baseline to 12 months the weight loss clearly did not match this. Reported changes in macronutrient composition were small (3–5 %) and protein differences at 12 months as assessed by 24 hour urinary urea were not statistically significant. Weight loss was related to reported compliance to the diets. Participants with the highest self management score lost 5·5 kg and lowered their HbA1c by 0·87 % while participants with the lowest score had no changes in either variable. The study clearly showed the difficulty of implementing a weight loss strategy for participants with type 2 diabetes in a routine clinical environment.

In contrast another 6 month hospital based study in North Carolina achieved a weight loss of 11·1 kg and a reduction in HbA1c of 1·5 % with an Atkins diet[54]. The calorie-reduced low GI control group also did very well with a weight loss of 6·9 Kg and an HbA1c fall of 0·5 %. Medications were reduced substantially in both groups but 42 % of volunteers dropped out. A study in New York with 105 participants produced much lower weight loss (3·4 %) at 12 months with no differences between the low carbohydrate and low fat diets and no changes in HbA1c[55]. Similarly in a general practice study 144 participants were enrolled in a test of an Atkins diet compared with a low fat diet for 2 years. Only about 50 % returned at 2 years but records could be extracted for another 57. There was a minor weight loss which did not differ by diet and no changes in HbA1c at 6,12 or 24 months[56]. A Canadian study that reduced carbohydrate

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by 13 % for 6 months had no effects on body weight or HbA1c[57].

People with type 2 diabetes have a better weight and lipid profile at 1 year after following a 12 week high protein diet compared with those who followed a high carbohydrate diet[58].

Although a lower carbohydrate, higher protein diet may lower HbA1c in some studies the effects in others is unexpectedly disappointing.

Acute single meal effects of protein on glycaemic control

Eight type 2 diabetic patients each ingested 350 ml beef soup 30 min before a potato meal; 55 g whey was added to either the soup (whey preload) or potato (whey in meal) or no whey was given. Gastric emptying was slowest after the whey preload ($P<0{\cdot}0005$). The incremental area under the blood glucose curve was lower after the whey preload and whey in meal than after no whey ($P<0{\cdot}005$). Plasma glucose-dependent insulinotropic polypeptide, insulin, and cholecystokinin concentrations were higher on both whey treatments than after no whey, whereas glucagon-like peptide 1 was greatest after the whey preload ($P<0{\cdot}05$). These data suggest that protein has more significant effects on glucose homeostasis other than just replacing carbohydrate[59]. Much more research needs to be done in this area, especially in long term weight stable studies.

Preservation of lean mass

Much attention has been focused on the ability of a high protein diet to reduce the amount of lean tissue lost during weight loss. Krieger[33] in his meta analysis of high protein, reduced carbohydrate diets found that a daily protein intake of 1·05 g/kg preserved about 0·6 kg of lean mass more than a lower protein diet. In studies longer than 12 weeks (7 studies only) the difference increased to 1·2 kg. There were no effects on fat mass. In an unpublished meta analysis we have examined 29 studies with a duration of 12 weeks or longer and found no difference on lean mass loss between high and normal protein weight loss diets although there were small but statistically significant effects on fat mass.

Donald Layman has been a very strong advocate of high protein diets for lean mass preservation and believes that an intake of 2·5 g of the essential branched chain amino acid leucine is required at each meal with a minimum of 10 g/day[60]. In his 12 month study of a comparison of a protein intake of 1·6 g/kg (carbohydrate/protein ratio of $<1{\cdot}5$) vs 0·8 g/kg (carbohydrate/protein ratio of $>3{\cdot}2$) absolute lean mass loss was the same in each group (2·6 and 2·7 kg) but change in % fat mass loss differed (5 % vs 3 %) so that there was a relative sparing of lean mass compared with fat mass with a 2 kg greater fat loss in the high protein group[38]. Whether this difference in lean and fat mass translates into clinical differences in insulin sensitivity and glucose control is not clear as the evidence is quite contradictory with increases in fasting glucose[61] as well as no change relative to a high carbohydrate diet[34].

Blood pressure

In weight stable studies Hodgson *et al.*[62] have demonstrated that an increase in protein of about 5 % of energy in exchange for carbohydrate lowers BP by about 5 mm Hg in hypertensive people. The OmniHeart study showed similar effects (3·5 mm Hg in hypertensives[63].

Although a high protein weight loss diet over 12 weeks had no beneficial effects on insulin sensitivity or HbA1c, it did lower blood pressure quite significantly (10/18 mm Hg) even though weight loss was small and not different from the high carbohydrate diet (2·3 and 2·5 kg)[64].

Side effects

It is commonly stated that a high protein diet could potentially reduce bone density and have adverse effects on kidney function, particularly in those with kidney disease. We have shown no adverse effects of a high protein diet in a 2 year weight loss study in postmenopausal women and no adverse effects on renal function in 40 patients with type 2 diabetes and microalbuminuria in a one year weight loss study (P. Clifton, unpublished data).

Summary

High protein diets (*ad libitum* or energy controlled) increase the loss of fat mass relative to lean mass in many studies with a clear reduction in plasma triglyceride. The rise in HDL cholesterol seen with high protein Atkins style diets may not be beneficial for vascular function and high saturated fat versions of the low carbohydrate diets should be avoided. Replacement of carbohydrate with protein lowers glucose and improves HbA1c and is worth considering as a dietary option in type 2 diabetes.

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