Influence of fat and carbohydrate proportions on the metabolic profile in patients with type 2 diabetes: a meta-analysis


CRD summary
This review found that replacing dietary fat with carbohydrate deteriorated insulin resistance in patients with type-2 diabetes. Generally the review was well conducted, but failure to present adequate details of the validity assessment mean that the authors’ conclusions should be interpreted with some caution.

Authors’ objectives
To determine the effect of replacing dietary fat with carbohydrate on glucose and lipid parameters in patients with type 2 diabetes.

Searching
MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to 2007. Search terms were reported. Reference lists of retrieved studies were screened. The review was restricted to published English language studies.

Study selection
Randomised controlled trials (RCTs) that compared low fat high carbohydrate diets (LFHC) with high fat low carbohydrate (HFLC) diets, of at least one week duration, in patients with type 2 diabetes, were eligible for inclusion. Included trials were required to provide data on fasting plasma glucose and fasting insulin. LFHC diets were defined as having a relatively high carbohydrate to fat ratio whereas the HFLC diets had low carbohydrate to fat ratios. Both parallel group and cross-over studies were eligible. Trials that included an intervention with a change in the content or quality of carbohydrate, such as an increase in fibre or whole grains, were excluded. Trials of very low calorie or enteral (not oral) diets and those in which the dosage of hypoglycaemic agents was changed during the intervention period were also excluded. The following metabolic outcomes were considered: haemoglobin A1C, fasting plasma glucose, fasting insulin, total cholesterol, fasting triglycerides, low density lipid cholesterol, high density lipid cholesterol, and two-hour postprandial levels of glucose and insulin.

Carbohydrate to fat ratios ranged from 0.60 to 1.56 in the HFLC diets and from 1.67 to 7.30 in the LFHC diets. The intervention duration ranged from 10 days to six weeks. Across all included trials, mean age was 55 years, the proportion of men was 63%, mean body mass index (BMI) was 28, hypoglycaemia agents were used in 52%, and mean diabetes duration was six years.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Trial quality was assessed using the Jadad scale. The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted as baseline and final means and statistical dispersion for each group for each of the metabolic outcomes was assessed. If data were not reported for the exact outcomes required, these were calculated using criteria defined in the paper. If necessary, measures of means and dispersions were estimated from figures. Mean differences between LFHC and HFLC groups were estimated by subtracting changes from baseline to final values in the HFLC group from that in the LFHC group. Standard errors (SE) for change from baseline values were directly extracted or estimated from the baseline and final values. Percentage change from baseline was calculated by dividing the mean change from baseline and its standard error by the baseline values.

Data were extracted by one reviewer and checked by a second. Disagreement was resolved through discussion with a
third reviewer, when necessary.

**Methods of synthesis**

Data on difference in percentage changes from baseline values were pooled separately for each outcome using fixed-effect models. Heterogeneity was assessed using the Q statistic. In the presence of significant heterogeneity, meta-analysis was repeated using random-effects models. Stratified analysis based on the following variables was carried out: study design, intervention period, proportion of women, mean age, BMI, proportion using hypoglycaemia agents, carbohydrate to fat ratio in the LFHC and HFLC groups, prescription of the monounsaturated fat diet, and prescription of a weight-loss or weight-maintenance diet. Meta-regression analysis was conducted to investigate the effects of age, BMI and carbohydrate proportion in each diet as continuous variables. Publication bias was assessed using the Begg and Egger tests. The trim-and-fill technique was used to investigate the impact of any suggested bias.

**Results of the review**

Twenty two trials reported in 19 publications were included (n=306 participants). Out of the 19 publications, 10 described the number of withdrawals (range 0 to 25%), none described methods of randomisation, and 17 used a cross-over design.

There were no significant differences in haemoglobin A1C (10 trials), fasting plasma glucose (22 trials), total cholesterol (20 trials), or low density lipid cholesterol (16 trials) between the two diets. Low fat high carbohydrate (LFHC) diets led to significant increases in fasting insulin (8.4%, 95% CI: 1.3 to 15.6; 22 trials), two-hour fasting insulin (12.8% (95% CI 5.2 to 20.4; nine trials), two-hour glucose (10.3%, 95% CI 6.7 to 13.9; 10 trials), triglycerides (13.4%, 95% CI 7.1 to 19.8%, 22 trials) and decreased high density lipid cholesterol (-5.6%, 95% CI -8.4 to -2.9; 20 trials). There were positive associations among the magnitude of changes in fasting plasma glucose, fasting insulin and triglycerides. Results for heterogeneity analyses were not presented, but the authors did state that heterogeneity was reduced when a number of outlying trials were removed from the analysis.

Stratified analyses suggested that fasting insulin was only increased in patients aged less than 55 years, in those with a BMI less than 28, those not taking hypoglycaemic agents, those with a carbohydrate to fat ratio in the LFHC of at least 3, and those in whom the high fat low carbohydrate (HFLC) diet was not a monounsaturated fat diet. Triglycerides showed significantly greater increases following: LFHC diet when it consisted of a monounsaturated fat diet compared with a general LFHC diet; LFHC and HFLC diets which were not aimed at weight loss compared with those that were aimed at weight loss.

Overall, there was no evidence of publication bias.

**Authors’ conclusions**

Replacing dietary fat with carbohydrate deteriorated insulin resistance, while the adverse effect on triglycerides from the LFHC diet could be avoided by restricting energy intake to a degree sufficient for the attainment of weight reduction.

**CRD commentary**

The review addressed a focused question and inclusion criteria were clearly defined. The literature search was adequate for published studies, but there was a possibility of language and publication bias as the review was restricted to published English language trials. This was considered in the analysis. Appropriate steps were taken to minimise bias and error in the extraction of data, but it was not clear whether such steps were also taken for the selection of studies and quality assessment. Although appropriate criteria were used to assess trial quality, the results of the quality assessment were not fully reported or considered in the analysis. Methods of meta-analysis were appropriate and relevant subgroup analyses were conducted. Generally the review was well conducted, but failure to present adequate details of the validity assessment mean that the authors’ conclusions should be interpreted with some caution.

**Implications of the review for practice and research**

**Practice:** The authors stated that replacement of dietary fat with carbohydrate is not recommended for improvement of insulin resistance in patients with type 2 diabetes under conditions where total energy and protein intake and the content
of carbohydrate are similar, and the proportion of carbohydrate to total energy is at least 30%.

**Research:** The authors stated that future studies should aim to provide a possible explanation for the greater adverse effect on fasting insulin of the LFHC diet (especially in younger and leaner individuals), should identify the long-term effect and safety of a low-carbohydrate diet on factors other than metabolic effect, and should address whether medication status could influence the effect of changing dietary carbohydrate to fat ratio in patients with type 2 diabetes.

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