Very-low-carbohydrate ketogenic diet v low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials

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CRD summary

This review concluded that individuals assigned to a very-low-carbohydrate ketogenic diet achieved greater long-term reductions in body weight and certain blood cardiovascular risk factors than those assigned to a low fat diet. The conclusions of this well-conducted systematic review are likely to be reliable but the magnitude of the results were of little clinical significance.

Authors' objectives

To compare a very-low-carbohydrate ketogenic diet with a low fat diet in overweight and obese individuals, in terms of long-term weight loss.

Searching

MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Science Direct, Scopus, LILACS, SciELO, ClinicalTrials.gov, OpenGrey.eu, DissOnline.de, NYAM.org and Clinical Evidence were searched to August 2012 with no date or language restrictions. The authors stated that the search strategy was available online.

Study selection

Randomised controlled trials (RCTs) that compared a very-low-carbohydrate ketogenic diet with a low fat diet in overweight and obese adults (older than 18 years with a mean body mass index greater than 27.5 kg/m^2) and had a minimum follow-up of 12 months were eligible for inclusion. Studies of populations with other risk factors in addition to high body mass index were eligible for inclusion. The primary outcome of interest was body weight. Secondary outcomes were triacylglycerol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, systolic and diastolic blood pressure, fasting blood glucose, insulin, HbA_{1c} and C-reactive protein levels. A very-low-carbohydrate ketogenic diet was defined as a diet with no more than 50g of carbohydrates per day or 10% of daily energy from carbohydrates. A low fat diet was defined as a restricted-energy diet with less than 30% of energy from fat. Studies with a concomitant pharmacological intervention were excluded from the review.

Around half of the included studies were conducted in USA; others were in UK, Australia, New Zealand and Israel. Around half of the included studies enrolled patients with risk factors – cardiovascular risk factors and type 2 diabetes – in addition to high body mass index. The average age of participants ranged from 39.8 to 60 years. Mean body mass index ranged from 30.7 to 42.9 kg/m^2. Where reported, average carbohydrate intake per day ranged from 36g to 190g or 33% to 47% of daily energy from carbohydrates.

Two reviewers independently assessed studies for inclusion.

Assessment of study quality

The quality of the included studies was assessed independently by two reviewers according to Cochrane Handbook recommendations. Criteria assessed were adequacy of sequence generation, allocation concealment, blinding of outcome assessors, handling of missing data and selective outcome reporting.

Data extraction

Mean differences between baseline and final values for each outcome were extracted by two reviewers; disagreements were resolved by consensus. Where necessary, study authors were contacted for further information. Imputations were performed where adequate data were unavailable; the authors stated that these imputations were shown in online supplementary material.

Methods of synthesis

Trial results were pooled using a random-effects model and weighted mean differences (WMD) and 95% confidence intervals (CI) were presented. Heterogeneity was assessed using X^2 and I^2 statistics. Significant heterogeneity was

explored by repeating the analysis and removing one trial at a time. Meta-regression was used to assess whether methodological features were affecting the results.

Subgroup analyses were performed according to risk of bias, use of intention-to-treat analysis and studies with 24 months of follow-up. Publication bias was assessed using funnel plots and Egger's test.

Results of the review

Thirteen RCTs (1,569 participants) were included in the review. Nine RCTs were considered to have a low risk of bias although two of these trials did not report the sequence generation method and seven did not report using any measure to conceal the allocation. Five trials were categorised as having a high risk of bias because they used a per-protocol analysis. There was no evidence of selective outcome reporting. Dietary counselling was considered to be adequate in six trials. The proportion of drop-outs ranged from 13.3% to 84.5%.

Patients assigned to a very-low-carbohydrate ketogenic diet had statistically significant greater weight loss than those assigned to a low fat diet (WMD -0.91kg, 95% CI -1.65 to -0.17; 13 RCTs; 1,415 patients). There was no evidence of significant heterogeneity (I^2=0%).

Patients assigned to a very-low-carbohydrate ketogenic diet had significantly decreased triacylglycerol (WMD -0.18mmol/L, 95% CI -0.27 to -0.08; 12 RCTs; 1,258 patients) and diastolic blood pressure (WMD -1.43mmHG, 95% CI -2.49 to -0.37; 11 RCTs; 1,298 patients) and significantly increased HDL cholesterol (WMD 0.09mmol/L, 95% CI 0.06 to 0.12; 12 RCTs; 1,257 patients) and LDL cholesterol (WMD 0.12mmol/L, 95% CI 0.04 to 0.2; 12 RCTs; 1,255 patients) compared with patients on a low fat diet. There was no significant heterogeneity for any of these outcomes.

There was no significant difference between treatment groups in changes in systolic blood pressure (11 trials), fasting blood glucose (eight trials), insulin (six trials), HbA_{1c} (four trials) and C-reactive protein (four trials).

Subgroup analyses were generally consistent with the main results, except for the subgroup analysis of trials with 24 months of follow-up (four trials) in which most of the results were no longer statistically significant.

There was no evidence of significant publication bias for the primary outcome.

Authors' conclusions

Individuals assigned to a very-low-carbohydrate ketogenic diet achieved greater long-term reductions in body weight, triacylglycerol and diastolic blood pressure and greater increases in LDL cholesterol and HDL cholesterol levels than those assigned to a low fat diet.

CRD commentary

The review question and inclusion criteria were clear. An extensive search strategy included grey literature databases and no language restrictions were applied so potential for publication bias and language biases was reduced. Publication bias was assessed appropriately and was not found to be significant for the primary outcome. Efforts were made to reduce potential for reviewer error and bias throughout the review process. The quality of the included studies was assessed and the results of the assessment were discussed and included in subgroup analyses. The synthesis appeared appropriate.

This was a well-conducted systematic review and the authors' conclusions are likely to be reliable. The authors acknowledged that in the long term and when compared with conventional therapy, the results appeared to be of little clinical significance despite their statistical significance (such as weight loss of 0.91kg) and this was not reflected in their conclusions.

Implications of the review for practice and research

Practice: The authors stated that health professionals should consider the advantages and disadvantages of recommending a very-low-carbohydrate ketogenic diet. Consider patients' willpower as the therapy prominently altered individuals' daily habits.

Research: Future trials should focus on dietary adherence. Investigations beyond that of blood cardiovascular risk factors merited further study (such as hepatic lipid infiltration, endothelial function, general cardiovascular events and

renal function).

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