Low-carbohydrate ketogenic diet and the combination of orlistat with a low-fat diet lead to comparable improvements in weight and blood lipids, but LCKD more beneficial for blood pressure

Christopher D Gardner


**Context**

After decades of ‘low-fat’ being promoted as the most appropriate dietary approach to weight loss,1 2 the unabated rise in obesity over the same period led to suggestions to consider alternative dietary strategies, the most prominent being ‘low-carb’. Since 2003, more than a dozen randomised controlled trials have conducted head-to-head comparisons of low-fat and low-carb diets. In general, the low-carb diets have proven to be as or more effective than the low-fat diets for weight loss and for some related metabolic variables among the populations studied.3–6 Consistent findings in the trials to date have been that overall success at 1–2 years was modest for all diet groups, that long-term dietary adherence and participant retention were less than optimal, and that weight regain was common. In other words, no single diet has emerged as clearly superior. Additional similar trials at this time are unlikely to change these general conclusions. However, alternative hypotheses that expand the low-fat versus low-carb question may still be of interest. The recent publication by Yancy and colleagues added a pharmacological therapy to the basic low-fat versus low-carb design.

**Overview**

The study was conducted among 146 adults (mean age 52 years and mean body mass index (BMI) 39 kg/m2), of whom 72% were men, 55% were black and 32% had type 2 diabetes. Study subjects were free-living individuals randomly assigned to either a low-fat diet with the addition of an inhibitor of dietary fat absorption, orlistat (O+LFD), or to a low-carbohydrate ketogenic diet (LCKD) for 48 weeks. The dietary modification component was delivered as 18 sessions of group instruction for both treatment arms. At 48 weeks, 88% and 79% of participants completed study measurements in the O+LFD and LCKD groups, respectively. Weight loss (average 8.5% for O+LFD and 9.5% for LCKD) and improvements in serum lipid and glycaemic parameters were similar in both groups. The only significant difference between groups was greater improvement in blood pressure for LCKD.

**Notable aspects of the study conduct and outcome**

The study had many positive attributes. Participant retention was high, and its diet assessment methods were more rigorous and extensive than those used in most other studies. The diet assessment results suggest that both diet groups achieved and maintained substantial dietary modifications. The laudable dietary adherence throughout the 48-week protocol may help explain why these investigators achieved and maintained a higher average weight loss than many previous studies.

Other notable aspects include the high proportion of men in the study and the high average baseline BMI of 39 kg/m2. There may have been gender differences in response to these diets, but it is unlikely there was sufficient statistical power to effectively test for an interaction by gender. The relatively high baseline BMI suggests these results should be interpreted cautiously when extrapolating them to people who are simply overweight or at lower levels of obesity.

**Limitations of the study design and significant findings**

One novel contribution of the study design was the inclusion of pharmacotherapy in one of the treatment arms. However, given that the function of orlistat is to block the absorption of dietary fat, one important limitation of the study was the absence of an O+LCKD treatment arm, which would have had a higher intake of dietary fat.
and therefore potentially more opportunity to observe the benefit of adding the orlistat. (One alternative would have been a $2 \times 2$ design of LFD versus LCKD, with or without orlistat, which would have required a substantially larger total sample size.) Although greater blood pressure lowering in the LCKD group was reported, both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher at baseline for the LCKD group, and the SBP and DBP were virtually identical in the two treatment arms at the end of the study, thus diminishing the importance of this finding.

Implications and future studies

The results of this trial reinforce previous findings that dietary macronutrient manipulations, even with the addition of a fat-absorption-inhibiting pharmacotherapy, lead to negligible differences in average weight loss success.\(^7\)

What is probably the richest area of continuing research in this field is powerfully presented in figure 3 of the study, which demonstrates that the 48-week weight loss in both treatment arms ranged from 0% to 30%. Finding ways to explain the variability within a diet group and using this knowledge to individualise dietary recommendations – rather than seeking an optimum diet for the general population – should be the focus of future studies.

Competing interests None.

References