# Low-carbohydrate diets, obesity and type 2 diabetes: A review

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**ABSTRACT**

*This review examines the effects of low-carbohydrate, high-protein diets (LCHO) (<150g carbohydrate/d) on glycaemia and cardiovascular risk, energy expenditure, appetite and satiety, liver and kidney function, bone metabolism, and possible adverse effects in type 2 diabetes mellitus (T2DM). At this stage, there is evidence to suggest that the use of lower carbohydrate diets improves glycaemia, cardiovascular risk and liver function in patients with T2DM and broadens patient choice as LCHOs provide an alternative to the standard dietary interventions. However, there is still a lack of evidence for the use of these approaches in the longer term.*

**INTRODUCTION**

Obesity is the main aetiological factor in the development of type 2 diabetes mellitus (T2DM) with 70–80% of type 2 diabetes patients presenting with overweight and obesity (body mass index (BMI) >30 kg/m$^2$). It has been shown that a low-carbohydrate, high protein (LCHO) diet (<150g carbohydrate/d) (1) can improve glycaemic control and results in weight loss in type 2 diabetes mellitus (T2DM).This growing evidence was acknowledged by the American Diabetes Association (ADA) and Diabetes UK, who have recently updated their position statements and recognised LCHOs as a treatment option for obese individuals with T2DM (2,3).

In this brief review, we examine the effects of LCHOs on glycaemia and cardiovascular risk, energy expenditure, appetite and satiety, kidney function, bone metabolism, liver function and possible adverse effects in T2DM.

## GLYCAEMIA AND CARDIOVASCULAR RISK

LCHOs, either ketogenic or not, are effective at lowering blood glucose levels. When a diabetic person is fasting, the rate of glycogenolysis is decreased due to depleted stores of glycogen, which results in a decrease in fasting blood glucose (4). The responses of patients with T2DM to different dietary macronutrient composition have previously been investigated. In 2003, Gannon and colleagues demonstrated that an elevated protein intake significantly decreased postprandial glucose levels and improved overall glucose control (based on $HbA_{1c}$ values) in patients with T2DM. There was no difference in weight loss, therefore it was suggested that the observed differences in blood glucose responses were due to the variation in the protein: carbohydrate ratio (5). A year later, Nuttall and Gannon (6) reported similar results in patients with T2DM, when they observed that replacing some of the dietary carbohydrates with protein reduced 24h integrated plasma glucose concentration and decreased postprandial glucose concentration (4). In 2006, Nuttall and Gannon did a similar 5-week-long study on patients with untreated T2DM, this time examining the metabolic responses to an LCHO (CHO, 20 %; P, 30 %, F, 50%). As well as the improved glucose control, they reported improved nitrogen balance in these patients (7).

In several reviews (8,9), the conclusion about the use of high protein diets indicated that there were improvements in triacylglycerol and high density cholesterol but unfavourable changes in low density lipoprotein cholesterol when a low-carbohydrate approach is used to achieve weight loss. However, Sharman *et al.* (10) demonstrated that the increase in low-density cholesterol was accompanied by a change in low-density cholesterol particle size resulting in a less atherogenic profile.

A recent meta-analysis of restricted carbohydrate diets in patients with T2DM (11) further supported the use of LCHOs in the treatment of T2DM. The results of the meta-analysis suggested that even moderate decreases in carbohydrate intake improved fasting glucose, $HbA_{1c}$ and triacylglycerols in patients with T2DM. Results from more recent trials lasting a year or longer indicated equal lowering blood glucose effect of low-fat and low-carbohydrate diets (12-14), while one reported greater improvements following a low-carbohydrate diet (15).

## ENERGY EXPENDITURE

Low-carbohydrate, high-protein diets appear to be more efficient in enhancing weight loss than conventional diets in the short term. Advocates for these diets claim that this success is partly due to increased energy expenditure. The rate of energy expenditure increases after a meal due to the costs of the digestion, absorption and the energy needed to store fuel (16). This is referred to as the thermic effect of food (TEF). It was shown that a high-protein meal compared with a standard-protein meal, has a greater increase in TEF and can reduce the decrease in the TEF after weight loss (17-19). Although it can be theoretically calculated that TEF enhances weight loss, it has not been observed in short or long term (19).

Several studies agree that the decrease in resting energy expenditure (REE) which accompanies weight loss is independent of diet macronutrient composition. Reduction in REE is expected to occur with the loss of both fat mass and fat free mass (FFM) (20). As REE depends hugely on the amount of FFM, then preservation of FFM, which can take place on energy restricted high-protein diets, can reduce the fall in REE. This was observed by Baba and co-workers (21) who reported that patients on a high-protein diet (45% P, 25% CHO) had 12% higher REE than those on a high-carbohydrate diet (12% P, 58% CHO). They suggested that it may have been due to the formation of potentially thermogenic serotonin and dopamine in peripheral tissues. Luscombe and co-workers (17) on the other hand, did not report REE to be increased by a high-protein diet (28% P, 42% CHO), but observed a blunting in the normal fall in energy expenditure seen during weight loss in T2DM patients. This disparity could be explained by different percentages of protein in the high-protein diets.

**APPETITIE AND SATIETY**

Several studies have reported that LCHOs have better appetite suppressing effects compared to low-fat diets. In a single-meal study, Luscombe-Marsh and colleagues (19) reported that the amount of food desired by obese hyperinsulinaemic subjects over a 3-h period following a test-meal was smaller after the high-protein low-fat meal than after an isocaloric standard-protein, high-fat meal. Similarly, Boden and colleagues (22) showed that despite a 1000 kcal lower energy intake during 14 days on LCHO (ad libitum with up to 21g of CHO per day) hunger levels were similar to those of a low-fat diet in obese patients with T2DM. The restriction of energy intake occurs naturally when carbohydrates account for 5–10% of the total energy of the diet (1). Similarly, in a cross-over randomised study, Johnstone et al (23) demonstrated that, in the short term, a LCHO ketogenic diet resulted in a greater significant reduction in hunger and lower food intake when compared to a high protein medium-carbohydrate non-ketogenic diet.

It is generally suggested that greater short-term improvements in LCHOs are likely to be a result of limited food choices, increased amount of protein, thermic effect of the diet, lower serum insulin concentrations, ketosis and loss of energy through ketonuria. However, the extents of these effects are still being debated (23-27).

**KIDNEY FUNCTION AND BONE METABOLISM**

Disturbances of renal function and bone metabolism are often reasons for rejecting LCHOs as a weight loss therapy. According to the ADA, a very high-protein diet is especially risky for patients with diabetes, because it can speed the progression, even for short lengths of time, of diabetic renal disease (28). However, Scottish Intercollegiate Guidelines Network's (2010) guideline on management of diabetes states that high protein intake (>1.0 g/kg) is not recommended only in patients with stage 4 chronic kidney disease; in patients with early stages of kidney disease, dietary protein restrictions (< 0.8 g/kg) are not required (29). Most of the studies examining LCHOs did not report adverse effects on either

kidney function or bone metabolism. In a study by Noakes et al (30) markers of renal function did not differ from baseline for neither high-carbohydrate, normo-protein (58 g/d) nor high-protein (104 g/d) diets. The study also did not report adverse effects on bone metabolism (30). In addition, a recent randomised controlled trial demonstrated that renal function was not adversely affected by weight loss on a LCHO in obese but otherwise healthy individuals (31). Nevertheless, more research is required to fully assess the effect of a LCHO on kidney function in T2DM.

**LIVER FUNCTION**

The burden of liver disease in patients with T2DM is significant and the prevalence of elevated liver enzymes in T2DM is quite high. Kotronen et al. (32) have reported that people with T2DM have 80% more fat in the liver than healthy people matched for age, weight and sex. Elevated levels of alanine aminotransferase (ALT) (found in 16% of people with T2DM) and gamma-glutamyl transferase (GGT) (found in 23% of people with T2DM) were associated with BMI, metabolic control and the presence of metabolic syndrome (33). The aetiologies of elevated liver enzymes vary, but a common one is non-alcoholic fatty liver disease (NAFLD). Elhayany and colleagues (34) reported that ALT levels dramatically improved after 12 months on a reduced carbohydrate Mediterranean diet. Interestingly, this improvement was more pronounced on this diet than on a standard Mediterranean diet or on a diet recommended by the ADA (35). Similar outcomes were reported earlier by Ryan and colleagues (36) who suggested that, for the obese insulin resistant patients, diet moderately lower in carbohydrate improved ALT levels greater than a high carbohydrate diet, apart from equal weight loss. The authors suggested this to be an effect of overall decreased insulin levels.

**ADVERSE EVENTS**

Most of the adverse effects of LCHOs are usually reported during the first two weeks. These may be due to the loss of total body water and it may be attenuated by drinking more (37). Other adverse effects reported were constipation, headache, halitosis, muscle cramps, diarrhoea, general weakness and rash (37). Moreover, due to muscle glycogen depletion, fatigue was observed during exercise (28). Although these side effects are generally transient, patients with diabetes or hypertension who go on LCHOs are advised to be under the care of a clinician, because sudden changes in the proportions of macronutrients in the diet may influence their drug requirements (1).

One of the concerns about LCHOs is the limitation of fruits, vegetables, cereals, grains and low-fat milk. According to the AHA, these restrictions are likely to cause deficiencies in vitamins and minerals and inadequate fibre intake (28). The recommended intake of these nutrients was shown to lower blood pressure (28); and reduced fibre intake could have long term adverse effects, such as increased risk of bowel cancer (22). However, there is no evidence that diabetic patients would benefit from increased amounts of fibre higher than the RDI (2). To our knowledge, none of the studies investigating LCHOs

reported nutrient deficiencies. Nevertheless, vitamin and mineral supplements are generally recommended to minimise the risk of deficiencies when following an LCHO (1).

## DISCUSSION AND CONCLUSION

Trials investigating the use of LCHOs have common limitations. Firstly, it may be difficult to distinguish the effects of an LCHO and dietary supplements provided. Secondly, in the case of studies with small numbers of participants / high dropout rates, results must be considered as preliminary (38). Although a higher attrition rate was observed on the low-fat diets compared with LCHOs (9), compliance to dietary interventions are often poor (39) and usually decrease after 6 months (25,28,40). Finally, the use of drugs confounds the contribution of the diet to the changes in body measurements, biological markers, blood lipids, and cardiovascular risk.

More research is required to determine the best way of delivering dietary therapy to achieve long-term weight reduction and optimum metabolic control in patients with T2DM. Identification of patient-specific dietary therapy remains the ideal goal. No one approach to diet and food-based therapies is applicable to all patients. At this stage, there is evidence to suggest that the use of lower carbohydrate diets improve glycaemia, cardiovascular risk and liver function in patients with T2DM and broadens patient choice as LCHOs provide an alternative to standard dietary interventions. However, there is still a lack of evidence for the use of these approaches in the longer term. Further work is therefore needed to identify patient-matched diet treatment for long-term sustained weight loss, possibly in association with drug-based therapies.

Sentences that stress the main points of the article:

1. Evidence suggests that LCHOs improve glycaemia, cardiovascular risk and liver function in T2DM.
2. LCHOs widen patient choice by providing an alternative to standard dietary interventions.
3. There remains a lack of evidence for the use of LCHOs in the longer term.

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