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REVIEW ARTICLE

A review of low and reduced carbohydrate diets and weight loss in type 2 diabetes

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Abstract

Background Recent evidence from randomized controlled trials of hypocaloric low carbohydrate diets in people without diabetes has shown that they promote significant weight loss over the short term. There is very little evidence for any effects of reduced carbohydrate intakes on body weight, glycaemia and cardiovascular risk in people with type 2 diabetes.

Methods An electronic search was performed using MEDLINE (1966 to March 2007), EMBASE (1988 to March 2007) and Cochrane Central Register of Controlled Trials (1991 to March 2007) using the keywords low carbohydrate, type 2 diabetes and weight loss. Studies including subjects with type 2 diabetes who adopted a reduced carbohydrate weight loss diet were identified. Data were extracted on study design, weight loss, effects on glycaemia and cardiovascular risk and potential adverse effects.

Results Six studies investigating the effects of hypocaloric reduced carbohydrate diets in people with type 2 diabetes were identified. The studies were heterogenous and most included small numbers, were short-term and provided varying amounts of carbohydrate. No studies were identified that were both low carbohydrate (<50 g day^{-1}) and also designed as randomized controlled trials. All studies reported reductions in both body weight and glycated haemoglobin, with no deleterious effects on cardiovascular risk, renal function or nutritional intake.

Conclusions Conclusions are limited by study design and small numbers, but it appears that reduced carbohydrate diets are safe and effective over the short term for people with type 2 diabetes.

Conflict of interests, source of funding and authorship

There are no conflicts of interest to declare.

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PAD designed the study, collected and analysed the data, wrote and critically reviewed the manuscript and approved the final version submitted for publication.

Background

The health benefits of weight loss for overweight and obese people with type 2 diabetes are now well established (Aucott *et al.*, 2004), but controversies remain over the most effective dietary intervention to promote successful weight loss (Moore *et al.*, 2004). The majority of people with diabetes who successfully lose weight will regain the lost weight over subsequent months or years (Wadden *et al.*, 2004). All national and international diabetes organizations promote weight loss by a combined strategy of increased physical activity and a reduction in energy intake achieved by reducing total fat, saturated fat and processed carbohydrate, but they continue to recommend relatively high total carbohydrate intakes of between 45–60% energy intake (Canadian Diabetes Association, 1999; EASD, 2000; Nutrition sub-committee of the Diabetes Care Advisory Committee of Diabetes UK, 2003; Bantle *et al.*, 2006). There is limited evidence that high carbohydrate diets may stimulate appetite and increase energy intake in people with the metabolic syndrome and type 2 diabetes (Boden *et al.*, 2005) and claims have been made that low fat, high carbohydrate diets may exacerbate obesity and hyperglycaemia (Arora & McFarlane, 2005). This has led to some discussion about the optimal amount of carbohydrate in the diets of people with diabetes to induce weight loss and improve glycaemic control (Mann & McAuley, 2007) and an investigation of the safety and efficacy of low carbohydrate diets (Kennedy *et al.*, 2005).

Low carbohydrate diets, of which Atkins is probably best known, have been popular for weight reduction since the 1960s. Reduction in carbohydrate intake (and thus the availability of glucose) stimulates fat oxidation to supply energy, which results in loss of body fat stores and ultimately weight loss (Adam-Perrot *et al.*, 2006). There is now substantial evidence from randomized controlled trials for the positive effect of low carbohydrate diets for weight loss in people without diabetes over the short term (Foster *et al.*, 2003; Samaha *et al.*, 2003; Stern *et al.*, 2004; Volek *et al.*, 2004; Yancy *et al.*, 2004), but there is limited evidence for the use of these diets over the longer term and in people with type 2 diabetes. It has been proposed that the mechanism of action of low carbohydrate diets would benefit people with type 2 diabetes but whether there would be any added effect over and above reduction in energy intake with associated weight loss remains open to question (Arora & McFarlane, 2005).

The benefits of improvement in glycaemic control for people with diabetes were established by the results of the United Kingdom Prospective Diabetes Study in 1998 (UKPDS, 1998). Weight loss improves insulin sensitivity and lowers glycated haemoglobin (A1c) in people with diabetes, but glycaemia *per se* is not the full picture for risk reduction in type 2 diabetes (Aucott *et al.*, 2004). Other risk factors include high blood pressure, alterations in lipid levels and central obesity, and all are associated with insulin resistance. This cluster of risk factors is found in overweight and obese people with type 2 diabetes and is referred to as the metabolic syndrome (Alberti *et al.*, 2006). The presence of metabolic syndrome increases cardiovascular risk, which remains the leading cause of death for people with type 2 diabetes (Williams & Pickup, 2000) . The evaluation of weight reducing diets, including low carbohydrate diets, should investigate effects on glycaemic control, measures of insulin resistance and cardiovascular risk reduction in people with type 2 diabetes.

Definition of low and reduced carbohydrate diets

Low carbohydrate diets have been called a variety of names, including ketogenic diets, high protein diets and high fat diets. Some high fat and high protein diets are not particularly low in carbohydrate and it has been proposed that the term low carbohydrate should include any diet providing ≤ 50 g carbohydrate per day (Volek & Westman, 2002; Adam-Perrot *et al.*, 2006). Although there are differences between individuals in blood ketone levels with various amounts of dietary carbohydrate, it has been shown that ketosis readily occurs at carbohydrate intakes below a level of 50 g day^{-1} (VanItallie & Nufert, 2003).

For the purposes of this review, low carbohydrate refers to a diet providing ≤ 50 g of carbohydrate per day, and reduced carbohydrate refers to any dietary intervention designed to lower usual carbohydrate intake.

Mechanism of action of reduced carbohydrate diets

All carbohydrates are digested to glucose and this is the preferred metabolic fuel in all tissues of the body. Consumption of excess energy (whether as protein, fat or carbohydrate) results in deposition of fat by the process of lipogenesis. Reduced carbohydrate diets, which are designed to limit both energy intake and available glucose, result in increased fat oxidation to supply energy needs and ultimately lead to weight loss (Adam-Perrot *et al.*, 2006).

Fat oxidation leads to the production of ketone bodies, a by-product of short-chain fatty acid breakdown, and these ketone bodies can be metabolized to produce energy. Ketone levels are raised in most fasting subjects where fat oxidation is providing energy, although levels do not rise to those observed in diabetic ketoacidosis, as the presence of insulin inhibits acceleration of ketone production. There has been much discussion over the role of ketones in the mechanism of weight loss in low carbohydrate diets; animal models suggest that circulating ketones have a direct effect on appetite by increasing satiety (Volek & Westman, 2002). There is some contradictory evidence for the effects of mild dietary-induced ketosis, with one study reporting that ketogenic low carbohydrate diets have a more favourable effect on glycaemia (Gumbiner *et al.*, 1996) and a more recent report stating that ketogenic diets have no metabolic advantage over nonketogenic low carbohydrate diets (Johnston *et al.*, 2006).

Restriction of carbohydrate intake is usually accompanied by a reduction in total energy intake leading to weight loss; there is now evidence from trials of low carbohydrate diets in people without diabetes that energy restriction accounts fully for all weight loss in individuals adopting these diets (Bravata *et al.*, 2003).

Reduced carbohydrate diets and type 2 diabetes

Metabolic studies in people with type 2 diabetes on reduced carbohydrate diets have shown that low carbohydrate diets have direct effects on glucose metabolism by reducing plasma glucose levels (Gannon & Nuttall, 2004), increasing insulin sensitivity (Boden *et al.*, 2005) and reducing postabsorptive glycogenolysis (Allick *et al.*, 2004).

There is now robust evidence from randomized, controlled trials for the effect of reduced carbohydrate diets over the short term in people without diabetes, but there remains limited evidence for people with type 2 diabetes (Kennedy *et al.*, 2005). Published studies in people with type 2 diabetes have involved small numbers of subjects, lacked a control group, had high attrition rates, had short follow-up periods or used a relatively moderate carbohydrate restriction. At present, there are no published studies of randomized controlled trials including an intervention diet which provides ≤ 50 g day^{-1} carbohydrate in people with type 2 diabetes. An electronic search was performed using MEDLINE (1966 to March 2007), EMBASE (1988 to March 2007) and the Cochrane Central Register of Controlled Trials (1991 to March 2007) using the search terms low carbohydrate, type 2 diabetes and weight loss. All studies relating to intervention trials of low carbohydrate diets in people with type 2 diabetes were included. Six trials were identified and included in this review. Of these six trials, only one was a randomized controlled trial, two were designed as cross-over trials and the remaining three trials were single-arm intervention studies. The follow-up period of these trials tended to be of short duration and ranged from 14 days to 22 months, and only two studies reported data beyond 6 months. There was little consistency in the amount of carbohydrate included in the intervention arms of these studies, with the lowest intake being reported as <20 g day^{-1} and the highest as 95 g day^{-1}. In addition, the number of subjects in each study was in the range 10–102 and, where age was reported, the studies included subjects in late middle-age (average age 51–66 years). Table 1 summarizes the details of the clinical trials of hypocaloric, reduced carbohydrate diets in people with type 2 diabetes that have been published to date.

Weight and glycaemic control

Table 2 shows changes in weight, body mass index and A1c from baseline for each study in people with type 2 diabetes. A short-term, 8-week cross-over study in 28 individuals receiving a diet providing 25% energy as carbohydrate showed significant reductions in weight and A1c compared to a diet providing 55% energy from carbohydrate after cross-over for 12 weeks (Gutierrez *et al.*, 1998). An intervention study of a low carbohydrate diet (<40 g day^{-1}) in 88 subjects reported significant reductions in both A1c and body weight at 1 year (Robertson & Broom, 2002).

Table 1 Details of clinical trials of hypocaloric, low carbohydrate diets in people with type 2 diabetes

Author	No. of subjects	Age (years)	Male/ female	Type of study	Carbohydrate intake (g day^{-1})	Duration of study
Gutierrez *et al.* (1998)	28	66.4	8/20	Cross-over	25% total energy*	8 weeks
Robertson & Broom (2002)	88	ND	42/46	Single-arm intervention	≤ 40	12 months
Boden *et al.* (2005)	10	51	3/7	Cross-over	21	14 days
Yancy *et al.* (2005)	28	56	20/8	Single-arm pilot intervention	≤ 20	4 months
Nielsen *et al.* (2005, 2006)	31 (16 intervention/15 control)	ND	ND	Nonrandomized intervention with comparison control group	75–95	6 months
	28 (16 intervention/7 cross-over/5 control)	ND	ND	Retrospective follow-up of above study	ND	22 months
Daly (2006a)	102 (51 intervention/51 controls)	58.7	49/53	Randomized controlled trial	70	3 months
Daly *et al.* (2006b)	206	ND	ND	6-month follow-up data from above study	ND	6 months

ND, no data reported.
*No details of absolute carbohydrate intake given.

Table 2 Changes from baseline in body weight, body mass index (BMI), and glycated haemoglobin (A1c) in studies of hypocaloric, low carbohydrate diets in people with type 2 diabetes

	Weight (kg)			BMI (kg m^{-2})			A1c (%)		
Author	Baseline	Weight loss	*P*-value	Baseline	Change	*P*-value	Baseline	Change	*P*-value
Gutierrez *et al.* (1998)	76.2	1.2	ND	28.5	−0.4	ND	9.7	−1.7	<0.05
Robertson & Broom (2002)	109.6	7.2	ND	38.6	−2.5	ND	9.6	−0.8	ND
Boden *et al.* (2005)	114.8	2.0	0.042	40.3	−0.8	ND	7.3	−0.5	0.006
Yancy *et al.* (2005)	131.4	8.7	<0.001	42.2	−2.8	<0.001	7.5	−1.2	<0.001
Nielsen *et al.* (2005)	100.6	11.4	<0.001	36.1	−4.1	<0.001	8.0	−1.4	<0.001
Nielsen *et al.* (2006)	ND	8.6	<0.001	ND	−3.2	<0.001	ND	−1.1	<0.001
Daly (2006a)	102.0	3.6	0.001*	36.1	−1.3	ND	9.1	−0.55	0.132*
Daly *et al.* (2006b)	ND	3.8	<0.0005*	ND	ND	ND	ND	−0.48	NS

ND, no data reported; NS, not significant.
*Significance assessed by comparison with changes from baseline in the control group.

A short-term inpatient study (21 g day^{-1} carbohydrate) over 14 days in 10 obese subjects reported greater weight loss and significant improvements in glycaemic control and insulin sensitivity (Boden *et al.*, 2005). A more recently published intervention study reported improvements in A1c and body weight over 16 weeks with a 20 g day^{-1} carbohydrate intake in 28 subjects (Yancy *et al.*, 2005). A nonrandomized study in 31 diabetic subjects compared a 20% carbohydrate diet (equivalent to 85–96 g day^{-1} for men and 75–85 g day^{-1} for women) with a low fat diet (25% energy as fat) over 6 months and reported significant reductions in weight and A1c (Nielsen *et al.*, 2005). This benefit remained at 22 months retrospective follow-up. Interestingly, seven of the original 15 controls had crossed over to the reduced carbohydrate diet after the 6 months intervention and these data are included in the follow-up report at 22 months (Nielsen & Jonsson, 2006). A recent and larger scale randomized trial of 102 patients with type 2 diabetes compared a prescribed 70 g day^{-1} carbohydrate intake (actual reported intake 109.5 g day^{-1}) with a low fat diet (<35% energy as fat) and showed a significant reduction in body weight and improvement in lipid profile, but no significant change in A1c over 3 months compared to a control group (Daly *et al.*, 2006a). Data for 206 subjects at 6 months showed maintenance of significant weight loss, but no change in differences in A1c between the two groups (Daly *et al.*, 2006b).

Other studies that have been published show a positive effect of reduction in carbohydrate intake in people with diabetes but, because these studies either included a small diabetic sub-group (54 of 132 subjects) and did not fully report changes in the sub-group (Stern *et al.*, 2004) or used a relatively high carbohydrate intake (138 g day^{-1}) (Sargrad *et al.*, 2005), they have not been included in this review. Two studies also excluded from this review investigated the effect of a eucaloric low carbohydrate diet on glycaemic control in people with type 2 diabetes and have shown positive metabolic effects of low carbohydrate diets in the absence of weight loss, including reductions in glucose and insulin levels, A1c and triglyceride levels (Allick *et al.*, 2004; Gannon & Nuttall, 2006).

It can be seen from Table 1 that only three of these studies reduced carbohydrate intakes to <50 g day^{-1}, and that two of these three studies were of short duration (less than 6 months). The lack of randomized controlled trials in this area, and the varying amounts of carbohydrate prescribed in the trials to date, make it difficult to reach significant conclusions about the role of carbohydrate in weight loss and glycaemic control for people with type 2 diabetes.

Body composition

All these published studies report significant weight loss with hypocaloric, reduced carbohydrate diets in people with type 2 diabetes. A theoretical view is that the majority of weight loss observed with reduced carbohydrate diets is due to water losses associated with glycogen depletion and increased urinary ketone secretion (Denke, 2001). However, this is not supported by the evidence provided by two of the studies in diabetic subjects investigating body composition, which showed that the majority of weight loss is explained by a reduction of body fat rather than fluid loss (Boden *et al.*, 2005; Yancy *et al.*, 2005).

Fat distribution, and specifically high levels of visceral fat, is a known risk factor for heart disease and diabetes and changes in intra-abdominal fat were investigated by two studies. Both report a positive effect of a reduction in carbohydrate intake; one reports a 5% decrease in waist circumference from 130 to 123 cm ($P \leq 0.001$) (Yancy *et al.*, 2005) and another reports a loss of 4.4 cm over 6 months ($P \leq 0.001$) (Daly *et al.*, 2006b).

Medication

The majority of studies in people with type 2 diabetes have included subjects taking a variety of glucose-lowering therapies, including metformin, thiazoladinediones, sulphonylurea and insulin. The studies that report changes in medication as a result of adopting a reduced carbohydrate diet have recorded either reduction or discontinuation of this medication (Gutierrez *et al.*, 1998; Boden *et al.*, 2005; Yancy *et al.*, 2005; Nielsen & Jonsson, 2006). For example, Daly *et al.* (2006a) reported that insulin doses were reduced in 85% of those adopting a reduced carbohydrate diet compared to 22% of the low fat group. Robertson & Broom (2002) stated that, before adoption of a reduced carbohydrate diet, all sulphonylurea therapy was stopped and insulin doses reduced by 50%.

Attrition rates

Attrition rates in dietary intervention studies are traditionally high, commonly between 30–60% (Dansinger *et al.*, 2005). In these short-term studies in people with diabetes, attrition rates ranged from no drop-outs for the short-term studies over 2 and 8 weeks, to 10–25% attrition for those conducted over 3 months to 2 years. These rates are relatively low, but little is known about attrition rates for most reduced carbohydrate intervention studies over the longer term.

Potential adverse effects of reduced carbohydrate diets

Intuitively, it has been assumed that reduced carbohydrate diets, by definition, provide higher amounts of both fat (especially saturated fat) and protein in the diet. Potential adverse effects associated with this dietary change include dyslipidaemia as a result of a high fat intake, and a decline in renal function and increased calcium loss from bones as a result of increased protein intake (Kennedy *et al.*, 2005). In addition, reduced carbohydrate diets may compromise nutritional intake as they may result in low intakes of dietary fibre, fruit, vegetables and milk products. At present, there is little evidence for the safety of reduced carbohydrate diets in people with type 2 diabetes over the long term.

Cardiovascular risk

Concern has been expressed about the effect of high fat intakes on blood lipid levels and risk of cardiovascular disease. This view is largely refuted for people without diabetes by a meta-analysis of the effect of low carbohydrate diets that shows favourable changes in triglyceride and HDL cholesterol, but higher LDL cholesterol (Nordmann *et al.*, 2006). A recent review of aspects of low carbohydrate diets in people without diabetes reports significant reductions in both post-prandial lipaemia and fasting triglyceride levels (Adam-Perrot *et al.*, 2006). Evidence from long-term studies in people with diabetes is lacking; from the studies reported in Table 1, only four authors report changes in lipid levels and these are summarized in Table 3. Two studies report a significant reduction in triglyceride levels, with no significant changes in total cholesterol, HDL cholesterol or LDL cholesterol (Boden *et al.*, 2005; Yancy *et al.*, 2005). Nielsen *et al.* (2005) and Nielsen & Jonsson (2006) did not report levels of LDL cholesterol at either 6 or 22 months follow-up, but stated there was a significant rise in HDL cholesterol from baseline and no significant change in triglyceride and total cholesterol levels. Daly *et al.* (2006a) does not report absolute values for total, HDL and LDL cholesterol at 3 months, but states that there was significant reduction in the ratio of total:HDL cholesterol in the group allocated a reduced carbohydrate intake. Lipid levels have not yet been reported for this study at 6 months follow-up.

Table 3 Effect of low carbohydrate diets on lipid levels in people with type 2 diabetes

	Total cholesterol (mmol L^{-1})			HDL cholesterol (mmol L^{-1})			LDL cholesterol (mmol L^{-1})			Triglycerides (mmol L^{-1})		
Author	Baseline	Change	*P*-value	Baseline	Change	*P*-value	Baseline	Change	*P*-value	Baseline	Change	*P*-value
Boden *et al.* (2005)	4.68	−0.44	<0.02	1.16	−0.02	NS	2.61	−0.05	NS	1.84	−0.65	<0.001
Yancy *et al.* (2005)	4.61	−0.07	NS	0.92	+0.07	NS	2.51	+0.26	NS	2.69	−1.12	0.001
Nielsen *et al.*	5.6	+0.5	NS	1.1	+0.2	<0.001	3.9*	+0.3*	ND	1.4	0	NS
(2005, 2006)	ND	−0.1	NS	ND	+0.2	<0.001	ND	−0.2*	ND	ND	0	NS
Daly (2005)	4.89	ND	ND	1.2	ND	ND	2.6*	ND	ND	2.5	−0.67	0.223

HDL, high-density lipoprotein; LDL, low-density lipoprotein; ND, no data reported; NS, not significant.
*Calculated from published data.

The main trend from these studies appears to be a reduction in triglyceride levels with no significant change in other lipid levels and little evidence for any increased cardiovascular risk in people with type 2 diabetes. However, these results must be interpreted with caution as these studies are short-term and most lack a control group.

Renal function

Nutritional recommendations for people with diabetes promote a moderate protein intake to reduce the risk of renal disease. Reduced carbohydrate diets are assumed to include larger quantities of dietary protein and this may have an impact on renal function. However, only two of the studies in people with type 2 diabetes have investigated renal function. One study over 2 weeks reported a small but significant rise in mean blood urea nitrogen, but no changes in serum creatinine and uric acid levels and no changes in urinary creatinine and albumin excretion (Boden *et al.*, 2005). Yancy *et al.* (2005) reported a reduction in serum creatinine and an increase in urea nitrogen over 16 weeks. Neither of these changes reached statistical significance. Counter-intuitively, a recent case-study reported that a low carbohydrate diet was successful in preventing end-stage renal failure in one individual (Nielsen *et al.*, 2006). There are no data from long-term studies in people with or without diabetes to either support or refute claims that reduced carbohydrate diets impair renal function and further research is needed in this area (Bantle *et al.*, 2006).

Calcium balance

There have been suggestions that reduced carbohydrate diets may have a negative impact in bone health and calcium metabolism as the acidosis associated with the presence of ketones, coupled with high protein intakes, promotes urinary calcium loss (Adam-Perrot *et al.*, 2006). There is very little evidence for the effects of reduced carbohydrate diets on calcium metabolism. One study in people without diabetes showed no effect of increased dietary protein over the short term (Kerstetter *et al.*, 2005) and only one study in people with diabetes investigated effects on serum calcium levels (Yancy *et al.*, 2005). This study reported no change in serum calcium levels over 16 weeks in individuals adopting a low carbohydrate diet. There is no evidence for the effects of reduced carbohydrate diets on calcium balance and risk of osteoporosis in the long term.

Dietary intake

A major criticism of reduced carbohydrate diets is that they may be nutritionally inadequate because they restrict consumption of foods generally associated with good health: fruit, vegetables, starchy foods and milk products (Adam-Perrot *et al.*, 2006).

There is no evidence at present to support or refute these claims. Two studies in people with diabetes reported dietary intake and found that, although there was a highly significant decrease in both energy and carbohydrate intake, absolute intakes of both protein and fat did not change significantly (Boden *et al.*, 2005; Yancy *et al.*, 2005). A third study (Daly *et al.*, 2006a) reported that there were significant increases in the amount of protein and fat in the diet of a reduced carbohydrate group compared to a control group receiving low fat advice, but the study comprised a comparison between groups after the intervention and did not include any data at baseline. However, although absolute protein and fat intakes were higher in the reduced carbohydrate group, these still remained lower than maximum recommended levels. In addition, the reduced carbohydrate group ate similar amounts of fruit and vegetables and significantly more oily fish than the low fat group. Calcium intakes were similar between the groups, but fibre intakes were significantly lower in the reduced carbohydrate group. The long-term nutritional effects of reduced carbohydrate diets in people with type 2 diabetes are unknown.

Conclusions

In summary, the available evidence shows that, in all intervention studies of reduced carbohydrate diets in people with type 2 diabetes, there were reductions in both body weight and A1c. No study published to date has shown a deleterious effect on glycaemic control or cardiovascular risk factors, but these findings should be interpreted with caution because the majority of studies lacked a control group and were of short-term duration. At present, it appears that low carbohydrate diets may be useful over the short term to promote weight loss in people with type 2 diabetes, but there is no evidence that these diets are more successful over the long term than traditional approaches. More research is needed to investigate the long-term effects of these diets on weight loss, glycaemic control, lipid levels, calcium metabolism and nutritional adequacy in people with diabetes.

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