Low Carbohydrate Diet

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Low-carbohydrate diets are increasingly used to help patients with obesity and type 2 diabetes. We sought to provide an overview of the evidence for this treatment approach, considering the epidemiology and pathophysiology of obesity and diabetes in terms of carbohydrate excess. We describe the mechanistic basis for the clinical benefits associated with nutritional ketosis and identify areas of practice where the evidence base could be improved.

Keywords: Type 2 diabetes ; obesity ; low-carbohydrate diets

1. Introduction

The continuum of the degree of carbohydrate restriction that exists in contemporary clinical practice is illustrated in Table $1^{[\underline{1}]}$, with general agreement that less than 20 g per day is a "very low" carbohydrate intake (though some use a threshold of less than 50 g), equivalent to about 10% of total energy intake. The threshold for "low" carbohydrate intake is usually accepted as less than 130 g/day, equivalent to less than 26% of total energy from carbohydrates. Consumption greater than 230 g per day is consistent with no restriction of carbohydrate, although we find that many of our patients with diabetes or obesity exceed several times this amount on a daily basis. In general, the greater the degree of carbohydrate restriction, the greater the degree of ketogenesis, such that carbohydrate intakes of more than 50 g per day are not usually sufficient for ketogenesis^[2]. Hence, "low-carbohydrate" and "ketogenic" are not synonymous dietary terms, but do overlap.

2. Guidelines Endorse Low-Carbohydrate and VLCKD Diets.

Doctors, nurses and other health care professionals ought to be aware that the use of low-carbohydrate and VLCKD diets in patients with obesity or type 2 diabetes is in fact supported by several sets of guidelines from international bodies and professional groups, as outlined in Table 2. For example, the most recent guidance from the American Diabetes Association is unequivocal in stating that "Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycemia and may be applied in a variety of eating patterns that meet individual needs and preferences".^[3]. In the UK, pragmatic infographic resources based on the glycaemic load of various foods are available from the National Institute for Health and Care Excellence (NICE) (created by one of the authors (D.U.)^[4]. See Figure 2 for an example. These help patients understand the glycemic "consequences" of their dietary choices. For example, a 150 g bowl of boiled rice has approximately an equivalent impact on blood glucose levels as ten standard teaspoons of table sugar.

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3. Early De-Prescription is Important

Although research data are relatively scarce on optimal patterns of medication usage early in low-carbohydrate and ketogenic diets, we have found that early and intensive de-prescribing is often required, particularly in patients with diabetes^[5]. In particular, rapid titration of insulin is obviously important in order to prevent potentially serious hypoglycemia. (This clearly applies only to patients with an established diagnosis of insulin requiring type 2 diabetes, as opposed to type 1 diabetes: Low-carbohydrate diets have been shown to reduce adverse events and improve control in observational studies in patients with type 1 diabetes^[6], but we have not considered this further here.) In general, we tend to stop all fast-acting insulin at the time of initiation of VLCKD and, if not stopping basal insulin completely, by then reducing the dose by between 50% and 80%. This mandates four-times-daily monitoring of capillary blood glucose levels in the hours and days after significant decreases in carbohydrate intake. We have found that it is essential that these patients have immediate access to a diabetes nurse, primary care doctor, consultant or dietitian with

experience of low-carbohydrate diets during this time. In addition, we tend to stop sulphonylurea drugs completely at initiation of the diet because of the risk of hypoglycemia. Conversely, we tend to continue metformin given its insulinsensitizing effects, cardiovascular benefits. and very low risk of hypoglycemia. We take an individualized approach to titrating gliptins or glitazones, informed by baseline HbA1c and patient preference. We often continue glucagon-like peptide-1 (GLP1) receptor agonists. Given the potential risk of euglycemic diabetic ketoacidosis^[2] in patients taking sodiumglucose cotransporter-2 (SGLT2) inhibitor drugs, we always stop these if the diet is initiated.

4. Calorie Counting Is Not Required

Rather than emphasizing the need for patients to quantify their calorie intake, we ask them to focus on eating to comfortable satiation and then stopping. The effectiveness of calorie counting has been questioned^{[B][9]} [97,98] with well-described physiological "recidivism" with this approach^[10]. We take a more mechanistically intuitive approach, emphasizing to the patient that metabolic changes associated with their reduced carbohydrate intake may adjust their "hunger set-point" as outlined above. We often try to back this engagement and education up with graphical aids, emphasizing the physiological mechanisms underlying insulin resistance and their reversal with carbohydrate restriction, as shown in Figure 3. Our anecdotal experience of patients reporting significantly reduced hunger and increased satiety is consistent with studies on higher fat and protein diet influence on the physiological drivers of feeding behavior^{[11][12]}.

The second group of drugs that need consideration during a low-carbohydrate diet is antihypertensive medications. This is because the higher circulating insulin levels in insulin resistant type 2 diabetes patients can cause renal sodium retention, which may be reversed quickly with a reduction in insulin levels (as part of a low-carbohydrate diet), leading to enhanced renal sodium (and water) excretion and a lower blood pressure^[13]. We (D.U.) have described these changes in a cohort of 128 patients with type 2 diabetes on a low-carbohydrate diet for an average of two years^[14], where there was a reduction in systolic and diastolic blood pressure of 10.9 and 6.3 mmHg, respectively, despite a 20% reduction in anti-hypertensive medication usage. The risk of hypotension mandates cautious and frequent monitoring of patients' blood pressure and vigilance for symptoms of postural hypotension.

5. Monitor Cardiovascular Risk Factors

While all patients with obesity and type 2 diabetes should have cardiovascular risk factors monitored periodically, the potential increase in fat consumption that arises on a low-carbohydrate diet, in the context of historical epidemiological concerns that dietary fat might increase cardiovascular risk, makes the issue more pertinent. We have found that individuals concerned about the appropriateness of low-carbohydrate diets are either unfamiliar or don't accept recent nutritional epidemiological discoveries around the ineffectiveness of low fat diets to prevent cardiovascular disease^[15] and the benefits of low-carbohydrate intake^[16] and certain saturated fats, such as those from dairy, in reducing cardiovascular (and diabetes) risk^{[17][18]}. A recent meta-analysis suggested low-carbohydrate diets are superior to low fat diets in improving the lipid profile^[19]. While current guidelines on saturated fat are overdue a revision^{[20][21]}, it seems reasonable to reassure patients undertaking a low-carbohydrate diet, and their health care providers, that saturated fats from foods that are not ultra-processed are unlikely to do them harm, especially if they are losing weight and improving glycaemia while undertaking a low-carbohydrate approach. A second consideration is the increase in LDL-cholesterol that is described with some^[22] but not all^[23] low-carbohydrate interventions, but the fact that this appears limited to the large LDL subfraction^[24] suggests it is unclear whether it increases cardiovascular risk. Nonetheless, we routinely measure blood pressure, lipid profile and HbA1c in patients adhering to a low-carbohydrate or VLCKD and treat abnormal findings as we would in routine clinical practice, where they have not improved over time.

6. Ensure Adequate Fiber Intake

While the recommended intake of dietary fiber is 30 g per day (in the UK) the average intake is closer to 18 g per day. The reduction in wholegrain consumption associated with a low-carbohydrate diet could accentuate that deficit and low intake of dietary fiber is associated with an increased risk of metabolic^[25] and colonic^[26] disease. However, we have found in practice that adopting a low-carbohydrate diet which limits ultra-processed foods and includes nuts, seeds, non-starchy vegetables and low-carbohydrate fruits tends to lead to a net gain rather than a reduction in patients' dietary fiber intake compared to baseline.

Body	Guideline	Year	Recommendation
Diabetes UK (UK)	Diabetes UK evidence- based nutrition guidelines for the prevention and management of diabetes	2011	The Diabetes UK 2011 guidelines support the view that low- carbohydrate diets may be considered an option for weight loss in people with Type 2 diabetes when supported by a registered healthcare professional. ^[27]
Scientific Advisory Committee on Nutrition (UK)	Carbohydrates and Health	2015	It is recommended that the dietary reference value for total carbohydrate should be maintained at an average population intake of approximately 50% of total dietary energy. ^[28]

Table 1. Summary of current guidelines and consensus statements on the use of low-carbohydrate diets.

Body	Guideline	Year	Recommendation
SIGN Guidelines (UK)	Management of Diabetes —A National Clinical Guideline	2015	People with Type 2 Diabetes can be given dietary choices for achieving weight loss that may also improve glycaemic control. Options include simple calorie restriction, reducing fat intake, consumption of carbohydrates with a low rather than a high glycaemic index and restricting the total amount of dietary carbohydrate (a minimum of 50 g per day appears to be safe for up to 6 months). ^[29]
National Institute of Clinical Excellence (UK)	Type 2 diabetes in adults: management	2015	Individualise recommendations for carbohydrate and alcohol intake, and meal patterns.
American Diabetes Association and European Association for the Study of Diabetes (USA & Europe)	Management of Hyperglycaemia in Type 2 Diabetes. A consensus Report.	2018	Nutritional therapies: Low-carbohydrate, low-glycaemic index and high-protein diets, and the Dietary Approaches to Stop Hypertension (DASH) diet all improve glycaemic control, but the effect of the Mediterranean eating pattern appears to be the greatest. ^[30]
Diabetes Australia (Australia)	Low carbohydrate eating for people with diabetes —position statement	2018	For people with type 2 diabetes, there is reliable evidence that lower carb eating can be safe and useful in lowering average blood glucose levels in the short term (up to 6 months). It can also help reduce body weight and help manage heart disease risk factors such as raised cholesterol and raised blood pressure. All people with any type of diabetes who wish to follow a low carb diet should do so in consultation with their diabetes healthcare team. ^[31]
American Diabetes Association (USA)	Nutrition Therapy for Adults with Diabetes or Prediabetes: A Consensus Report	2019	Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycaemia and may be applied in a variety of eating patterns that meet individual needs and preferences. For select adults with type 2 diabetes not meeting glycaemic targets or where reducing anti-glycaemic medications is a priority, reducing overall carbohydrate intake with low- or very low-carbohydrate eating plans is a viable approach. ^[32]

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