REVIEW

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Carbohydrate-restricted diets and Type 1 diabetes mellitus: research considerations

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Purpose of review
Type 1 diabetes mellitus (T1DM) is managed via careful control of blood glucose, exogenous insulin, diet, exercise, and other physiologic factors. Interestingly, the dietary recommendations for T1DM have had very little systematic research. Many clinical observations, as well as emerging research studies, have noted that a carbohydrate-restricted diet can lead to normalization of blood glucoses with reduction in hypoglycemic reactions among motivated individuals.

Recent findings
In this paper, we review observations of carbohydrate restriction and propose a series of studies to test two levels of dietary carbohydrate intake for the management of individuals affected by T1DM. We recommend that the studies start in otherwise healthy adults with hemoglobin A1c $>$ 8%, and then progress to more complicated populations including children, those with secondary complications and/or good glycemic control. Larger, long-term studies would then address growth in children, and diabetic complications including cardiovascular outcomes.

Summary
Due to the clinical observations of improvements using carbohydrate-restricted nutrition for T1DM, we recommend that these types of studies addressing the level of dietary carbohydrate be urgently conducted.

Keywords
carbohydrate-restricted diets, low-carbohydrate diets, Type 1 diabetes mellitus

INTRODUCTION

Type 1 diabetes mellitus (T1DM) affects 1.25 million adults and children in the USA, accounting for 6% of all cases of diabetes. T1DM is an autoimmune disease that leads to the destruction of the pancreatic beta cells, leading to a loss of insulin and amylin secretion. T1DM is managed by lifelong exogenous insulin and control of blood glucose. Both the standard diabetes protocol and the restricted carbohydrate approach strongly rely on the careful consideration of dietary macronutrient content. The current dietary approach recommended by the American Diabetes Association states, 'There are a few key themes to a healthy diet: lots of fruits and veggies, plenty of whole grains and fiber, and limits on certain proteins, added sugars, and solid fats.' Injected mealtime bolus insulin is to be adjusted to the carbohydrate intake, typically 1 unit of insulin for every 15 grams of carbohydrate [1]. The traditional treatment of T1DM with high dietary carbohydrate and medication use has not solved the long-term complications of T1DM. Over time, the current management of T1DM has not generally led to improvements in glycemic control [2].

Carbohydrate-restricted diets have been used in the past to treat T1DM, and it is not clear what evidence compelled the dietary recommendations to change to the higher carb standards [3]. Several recent reviews were unable to document a study that proved that higher levels of dietary carbohydrate, the current recommendation, was superior to the previously employed carbohydrate-restricted diets [4▪,5,6].

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KEY POINTS

- There are very few studies addressing the dietary pattern for individuals affected by Type 1 diabetes mellitus.
- Using carbohydrate-restricted dietary patterns are effective in motivated clinical populations to improve glycemic control in Type 1 diabetes.
- These clinical observations should be expanded into larger, well-controlled studies, so that risks and benefits can be more fully elucidated.

Clinical observation of carbohydrate restriction and Type 1 diabetes mellitus

The ideal diabetes treatment would achieve and maintain blood glucose levels in normal ranges, minimal hypoglycaemia, and excellent quality of life (Table 1). Because the most powerful dietary contributor to increased glucose levels is carbohydrate, it is sensible to lower the carbohydrate intake to control blood glucose levels. This physiologic understanding led several physicians and researchers with T1DM to use a carbohydrate-restricted diet for themselves and for their patients [7–11]. This alternative 'low carb' approach is gaining popularity because of the remarkably quick response to normalize the blood glucose and the easy ability of sharing these results on social media. One social media group has a following of many members, and a published survey of these members showed that motivated individuals ($n = 300$) remarkably attained normal glycemic control with concomitant reduction in insulin and hypoglycemic reactions [12]. Based on these clinical observations, we have proposed the following next steps for systematic study.

Study proposal: carbohydrate restriction vs. ADA diet for Type 1 diabetes mellitus

Research question

How does a carbohydrate-restricted diet (30 g/day) compare to the current american diabetes association (ADA) recommended diet for management of T1DM over a 6-month period?

Table 1. Criteria for the ideal treatment of Type 1 diabetes mellitus

Normal glycemic control
Minimization of hypoglycemia
Correction of other cardiometabolic risk factors (metabolic syndrome, hypertension)
Elimination, reduction, and removal of diabetic complications
Excellent quality of life

Study design

This study is a two-arm parallel-design randomized controlled trial over a 6-month period.

Study population

Thirty-four individuals with T1DM will be recruited to participate.

Inclusion criteria

(1) Diabetes mellitus, Type 1, confirmed by deficiency in c-peptide
(2) Age from 18 to 65 years old
(3) Hemoglobin A1c $> 8\%$

Exclusion criteria

(1) Unstable or serious medical condition
(2) Gastroparesis/severely impaired digestive motility as it adds additional complexities to proper basal-bolus management.

Intervention

Subjects will be randomized to follow one of 2 groups:

(1) ADA diet. This group will be given the book, The Type 1 Diabetes Self-Care Manual by Jamie Wood MD and Anne Peters MS [1].
(2) Carbohydrate-restricted diet. This group will be given the book, The Diabetes Solution and 'Diabetes University' instruction videos by Richard K. Bernstein MD [7].

A dietitian or clinical diabetes educator, familiar with both approaches, will assist in the teaching and monitoring of the dietary interventions.

Instruction for both groups:

All subjects will receive the same instruction regarding the use of combination basal and bolus insulin. Further systematic instruction will include proper injection sites, adjusting insulin to account for protein, understanding and accounting for effects of exercise on blood sugar, as well as managing during sick days that include dehydrating illness such as fever, diarrhea, and vomiting.

Blood glucose monitoring

Continuous and finger-stick glucose monitors will be provided for self-monitoring of blood glucose.

Insulin dosing

Because there are so many ways of prescribing insulin, some flexibility in the protocol is needed, but there needs to be a combination of basal and bolus insulin. The basal insulin can be provided as an insulin pump, or a long-acting insulin (e.g. lantus, levemir, or Tresiba).

Correcting low blood sugars

Low blood sugars are corrected to target using glucose and preferably liquid glucose, which is both fastest and most precise. Subjects will be asked to not use food to correct blood sugars as the action of meals is too slow, too imprecise, and may result first in hypoglycemia and then later hyperglycemia.

Correcting high blood sugars

High blood sugars may occur for a variety of reasons and require additional insulin outside the standard basal/bolus protocol. For corrections, small doses of rapid acting Novolog or Humalog can be used, and their speed of action can be increased via intramuscular injections into the deltoid.

Primary outcome

The primary outcome is hemoglobin A1c, and it will be measured at baseline, 3 months and 6 months.

Secondary outcomes

Adherence (daily reported carbohydrate), body weight (before and after the study), blood pressure, blood markers of metabolism for safety (complete blood count, comprehensive metabolic panel, lipid profiles), and number of hypoglycemic events. In addition, the study survey will also include data fields for age, gender, daily activity, total daily macronutrient content and ketone measurements (daily)

Duration

The subjects will be seen in the clinic every month for 6 months for continued education and measurements.

Sample size considerations

Using pilot data from the carbohydrate-restricted diet survey compared to several published studies, a sample size of 17 subjects per group would have 80% power to detect the difference between a HbA1c of 7.0% and 6.0% (SD = 1.35), using a two-sided p value of 0.05 [12–14].

DISCUSSION

The current dietary recommendations for T1DM have received very little comparative study to other diets, and strong clinical observation experience suggests that carbohydrate restriction is effective among motivated individuals. There is a strong rationale to lower the dietary carbohydrate for the treatment of a condition defined by elevated blood glucoses. The 'law of small numbers' provided a mechanistically obvious solution: restrict both carbohydrate quantity and all rapid acting carbohydrates [7]. Because of concerns about safety and feasibility for those who may not be so motivated, prospective studies are in order.

We have outlined the first of many possible studies to assess the safety and feasibility of a carbohydrate-restricted diet. In a similar fashion when studying a new drug, it is common to begin the research among healthy individuals, or in populations that would require little assistance—for example, motivated patients. Even though it would not require many research subjects to reject the null hypothesis, the more subjects enrolled will give a greater understanding of the safety and feasibility. If the initial study in healthy individuals looks promising, then subsequent studies can include individuals with medical co-morbidities, children, and have longer duration to determine any difference with respect to the complications of diabetes.

The concerns about carbohydrate-restricted diets for T1DM include ketoacidosis, hypoglycemic unawareness due to ketosis, an impaired sympathoadrenal response to hypoglycemia, growth retardation, and long-term cardiometabolic risk [15]. These concerns, however, are lessened when considering studies that show final stature stunting correlating with A1c of 7% and higher, as well as elevated A1c being the most potent predictor of cardiovascular diseases in T1DM [16,17]. Moreover, the ADA has recently adjusted their pediatric A1c guidelines to reflect mounting evidence demonstrating that chronically elevated levels of blood glucose can cause effects including abnormal brain development, increased heart problems, microvascular complications (e.g. diabetic nephropathy, neuropathy, and retinopathy), and increased mortality rates in children and adolescents with T1D [18]. Given these findings combined with the preliminary findings that 97% of individuals with T1DM attained the ADA goal when using a restricted carbohydrate diet (20–70 g), the possible benefits from this approach outweigh the theoretical concerns, but research is needed to determine the balance of these risks and benefits.

The manner in which these early studies are interpreted are reminiscent of the early reaction to the use of carbohydrate restriction for obesity and Type 2 Diabetes Mellitus. Initially, there were

many negative opinions to the approach because it was an approach that was unfamiliar to the mainstream teaching. Even though the efficacy was easy to prove, the studies required to prove 'safety' involve following hundreds or thousands of subjects in a careful manner. One important lesson from the use of carbohydrate-restricted diets for T2DM is that the interpretation of changes in serum lipid profiles must include the concept of 'metabolic syndrome [19▪].' Carbohydrate-restricted diets reduce cardiometabolic risk by addressing the metabolic syndrome [20].

Another lesson learned from the early research of carbohydrate-restricted diet research involved the therapeutic inertia of the standard instructional methods. Some practitioners have been trained in only one approach, and have difficulty teaching two approaches. For example, a nutrition expert may by default recommend 'lean meats' or 'low saturated fat choices', when the carbohydrate-restricted approach does not use this language. If the same nutrition educator is used, it is important for the educator to teach with 'equipoise' – in other words, in an unbiased manner without judging that one approach is better than another. If such a practitioner is not available, then there should be two diet educators. Another option would be to use educators who are very enthusiastic about teaching their approach, to enhance subject motivation. Furthermore, with T1DM, dietary considerations alone are not sufficient. Instructor expertise in determining basal-bolus programs and the many features of exogenous insulin dosing are critical – particularly so with the less well-known restricted carbohydrate approach.

CONCLUSION

Due to the biological rationale and clinical observations of successfully using carbohydrate-restricted nutrition for T1DM, we recommend that a systematic approach to assess the safety and efficacy be conducted. The clinical research interventions may benefit from including principles and practices taught by doctors and individuals who have experience with this approach.

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Conflicts of interest

D.T.D. has no conflicts of interest. E.C.W. receives royalties for the sale of diet books, and has equity in Adapt Your Life, Inc., a company based on low-carbohydrate concepts.

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