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Role of Low-Carbohydrate Diets in Diabetes Management

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Abstract

Low-carbohydrate diets (LCD) are gaining in popularity socially as well as clinically for the treatment of diabetes and weight management. While many health organizations across the globe have recognized LCD as an important dietary strategy for diabetic patients, some organizations promote primarily calorie-restricted diets (CRD). There are multiple reasons that LCD is an important tool in diabetes management that need to be discussed to add to the literature evidence for LCD efficacy. We present a brief overview of LCD utilization for glycemic control along with data gathered from different types of diabetes patients seen at Takao Hospital as well as the Japan Low Carbohydrate Diet Promotion Association.

Keywords: Glycemic control; Low carbohydrate diet (LCD); Calorie-restricted diet (CRD); Japan LCD Promotion Association (JLCDPA)

Introduction

Before the discovery of insulin in 1921, diabetic patients were treated by limiting carbohydrate intake [1], which was viewed as both safe and effective. Elliott Joslin, founder of the Joslin Diabetes Center, began using exogenous insulin in 1921/22 on some of his patients [2]. Once insulin became widely available it displaced low carbohydrate diets (LCDs) in the mainstream medical community, in large part due to Joslin's success. Diabetic patients with insufficient endogenous insulin secretion, e.g. type 1 diabetes (T1D), are generally treated with insulin in modern times as well. This is quite logical as the deficient substrate is directly replaced. Even when endogenous insulin is produced in excess due to insulin resistance, insulin replacement is commonly utilized when oral hypoglycemic agents (OHAs) and lifestyle modification are insufficient in controlling blood glucose (BG). In the case of type 2 diabetes (T2D), dietary modification is often recommended. Dietary focus in T1D tends to be primarily limited to counting carbohydrates to estimate exogenous insulin requirements. However, there are multiple reasons to encourage dietary modification as a pre-emptive measure in T1D patients rather than an afterthought merely to calculate insulin dosing. First, traditional diets restricting calories but not carbohydrates are less effective than LCDs at good glycemic control. Second, LCDs reduce quantitatively the requirement for antihyperglycemic medications. In many cases, LCDs eliminate the need for any medication. Third, some symptoms of metabolic syndrome improve. Some symptoms drastically improve within days of LCD initiation. There is a plethora of definitions for LCD. Feinman and Bernstein give tiered definitions of LCD [3]: i) Very low-carbohydrate ketogenic diet (VLCKD), ii) Low-carbohydrate diet: <130 g/day or <26% total energy, iii) Moderate-Carbohydrate Diet: 26%–45%, iv) High-Carbohydrate Diet: >45%. We separate LCD into three tiers based on a percentage of total dietary carbohydrate intake to aid in our scientific study. Super LCD, standard LCD, and petit LCD are defined as 12%, 26%, and 40% of daily caloric intake from carbohydrates, respectively [4]. The Japan Diabetes Society (JDS) is a major health organization in Japan that focuses on diabetes care. The JDS recommends that diabetic patients consume a calorie-restricted diet (CRD) high in carbohydrates. We use a CRD that consists of 60% carbohydrate based on historical

recommendations when testing glycemic control. The protocol followed at Takao Hospital is CRD on days 1-2 followed by super LCD on days 3-7 or 3-14, depending on the length of the study. BG monitoring was initially solely by glucometer, but CGM has recently been incorporated.

Super LCD in T2D Patients

Case 1 is a 74-year-old male diagnosed with T2D 22 years ago. He had an HbA1c of 6.7% and a weight of 67 kg at the time of diagnosis. Within one month of initiating the super LCD weight was decreased to 57 kg. HbA1c took months to improve as expected and has been maintained at 5.7% after stabilizing. The most recent labs in June 2023 are seen in (Table 1). No OHAs are used by this patient. Case 2 is a T2D female in her 50s who had a Time in Range (TIR) of 60% and 79% on days 1 and 2, respectively. TIR increased to 100% on day 6 and continued at 100% to completion on day. Time below range (TBR) was 21% on day 1 but trended downward to 0% on day 6 where it remained until completion on day 14. This is evidence that decreasing carbohydrate intake decreases hypoglycemic and hyperglycemic variability.

Table 1: *Recent laboratory data in 2023 for case 1.*

Test	Data	Unit	Range
Fasting BG	102	mg/dL	60-109
IRI	1.9	μU/mL	3-15
HbA1c	5.7	%	4.6-6.2
Glycosylated albumin	13.8	%	
B-hydroxybutyrate	137.0	μM/L	<76.0
Urine ketone bodies	+	+/−	−
Uric acid	3.6	mg/dL	3.4-7.0
TG	65	mg/dL	50-149
HDL-C	74	mg/dL	40-98
Calculated LDL-C	89	mg/dL	<140
Creatinine	0.69	mg/dL	0.6-1.1
Cystatin C	0.71	mg/L	0.53-0.95
TSH	1.0	mIU/L	0.61-4.23
FT3	3.0	pg/mL	2.1-4.0
FT4	1.1	ng/dL	0.8-1.8

Case 3 is a male T2D patient in his 50s who saw improvements after starting a super LCD. After just 7 months, HbA1c and weight down trended from 11.1% to 6.3% and 66 kg to 58 kg, respectively. After 7 years of super LCD HbA1c was 5.7 and weight 57 kg. Figure 1 shows the changes in HDL, LDL, HbA1c, and body mass over time.

Super LCD in SPIDDM Patients

Comparison of 12 T2D subjects with positive Glutamic Acid Decarboxylase antibody (GADA) (Group 1) versus 12 T2D subjects negative for GADA (Group 2) were conducted using CRD 1-2 days and super LCD for days 3-14 [5]. Both groups performed better as measured by meal tolerance test, post-prandial BG, and M value on the super LCD. However, Group 2 had better glucose control than Group 1, which could indicate progression to Slowly Progressive Insulin-Dependent Diabetes Mellitus (SPIDDM) in GADA positive T2D patients.

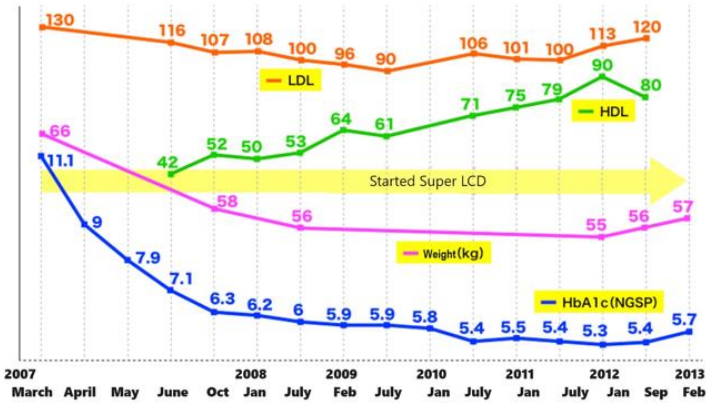

Figure 1: *Laboratory Data over Time for Case 2.*

Case 4 was found to be GADA positive and was diagnosed with SPIDDM in his 50s. He has been treated with a super LCD alone for more than 4 years [6]. The patient's IRI has been 3.0 μU/mL or less when measured. HbA1c has consistently been maintained at 6.0% or less and FBG ranges from 90-111 mg/dL. The patient may eventually require insulin. However, it appears that there is an increased latency to insulin dependence that may be attributable to super LCD adherence.

Super LCD in T1D Patients

Case 5 is a T1D patient in his 50s. After initiating the super LCD, insulin requirements were reduced while markers of glycemic control simultaneously improved [7]. CPR in January 2018 was 1.1 ng/mL and by mid-2022 it had decreased to 0.2 ng/mL, indicative of declining but continuing endogenous insulin production. This decline is associated with an increase in insulin requirement; however, the patient still requires less insulin than before starting the super LCD despite a decrease in CRP. In addition to reducing insulin requirement, LCD could prolong endogenous insulin production.

Case 6 is a male in his 50s that was diagnosed with T1D. He had a prolongation of the honeymoon phase by 16 months after the continuation of the super LCD [8]. Additionally, this patient was evaluated using the Takao Hospital protocol. TIR was 82% and 89% on days 1 and 2, respectively. Afterward, TIR increased to 100% on day 8 and continued at 100% to completion on day 14. This is another superb example showing both the short-term and long-term benefits of LCD implementation.

Case 7 is a 48-year-old female T1D patient who transferred to Takao Hospital for diabetes management and education to improve glycemic control. Her HbA1c was 11.6%, GADA 1130 U/mL, and Glycoalbumin (GA) was 24.2%. The insulin regimen on admission was 18 units of insulin glargine and insulin lispro 4-2-2 units. The patient was given the super LCD containing approximately 1600 kcal per day with 10 g of carbohydrates per meal (from non-starchy plant foods). She was monitored with CGM for 7 days. Insulin requirement was quickly decreased, and the regimen was revised to 10 units of insulin glargine and no Humalog by discharge on day 7. As seen in Figure 2, the calculated HbA1c was 6.5%. Glucose briefly exceeded 200 mg/dL on the third day but improved afterward. TBR was 14% and 21% on days 1 and 2, respectively but was 0% thereafter. This patient achieved better glycemic control by injecting less insulin. Hypoglycemia is avoided physiologically by gluconeogenesis and proper insulin dosing.

Case 8 is a 73-year-old female T1D patient who was referred for inpatient evaluation and treatment of T1D for 7 days at Takao Hospital. HbA1c and GA were 7.2% and 19.0%, respectively. CPR and urine C-peptide were 0.2 ng/mL (1.5-3.5) and 16.6 µg/day (29.2-167), respectively, indicative of minimal endogenous insulin secretion. The only agent used for glucose lowering was insulin degludec scale 9-10 units depending on morning FBG. The patient started a 1400 kcal per day super LCD and was monitored with concurrent CGM. Data can be viewed in Figure 3.

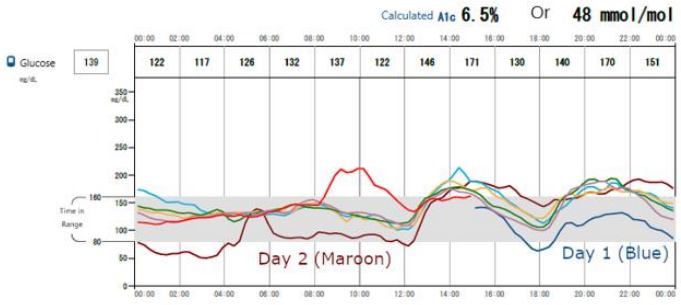

Figure 2: *Seven-day CGM data for Case 7.*

The estimated HbA1c over 7 days was 5.9%, indicating great improvement in glycemic control. The glucose range was set from 80-160 mg/dL. TBR was calculated to be 7% over the 7 days. Glucose never dropped below 66 mg/dL and was only below 70 mg/dL on 4 readings, however, the patient never complained of any symptoms of hypoglycemia. Good glycemic control was maintained on insulin degludec 9-10 units only. The patient was recommended to take miglitol 25mg only prior to carbohydrate intake upon discharge. This is another example of a simple and effective medication regimen made possible by dietary modification.

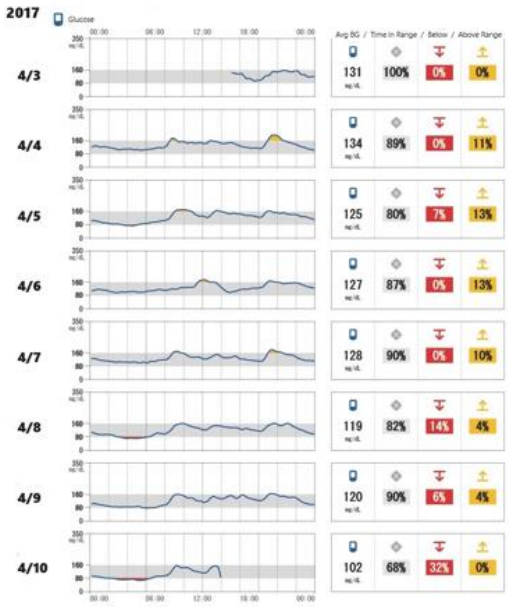

Figure 3: *Seven-day CGM data for Case 8.*

Considerations

There are growing data supporting the efficacy and safety of LCD. Conventional diets containing large amounts of carbohydrate result in postprandial hyperglycemia and huge BG fluctuations. LCDs prevent both postprandial hyperglycemia and BG fluctuations that are seen in conventional diets. Avoiding postprandial hyperglycemia and BG fluctuations, in addition to improvements in metabolic syndrome symptoms may help prevent diabetic complications. LCDs are also effective in decreasing insulin and OHA requirements in diabetic patients with impaired endogenous insulin production. Many T1D and SPIDDM patients benefit from the super LCD in both the short and long terms. It appears that LCDs can prolong the Honeymoon period in T1D patients. SPIDDM patients may eventually progress to insulin dependence. However, LCDs may slow progression in SPIDDM patients, as well. There is much more to learn in this regard, and we hope to stimulate efforts to work out the details in the future.

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