

RESEARCH PROPOSAL

A Randomized Controlled Clinical Nutrition Research Study

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1. Title: Increased Dietary Fiber Intake with Net Carbohydrate Compared to Total Carbohydrate Calculation on Hypoglycemic Episodes and Glycemic Control in Type 1 Diabetic Patients

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3. Relevant Background: Diabetes has rapidly increased in prevalence and now affects approximately 37.3 million, or 11.3% of the American population.¹ Nearly 1.9 million Americans have type 1 diabetes (T1D), including about 244,000 children and adolescents.¹ Sixty-four thousand people are diagnosed each year in the U.S.² 2.1 million people in the U.S. are expected to have T1D by 2040.² Potential complications in T1D are eye problems, foot problems, heart disease, high blood pressure, kidney disease, oral health problems, diabetic neuropathy, skin conditions, stroke, diabetic ketoacidosis (DKA), hyperglycemia, and hypoglycemia.³ Several factors affect blood sugar levels in T1D, and management is complex and highly individualized.³ The three main components of diabetes management include insulin, blood glucose monitoring, and carbohydrate counting.³ The amount of insulin needed throughout the day depends on several factors, including food types.³ It is crucial to understand how certain types of foods affect blood glucose.³ Hypoglycemia is an acute, potentially life-threatening, and the most common complication of diabetes treatment.⁴ Severe hypoglycemia is more common in T1D.⁴ Hypoglycemia is an event with a measured plasma glucose concentration of ≤ 70 mg/dL (≤ 3.89 mmol/L).⁴ Severe hypoglycemia is an episode in which the patient's blood glucose level is documented as <50 mg/dL (<2.78 mmol/L).⁴ Dietary fiber is one type of carbohydrate, just like sugars and starches, but it does not raise glucose levels because the body does not digest it.⁵ There are two types of fiber: insoluble and soluble.⁵ A high dietary fiber intake, particularly of the soluble type above the level recommended by the American Diabetes Association (ADA), improves

glycemic control.⁶ Soluble fiber is found in foods such as oats, peas, pears, beans, apples, bananas, avocados, apricots, nectarines, guavas, citrus fruits, carrots, sweet potatoes, broccoli, brussel sprouts, barley, turnips, figs, flaxseed, sunflower seeds, hazelnuts, and psyllium.⁷ More than 90% of women and 97% of men do not meet recommended intakes for dietary fiber.⁸ Fiber is promoted as part of a healthy dietary pattern and in diabetes management.⁹ The amount of fiber needed depends on age and gender.¹⁰ Based on Dietary Guidelines for Americans (DGA), healthy adults need between 25-38 grams of fiber a day on average.¹⁰ Carbohydrate (CHO) counting can help manage blood glucose levels and know how much insulin to take.¹¹ According to the Food and Drug Administration (FDA), total carbs are the total number of carbohydrates a serving size of a given food has.¹² Insulin-to-carb ratio calculates how much insulin to take to manage blood sugars after eating.¹³ Net carbs are the total amount of CHO in a food minus the fiber content.¹⁴ While soluble fiber does provide a few calories, it does not seem to increase blood glucose.¹⁴ The most recent research suggests that its effects in the gut help reduce blood sugar levels.¹⁴ Many studies have shown that soluble fiber may lead to better blood sugar control, increased insulin sensitivity, and the absorption of fewer calories.¹⁴ T1D patients must calculate their carb-to-insulin ratio based on their CHO intake.¹⁴ Calculating net CHO may help them dose insulin more accurately, thereby experiencing fewer hypoglycemic episodes and having blood glucose levels in the recommended time-in-range.¹⁴ Time-in-Range (TIR) is the amount of time those with diabetes spend with their blood glucose levels in a recommended target range and is represented as a percentage.¹⁵ Glucose goals vary for each person, but a typical target glucose range is 70 to 180 mg/dL.¹⁶ For most people with T1D, a TIR above 70% is recommended.¹⁶ It would help to aim at spending less than 4% (58 minutes) below 70 mg/dL, less than 1% (14 minutes) below 54 mg/dL, less than 25% (6 hours) above 180 mg/dL, and less than 5% (1 hour, 12 minutes) above 250 mg/dL.¹⁶ The ADA refers to

these as “time below range” (TBR) and “time above range” (TAR).¹⁷ In June 2019, the ADA published its first recommendations for TIR targets when using continuous glucose monitoring (CGM) in research and practice (Battelino et al., 2019).¹⁷ These guidelines are designed to help stay as healthy as possible while minimizing the risk of severe hypoglycemia.¹⁸ TIR has become a potentially more valuable method of assessing blood sugar management thanks to the development of continuous glucose monitoring (CGM).¹⁸ This study will determine if a diet rich in fiber will significantly affect diabetes control and glycemic excursions or the incidence of hypoglycemia.¹⁹ The aim of this study will compare the effects of calculating net CHO versus total CHO when consuming high-fiber intake and the impact on reducing hypoglycemic episodes and glycemic control in T1D patients followed for 12 months. We hypothesize calculating net CHO with increased dietary fiber intake can reduce the number of hypoglycemia episodes and regulate glycemic control in T1D patients.

4. Objective/Purpose: This study aims to compare the effects of increased dietary fiber intake with net CHO compared to total CHO on hypoglycemic episodes and regulate glycemic control in T1D patients.

5. Hypothesis: While consuming increased dietary fiber intake, calculating net CHO versus total CHO will have fewer hypoglycemic episodes in T1D patients and regulate glycemic control.

6. Procedures/Methods: *Sample:* Patient recruitment will occur at the Rochester Endocrinology Center (REC) in Rochester, New York. Patient eligibility criteria will consist of participants who are currently T1D patients at REC, are ≥ 18 years of age, diagnosed with T1D ≥ 12 months before the enrollment period, and use a continuous glucose monitor (CGM). Patients are excluded if they have significant uncontrolled T1D (hyperglycemia ≥ 250 within the past three months before screening), gestational diabetes, T2D, intend to become pregnant, are lactating, are currently on a

calorie-restricted diet (<1500 kcal/day) within the past three months before screening, used any illicit or investigational drug(s) within the past six months, or consume more than one serving alcoholic beverage per day. Recruitment will be done voluntarily using a survey and questionnaire method during the patient's routine office visit to their endocrinologist. All participants will provide written and verbal consent to participate in the trial. A nurse practitioner will obtain the participant's date of birth, sex, race, current medications, and medical history during the initial screening visit. All participants' CGM reports on the number of hypoglycemic episodes, glucose levels, A1C, and TIR percentages at every in-person session at baseline and at months 3, 6, 9, and 12 will be obtained. All participants will consume between 22-34g of dietary fiber daily, focusing mainly on soluble fiber from whole foods, along with receiving psyllium fiber supplements (Metamucil, P&C, Cincinnati, Ohio, USA) to achieve daily goal intake without calorie restriction. The United States Department of Agriculture's (USDA) Dietary Guidelines for Americans (DGA) was used to establish the baseline cutoff for meeting recommended dietary fiber intake.⁸ Males, 18-50 years of age, will take in at least 31-34g of fiber per day and 25-28g for females 18-50 years of age. If patients are over 50, the recommended daily fiber intake will be at least 22g for females and 28g for males. All participants will receive a premium version of a food tracker app (MyFitnessPal) to track total CHO, or net CHO, dietary fiber, and water intake. At baseline, a registered dietitian nutritionist (RDN) and certified diabetes care and education specialist (CDCES) will obtain a three-day dietary intake recall and provide nutrition education. The study dietitian will analyze the food diary to determine daily caloric intake and fiber intake using the MyFitnessPal program. At every in-person appointment for months 3, 6, 9, and 12, all participants will continue to meet with the RDN, CDCES, to encourage higher soluble fiber intake from whole foods. Patients will be asked to maintain their usual daily activities and, if exercising, report them

on the MyFitnessPal app. All patients, study coordinators, and medical doctors involved will not be blinded to the patient's assignment. After enrollment, patients will be randomized into two groups using a random number generator. One group will calculate their net carbs (total CHO - fiber = net CHO), and the second group will calculate their total CHO. *Intervention:* The intervention will be net CHO calculating. This experimental group will calculate net CHO for their carb-to-insulin ratio, which will determine how much insulin they need to give themselves. *Control:* The control, for all participants, will be the MyFitnessPal app and fiber intake. A control group will total CHO counting for their carb-to-insulin ratio. *Time Frame:* There will be 48 participants involved during the recruitment/washout period between December 2022 and March 2023, accounting for an attrition rate of 20%. During the washout period, subjects will be asked to lower their insulin dose for unexplained hypoglycemia and increase it for a pattern of hyperglycemia that lasts for two days. The total number of expected participants in the analysis will be 40 T1D patients. Participation length will be a 12-month commitment beginning in April 2023 with an anticipated completion of April 2024. *Primary and Secondary Endpoints:* The primary outcome is the average number of hypoglycemic episodes per week; the secondary outcomes will be A1C and the percentage of TIR calculations. Each will be assessed at baseline, 3 months, 6 months, 9 months, and 1 year.

7. Statistics: Statistical analysis will be performed using SPSS data software. A *p* value of <0.05 will be considered significant. The parametric statistical tests will be the independent and paired sample t-tests comparing the differences in the number of hypoglycemic episodes per week, A1C, and TIR percentage at each time point (0, 3, 6, 9, 12 months) between the net CHO and total CHO calculation groups and within each group compared to baseline respectively.

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