5:2 Intermittent Fasting benefits Early Type 2 Diabetes Treatment

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Introduction

Background and Context

Over 537 million adults were diagnosed with diabetes in 2021. As a global health challenge, is predicted to rise to over 783 million suffer in 2045. The condition has reached epidemic proportions in China, where the prevalence has surged to 12.4% among adults. These trends, such as dietary transitions, sedentary lifestyles and stress, show the urgent for innovative and long interventions[1].

Suitable weight loss benefits glycemic control because obesity is one of risk factors for type 2 diabetes mellitues (T2DM), which could exacerbates insulin resistance and glycemic dysregulation[2]. As a practical dietary intervention, the 5:2 intermittent fasting (5:2 IF) diet involves 2 non-consecutive fasting days (one-forth of the energy intake of a habitual diet) and 5 days of habitual intake per week, has shown promise in improving lifestyle modification to better glycemic control[3].

While pharmacological treatments are usually the primary choice for T2DM, they are usually accompanied by disadvantages such as high price, side effects and so on. Dietary interventions are more general-purpose in comparison. However, further research is required to validate its efficacy and safety, especially study in comparison with these drugs.

Problem Statement

Current treatment strategies for T2DM include pharmacological interventions such as metformin and empagliflozin, which are effective but may lead to side effects. There is a study illustrate metformin make gastrointestinal discomfort[4] and a research show empagliflozin make genitourinary infections[5].

While previous studies have demonstrated the potential of intermittent fasting in reducing body weight and improving hemoglobin A_{1c} (HbA_{1c}) levels[6], little is known about its efficacy compared to standard pharmacological therapies. Addressing these gaps is essential for developing comprehensive understanding of the way in which 5:2 IF strategies can be integrated into clinical practice as a workable alternative or complement to pharmacological therapies.

Research Questions

1. How does the 5:2 intermittent fasting compare to metformin and empagliflozin in improving glycemic control in patients with early-stage T2DM?

2. What are the effects of 5:2 intermittent fasting on other measures such as body weight, fasting glucose levels, and lipid profiles?

3. What are the side effects with the 5:2 intermittent fasting?

Relevance and Importance of the Research

Understanding the mechanisms of 5:2 intermittent fasting can inform broader strategies for addressing diabetes and its associated comorbidities, benefiting both individuals and healthcare systems globally. Improve patient adherence by offering a flexible and sustainable dietary approach.

By comparing 5:2 intermittent fasting with standard pharmacological treatments, this research can help nutritionists who seek to a sustainable lifestyle intervention. Besides, this study seeks to challenge prevailing assumptions that medication is inherently superior to lifestyle interventions for T2DM management and provide a foundation for exploring the long-term impacts of intermittent fasting on diabetes remission and cardiovascular health.

One of important features is the use of interactive web response system to randomize, the statisticians blinded to the study groupings during the data analysis.

Literature review

Key Concepts, Theories and Studies

Intermittent fasting (IF) in clinical practice provide 30–40% of energy requirements on fasting days and 100% or ~125% of energy requirements on non-fasting days[7]. The mechanisms of IF are complex and include eliminating or remediating damaged molecules and improving insulin resistance [8, 9]. Common protocols of IF consist of alternate-day fasting, time-restricted feeding and 5:2 intermittent fasting diet.

A previous study found that more than 100% of energy requirements on non-fasting days increased fasting insulin[10]. While in a 16-week randomized controlled trial (RCT), an alternate-day fasting program providing approximately 1200 kcal of energy on non-fasting days led to improvements in fasting triglycerides and insulin and weight loss[11].

5:2 intermittent fasting diet involves 2 non-consecutive fasting days (one-fourth the energy intake of habitual diet) and 5 days of habitual intake per week. Individuals with obesity have successfully lost weight with this diet through both short-term and long-term interventions[12]. A study found that a 12-month 5:2 intermittent fasting diet significantly decreased HbA_{1c} levels among patients with overweight or obesity and type 2 diabetes, compared with a continuous energy restriction diet[13].While these findings point the need for direct comparisons with pharmacological treatments to establish its benefits.

Key Debates and Controversies

Debates persist over its long-term sustainability and safety, particularly in individuals with T2DM who may be at risk for hypoglycemia. In earlier studies, the common adverse effects of IF included dizziness, headache, nausea, and temporary sleep disturbances. In a secondary analysis of dietary data of two studies of intermittent fasting 5:2 in New Zealand, Scholtens EL et al. found that although fibre intake of IF had lower than recommended and IF was safe and acceptable for weight-loss[14]. Critics also question the universality of fasting protocols, suggesting that individual factors such as age, gender, cultural dietary preferences, and comorbidities may affect outcomes. I think a daily multivitamin supplement and regular face-to-face interview can prevent the risk of complications.

Gaps in Existing Knowledge

There is limited research comparing its efficacy directly with first-line pharmacological treatments for early-stage T2DM. Current studies focus primarily on glycemic control and weight loss, with insufficient exploration of secondary outcomes like lipid metabolism, inflammation, and long-term sustainability. Its long-term impacts on diabetes remission unclear. This research would focus on a 5:2 IF plan change hemoglobin A_{1c} level in adults with early type 2 diabetes to explore its availability.

Research design and methods

Research design

This is a qualitative and experimental research which involve original data collection from participants. It is an intervention study designed by RCT to assess the efficacy of the 5:2 IF on glycemic control in adults with T2DM.

Methods and Sources

Participants aged 18 to 65 years with newly diagnosed T2DM, BMI of 24 or more and HbA_{1c} level of 7% to 9%. The pregnant or breastfeeding women, as well as participants who had used weight-loss drugs within the past 3 months should be excluded.

The randomization list of participants was generated by the stratified blocked randomization method using SAS software, in which stratification was based on the center (block size of 9)[15]. Within each stratum, participants were randomized using a block randomization method, with a block size of 9, in a ratio of 1:1:1 to receive either metformin, empagliflozin, or 5:2 IF. Both the lists for participant and treatment allocation were inputted into the interactive web response system.

At the study site, participants were administered treatment based on the randomization code and the corresponding treatment group obtained from the interactive web response system. Blinding of participants and investigators was not possible in this study. However, during the data analysis, the statisticians remained blinded to the study groupings.

During the 16-weeks period, the intervention group followed a 5:2 intermittent fasting, they consumed low-energy meal on two non-consecutive days of the week and follow their habitual diet on the remaining five days. The control group took metformin (Shanghai Bristol-Myers Squibb) or Empagliflozin (Shanghai Boehringer Ingelheim) continue with their usual diabetes diet without fasting. Metformin administered 0.5g twice a day, up to 2g/d based on tolerance[4]. Empagliflozin administered 10 mg once a day[5]. All participants received dietary guidance from nutritionists[16].

Change in HbA_{1c} levels from baseline was the primary outcome and secondary included BMI, waist circumference, hip circumference, diastolic blood pressure, fasting plasma glucose (FPG) level, fasting insulin level, fasting C-peptide level, lipid profiles (total cholesterol, triglycerides, high-density lipoprotein cholesterol [HDL-C], and low-density lipoprotein cholesterol-levels), and uric acid levels.

Used analysis of covariance model (ANCOVA) to compare changes in HbA_{1c} and other outcomes between groups, adjusting for confounding variables. Intention-to-treat analysis would be followed to account for the primary outcome. Besides, we need to consider an dropout rate.

Practical Considerations

The research was approved by the ethics committees of all participating centres, followed the International Conference on Harmonization Guidelines for Good Clinical Practice and the Declaration of Helsinki and adhered to the Consolidated Standards of Reporting Trials reporting guideline[17]. And all participants written informed consent.

Due to some participants found it challenging to adhere to the fasting protocol, account for dropout rate by increasing the sample size.

Implications and contributions to knowledge

Expected Results

Over the 16-week intervention period, patients in the 5:2 IF group would achieve a reduction in HbA_{1c} level. It would be significantly greater than the reductions saw with metformin and empagliflozin.

The 5:2 IF would approach result in weight loss, experience a notable reduction in fasting plasma glucose levels. Improvements in lipid profiles would be also observed. The 5:2 IF would lead to reduction in triglyceride levels and an increase in high-density lipoprotein cholesterol, suggesting potential cardiovascular benefits.

The entire experiment would carry out safely, the adverse effects would have a low incidence. Some participants may experience hypoglycemia.

Practical Implications

By directly comparing the 5:2 intermittent fasting regimen to first-line pharmacological treatments, the study aims to provide robust evidence for integrating this dietary approach into clinical guidelines. Encourage healthcare providers to prioritize dietary interventions over medication for newly diagnosed patients.

Health organizations and policymakers could use this evidence to design public health strategies focused on non-pharmacological, cost-effective diabetes management, potentially reducing healthcare expenditures.

Theoretical Implications

It will contribute to the comprehensive understandings of intermittent fasting's metabolic and physiological effects, particularly its role in improving glycemic control. By challenging traditional opinions about T2DM treatment, this research will pave the way for future research exploring non-pharmacological interventions for chronic diseases.

Research schedule

Research phase	**Objectives**	**Deadline**
Preparation	Abtain ethical approval and recruit participants.	15th July
Intervention	Implement the 16-week intervention and collect data.	6th August
Analysis	Perform statistical analysis.	7th September
Report Writing	Discussion and write paper.	30th September

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