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The Impact of Time-Restricted Eating and Intermittent Fasting on Glycemia, Body Weight, and Overall Well-Being in Patients with Type 2 Diabetes – A Review of Studies

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Abstract

Introduction

Intermittent fasting is becoming increasingly popular, particularly among individuals with obesity. One variation of this approach is time-restricted eating (TRE), which involves consuming meals only during a specific time window, typically lasting between eight to twelve hours each day.

Aim Of The Study

The objective of this article was to analyze studies conducted on both animal and human models. This analysis enabled a presentation of the benefits and potential risks associated with time-restricted eating in the context of type 2 diabetes.

Materials and Methods

In the study, scientific articles retrieved from the PubMed and Google Scholar databases were used, utilizing keywords such as "intermittent fasting and type 2 diabetes," "intermittent fasting and glycemia," "metabolic effects of fasting," and "intermittent fasting in animals,". Articles in languages other than English were excluded.

Summary

Various fasting types led to reduced HbA1c, weight loss, and improved well-being in experimental groups. Researchers emphasize the need for further trials involving larger groups and longer observation periods to objectively assess the long-term effects of TRE on T2D. Establishing these findings is essential to maximizing the benefits of fasting while minimizing the risk of hypoglycemia. If practiced cautiously under medical supervision, intermittent fasting

could serve as an effective and safe method for managing type 2 diabetes. Adjusting medication, monitoring glucose, and staying hydrated are crucial to minimizing hypoglycemia risk.

Keywords

time-restricted eating (TRE), intermittent fasting (IF), type 2 diabetes, hypoglycemia, body weight, glycated hemoglobin (HbA1c), well-being

Introduction

Type 2 diabetes (T2DM) is a metabolic disorder characterized by persistently high blood sugar levels, which can lead to various complications, potentially damaging organs and systems and increasing morbidity and mortality rates. The primary cause of T2DM is insulin resistance, particularly in the liver, skeletal muscles, and adipose (fat) tissue. Many individuals with type 2 diabetes also experience obesity, which further exacerbates insulin resistance in these tissues (1). One therapeutic approach that may help reduce body weight while maintaining normal glucose levels is time-restricted eating (TRE). This approach involves consuming meals within a specific time window, typically lasting 8 to 12 hours per day. Other popular forms of intermittent fasting (IF) include the 5:2 diet, early morning meal restriction, and the B2 regimen. The risk of hypoglycemic episodes may present an obstacle to the use of this method. However, in recent years, various forms of intermittent fasting (IF) have gained popularity, especially among individuals struggling with obesity.

Metabolic Effects of Fasting

Fasting, as a physiological state, induces numerous metabolic and hormonal adaptations that allow the body to survive in conditions of food scarcity. The first stage involves the use of glycogen reserves in the liver, which provide glucose for most tissues, including neurons. Once glycogen stores are depleted, the body shifts to burning fat, with lipolysis releasing free fatty acids, which are then converted into ketone bodies in the liver. Ketone bodies become the primary energy source for the brain, replacing glucose (2).

During fasting, there is a decrease in insulin and leptin levels, which helps mobilize fats and reduces glucose utilization by muscles. At the same time, levels of glucagon and growth hormone increase, supporting gluconeogenesis and lipolysis (3). Activation of AMPK (AMP-activated protein kinase) plays a key role in regulating cellular metabolism, particularly under nutrient deficiency. The inhibition of the mTOR (mechanistic target of rapamycin) pathway and the control of autophagy are the primary adaptive mechanisms that allow the body to maintain

energetic homeostasis (4),(5). Studies have shown there is also an increase in the levels of insulin-like growth factor binding protein (IGFBP), along with a decrease in the levels of IGF-1, amino acids, insulin, and glucose. It may effectively inhibit the growth of cancer cells while promoting the health of normal tissues (6). Additionally, the liver plays a key role in the adaptation to starvation, by increasing gluconeogenesis and ketogenesis activity. It ensures a stable energy level (7). In adipose tissue, there is a reduction in the activity of anabolic pathways, which leads to lipid mobilization and contributes to fat loss (8). Protective effects of fasting include reduced oxidative stress, decreased inflammation, activation of repair processes, and increased energy efficiency, which may contribute to slowing aging processes (9). Intermittent fasting may also affect cognitive function. Type 2 diabetes leads to cognitive dysfunction, and IF may help enhance the activity of signaling pathways related to neuroplasticity, improving memory and other cognitive functions. Intermittent fasting (IF) affects the increased expression of genes related to energy metabolism in the hippocampus, which may also translate into improvements in these processes (10), (11).

Numerous studies have used various types of fasting in animals. McCay's work in 1935 demonstrated that reducing food intake in rats was associated with lower rates of chronic diseases and increased lifespan (12). In studies involving diabetic mice, caloric restriction (CR) helped restore damaged beta cells in pancreatic islets, which may explain its beneficial effects on glycemic control. A reduction in triglyceride concentrations have also been observed. Other studies confirmed (13). Three weeks of caloric restriction (CR) improved glucose tolerance by lowering plasma glucose levels, as assessed during the oral glucose tolerance test (OGTT). Caloric restriction also increased the level of GLUT-4 protein in adipose tissue, which may have contributed to the improvement in glucose tolerance. Additionally, the use of time-restricted eating (TRE) reduced adipose tissue mass (14). Two other studies, one conducted at the Wisconsin National Primate Research Center (WNPRC) and the other at the National Institute on Aging (NIA), examined the impact of caloric restriction (CR) on the health and lifespan of rhesus monkeys. Both studies showed some health benefits of CR, but presented conflicting results regarding its effect on lifespan. The results from the University of Wisconsin study indicate that caloric restriction delayed the onset of age-related diseases such as diabetes, cancer, and cardiovascular diseases, as well as slowing brain atrophy and increasing survival rates (15). The NIA study, however, found that CR started at an older age (16-23 years) did not increase survival compared to the control group (16).

Research on mice showed that intermittent fasting (IF) alleviated diabetic retinopathy by lowering TNF-α mRNA levels in the retina and provided retinal protection by activating bile acid–activated G-protein coupled receptors, preventing the development of retinopathy (17).

Literature Review

Article C. Li et al.(18) presents the findings of a pilot randomized trial that evaluated the impact of a one-week fasting therapy on individuals with type 2 diabetes (T2D) and metabolic syndrome. The aim of the study was to determine whether this fasting approach could provide medium-term metabolic and clinical benefits compared to the standard medical care that primarily relies on pharmacotherapy. The trial included 46 participants, aged 25 to 75 years, who met the criteria for metabolic syndrome. They were randomly assigned to two groups. The experimental group underwent a one-week energy-restricted fast (300 kcal/day) based on the Buchinger method, which included two preparation days and a gradual reintroduction of solid foods afterwards. During the fasting period, participants were also advised to follow a Mediterranean diet. The control group only received recommendations for the Mediterranean diet. The intervention lasted one week, followed by a four-month follow-up period. Results showed that the fasting intervention led to a significant reduction in body weight (an average of −3.5 kg compared to −2.0 kg in the control group; $p = 0.03$) and waist circumference (−4.4 cm compared to −0.3 cm; $p = 0.001$). Furthermore, the fasting group experienced a notable decrease in blood pressure: systolic pressure decreased by −13.9 mmHg (compared to +0.4 mmHg in the control group; $p = 0.01$), and diastolic pressure decreased by −9.0 mmHg (compared to +3.2 mmHg; $p = 0.003$). The quality of life also improved in the fasting group, as measured by the WHO-5 index ($p = 0.04$). Although there were slight improvements in metabolic parameters such as HbA1c, insulin resistance (HOMA-IR), and lipid profiles, these differences were not statistically significant compared to the control group. The study concluded that one-week fasting therapy is safe and well-tolerated. No severe side effects were reported, and participants did not experience severe hunger. Three participants in the fasting group reported mild headaches during the first few days of fasting, and one participant experienced mild dizziness later on. Overall, hunger was not intensely felt by all participants.

The study by Corley et al. (19) aimed to assess whether the risk of hypoglycemia is higher when following two consecutive days of very low-calorie diet compared to two non-consecutive days of the same diet in individuals with T2D. The study included 41 adults with a BMI of 30–45 kg/m², treated with metformin and/or hypoglycemic medications, and HbA1c levels ranging from 50 to 86 mmol/mol (6.7%–10%). Participants were randomly assigned to one of two

groups following a diet of 2092–2510 kJ over two consecutive or non-consecutive days per week for 12 weeks. The study observed a difference in the incidence of hypoglycemia between the two groups. It also assessed changes in diet, quality of life, body weight, lipid levels, glucose, HbA1c, and liver function. The results indicated that fasting increased the risk of hypoglycemia, despite reduced medication dosages (hazard ratio 2.05, 95% CI 1.17 to 3.52). There was no significant difference between consecutive and non-consecutive fasting (hazard ratio 1.54, 95% CI 0.35 to 6.11). Participants in both groups showed improvements in body weight, HbA1c, fasting glucose, and quality of life.

The study by E. B. Parr et al. (20) aimed to evaluate the feasibility of time-restricted eating (TRE) for individuals with type 2 diabetes (T2D) and to assess its effects on dietary changes, blood sugar levels, cognitive functions, and mental well-being. Nineteen participants (mean ± SD; age: 50 ± 9 years, BMI: 34 ± 5 kg/m², HbA1c: 7.6 ± 1.1%) completed a six-week intervention in which they followed a daily eating window from 10:00 AM to 7:00 PM for approximately five days a week. The researchers found that total energy intake, macronutrient distribution, and the number of meals consumed did not significantly change during the four weeks of TRE. Participants reported adhering to the diet 43% of the time, indicating a degree of non-compliance. This suggests that prior studies employing self-reporting methods might have overestimated adherence to the diet. TRE was associated with a reduction in total reported energy intake of about 1000 kJ/day (approximately 11%). On days when all meals were consumed within the designated window, there was a decrease in carbohydrate and alcohol intake. Overall adherence to TRE correlated with lower carbohydrate consumption, indicating that TRE could help reduce the consumption of additional "daytime snacks" (such as ice cream, chocolate, and alcohol) and lead to a lower total energy intake. Most non-adherence occurred on weekends, primarily due to social events. On non-diet days, participants generally achieved their total daily energy intake in about 11 hours, compared to roughly 8.5 hours during TRE. Energy intake after 7:00 PM accounted for the majority of non-compliance cases (63%). There was a slight but non-significant improvement in HbA1c levels (-0.2 ± 0.4%; $p = 0.053$) and a decrease in the total glucose area under the curve (AUC) following the oral glucose tolerance test ($p = 0.056$). However, the change in HbA1c was less than the clinically significant threshold of -0.5% HbA1c. The intervention lasted only one month, which is shorter than the three months typically required to observe significant HbA1c improvements. Notably, TRE did not worsen glycemic control, even with the same energy intake during a shorter eating window. No clinically significant changes were found in depression, anxiety, eating behavior, sleep quality, or overall quality of life ($p > 0.05$ for all measures). The lack of change in mental well-being

markers indicates that TRE did not negatively impact these outcomes. The researchers noted statistically significant improvements in executive functions ($p = 0.004$) but also a deterioration in processing speed ($p = 0.02$), which was unexpected. Previous studies indicated that short periods of fasting do not typically affect processing speed, and no significant changes were observed in attention, visual learning, or working memory. After completing the four-week TRE intervention, qualitative interviews were conducted with participants using 13 open-ended questions. Participants reported challenges with morning or evening schedules, particularly related to "hunger," "missing morning coffee," and having to eat before 7:00 PM, which conflicted with family, social, or professional commitments. Some participants experienced hunger or anxiety about hunger, while others felt less hungry than anticipated. A few found that TRE helped eliminate nighttime eating, while others struggled to avoid nighttime snacks due to negative emotions such as stress or boredom. Additionally, some participants noted that TRE encouraged healthier and more balanced meal planning, while others resorted to pre-packaged or "junk" food due to inadequate meal planning. Participants expressed both positive and negative emotional responses to TRE; some appreciated the structure and routine, while others felt stress or anxiety trying to adhere to it. They emphasized that increased self-control heightened their awareness and responsibility for healthier eating. In conclusion, a four-week, nine-hour TRE regimen is feasible and achievable for individuals with T2D, with adherence significantly influencing daily energy intake.

The article by Obermayer et al. (21) evaluated the safety and effectiveness of intermittent fasting (IF) in patients with insulin-treated Type 2 Diabetes (T2D). The study involved 46 participants who were randomly assigned to one of two groups: an IF group ($n = 22$) that practiced fasting three days per week by consuming only 25% of their daily caloric intake on fasting days, and a control group ($n = 24$) that continued with standard care. All participants were placed on the same insulin regimen, specifically insulin glargine, and utilized continuous glucose monitoring with FreeStyle Libre. After a 12-week period, the IF group showed a significant reduction in HbA1c levels, with a decrease of 7.3 ± 12.0 mmol/mol, while the control group experienced a slight increase of 0.1 ± 6.1 mmol/mol ($p = 0.012$). Additionally, the average daily insulin dose decreased by 9 ± 10 IU in the IF group, whereas it increased by 4 ± 10 IU in the control group ($p = 0.008$). The IF group also experienced significant weight loss, averaging -4.77 ± 4.99 kg, in contrast to the control group, which gained an average of $+10.27 \pm 1.34$ kg ($p < 0.001$). Importantly, there were no instances of severe hypoglycemia, and all serious adverse events leading to hospitalization were not related to the fasting intervention. Furthermore, an improvement in the quality of life was reported in the IF group ($p = 0.043$).

The study conducted by Carter et al.(22) and published in JAMA Network Open in 2018, aimed to compare the effects of intermittent calorie restriction (CR) with continuous energy restriction on glycemic control and weight loss in patients with type 2 diabetes over a 12-month period. A total of 137 adults with type 2 diabetes were randomly assigned to one of two groups: the intermittent energy restriction (IER) group or the continuous energy restriction (CER) group. The IER group followed a diet of 500-600 kcal/day for 2 days each week and consumed a normal diet for the remaining 5 days. In contrast, the CER group adhered to a diet of 1200-1500 kcal/day for all 7 days of the week. The results showed that both the IER and CER groups experienced similar reductions in HbA1c levels after 12 months. The average change in HbA1c was -0.3% (SEM [0.1%]) for the IER group and -0.5% (SEM [0.2%]) for the CER group, with a difference of 0.2%, which fell within the equivalence margin of ±0.5%. Although both groups lost weight, the difference was not statistically significant; the average change in body weight was -6.8 kg for the IER group and -5.0 kg for the CER group, resulting in a difference of -1.8 kg, which did not fall within the equivalence margin of ±2.5 kg. No significant differences were observed between the groups concerning step count, fasting glucose levels, lipid levels, or the overall treatment effect score after 12 months. It was noted that 35% of participants using sulfonylureas and/or insulin experienced hypoglycemic or hyperglycemic events within the first two weeks of treatment.

Study	**Type of Intervention**	**Body Weight Reduction**	**Effect on HbA1c**	**Well-being/ Quality of Life**
Li et al. (2017)	Weekly fasting (Buchinger)	−3.5 kg (vs −2.0 kg in the control group, p = 0.03)	Trend toward improvement, no statistical significance	Improvement (p = 0.04)
Corley et al. (2018)	VLCD for 2 days a week	Weight loss in both groups (no significant differences)	Decrease in HbA1c in both groups without statistical differences	Improvement in both groups

Parr et al. (2020)	TRE (Nutrients)	No significant changes	HbA1c decreased by −0.2% (p = 0.053)	No significant changes
Obermayer et al. (2022)	IF (INTERFAST-2)	−4.77 kg (vs +1.34 kg in the control group, p < 0.001)	HbA1c decreased by −7.3 mmol/mol (p = 0.012)	Improvement (p = 0.043)
Carter et al. (2018)	IER (500–600 kcal/day for 2 days/week) vs CER (1200–1500 kcal/day for 7 days/week)	−6.8 kg (IER) vs −5.0 kg (CER), difference −1.8 kg (not statistically significant)	HbA1c: −0.3% (IER) vs −0.5% (CER), difference 0.2% (equivalence ±0.5%)	No data

Table 1. Summary of key results from cited randomized controlled trials

Discussion

Intermittent fasting (IF), particularly time-restricted eating (TRE), triggers various metabolic and hormonal changes that can benefit the body. Notable adaptations include a shift towards fat burning, increased insulin sensitivity, activation of cellular repair processes (such as autophagy), and reductions in oxidative stress and inflammation. Animal studies, particularly those involving mice, have shown that TRE can enhance glucose control, improve glucose tolerance, increase insulin sensitivity, and even promote the regeneration of beta cells in the pancreas. The impact of IF on glucose control appears to depend on the specific protocol used and the individual characteristics of the patient. The clinical trials reviewed included groups that varied in size from 19 to 137 participants, and the duration of interventions ranged from 4 to 48 weeks, with one study observing outcomes over 12 months. A study by C. Li et al. suggests that fasting therapy may effectively complement type 2 diabetes (T2D) treatment, especially in terms of weight reduction, waist circumference, blood pressure control, and improved quality of life. However, the authors noted several limitations, including a small sample size and the lack of health parameter measurements immediately after fasting. Differences in baseline characteristics between groups, such as fasting glucose levels or insulin resistance, may have

influenced the results. The authors call for future research with larger sample sizes and longer follow-up periods to better evaluate the effectiveness of combining prolonged fasting with intermittent fasting for more lasting effects. The study conducted by Corley et al. concluded that fasting, whether done on consecutive or non-consecutive days, increased the frequency of hypoglycemia in individuals with T2D who were on hypoglycemic medications. However, due to education and medication dose reductions, fewer hypoglycemic events occurred than expected. This study is one of the few to address the risk of excessively lowering blood sugar in individuals with T2D on intermittent calorie-restricted diets. It found a low risk of hypoglycemia when participants received weekly medical supervision, hypoglycemia education, and medication dose adjustments. The study by E.B. Parr suggests that a four-week, nine-hour TRE regimen is feasible and achievable for individuals with T2D. Given the relationship between food intake, effective diabetes management, and psychological and cognitive factors, future studies should continue to explore the effectiveness of TRE as a dietary strategy for T2D, particularly regarding psychological and cognitive outcomes. Future interventions should also assess TRE's potential for facilitating dietary changes and ensuring long-term adherence among individuals with T2D or those at risk of developing it. The study by Obermayer et al. shows that intermittent fasting three days a week can effectively enhance glycemic control, facilitate weight loss, and reduce insulin requirements in individuals with T2D, all while maintaining safety. One advantage of IF is its potential for easier adherence, as it does not require continuous calorie restriction. However, the study had limitations, including allowing participants to consume up to 25% of their daily caloric intake on fasting days, which may have influenced the results. Strengths of the study included its randomized controlled design, incorporation of intermittent scanning continuous glucose monitoring (isCGM), and metabolomic analysis. Future research with longer observation periods is needed to evaluate the long-term effects of intermittent fasting and to explore different types of fasting in this patient population. The results of the study by Carter et al. suggest that intermittent energy restriction is an effective dietary strategy for lowering HbA1c levels in patients with T2D and is comparable to continuous energy restriction. While intermittent energy restriction may offer advantages in terms of weight loss, further studies involving a larger number of participants are needed to confirm these findings. Overall, intermittent energy restriction appears to be generally acceptable for most patients with T2D. However, for patients using sulfonylureas and/or insulin, regular glucose monitoring is essential. Several limitations of the study were noted, including that participants had relatively well-controlled T2D, which may limit the generalizability of the results. Additionally, changes in medication could have influenced HbA1c level changes.

Participants also had more frequent contact with dietitians than is typical in clinical practice, potentially affecting the study results. Moreover, fingerstick blood glucose monitoring was the only method used to monitor glucose levels, which could have led to undetected hypoglycemic and hyperglycemic events.

Conclusion

Intermittent fasting (IF) has gained popularity as a flexible alternative to traditional dieting. Research indicates that IF can effectively reduce body weight, improve glucose control, and lower HbA1c levels. This dietary approach may also lead to a decrease in total daily calorie intake due to the limited eating window and increased sensitivity to satiety signals. Additionally, IF induces periods of energy deficit, positively influencing metabolic processes such as autophagy, which could help protect pancreatic beta cells. However, one significant challenge of IF is the heightened risk of hypoglycemia for individuals using insulin or other hypoglycemic medications. Therefore, implementing IF requires strict medical supervision and potential adjustments to medication dosages. Time-restricted eating (TRE) is another promising strategy that aligns calorie intake with the body's circadian rhythm. Research suggests that consuming meals earlier in the day can enhance insulin sensitivity, improve glucose tolerance, and promote weight loss. TRE may be particularly beneficial for individuals who find traditional low-calorie diets or more restrictive fasting difficult to maintain. Nonetheless, the short-term effects of TRE may not be as pronounced as those of continuous calorie restriction (CR) or IF, indicating that longer observation periods are necessary to fully assess its benefits. Despite encouraging findings, several limitations in the studies must be acknowledged. Many studies had small sample sizes and brief durations, making it challenging to generalize the results to larger populations. Additionally, the diversity in methodologies, including varying definitions of fasting protocols, complicates direct comparisons between studies. A critical challenge remains in identifying which patient groups will benefit most from each intervention and determining the best way to combine these approaches with other treatments, such as medication or physical activity. In clinical practice, it is essential to individualize therapy and prioritize patient education. While IF and TRE may provide alternatives for those struggling with conventional diets, not all fasting approaches will be suitable for every patient. For instance, individuals with type 2 diabetes who are on insulin must be cautious of the risk of hypoglycemia during fasting, necessitating close glucose monitoring and careful medication adjustments. Furthermore, the impact of these strategies on quality of life is a crucial consideration, as prolonged dietary restrictions may lead to fatigue or dissatisfaction, adversely affecting adherence to the regimen.

While therapies involving TRE or IF show great promise in managing type 2 diabetes more effectively, further high-quality research is needed to fully understand their mechanisms and broaden their clinical application.

Disclosure

Author's contribution

Conceptualization: Szymon Przemysław Stolarczyk and Borys Kuba Romańczuk; Methodology: Katarzyna Kamińska – Omasta; Software: Olga Krupa; Check: Daria Rybak and Kinga Furtak; Formal analysis: Magdalena Agata Czerska and Bartosz Omasta; Investigation: Zofia Wójcik and Paulina Dorota Pietrukaniec; Resources: Katarzyna Kamińska-Omasta and Zofia Wójcik; Data curation: Bartosz Omasta; Writing -through preparation: Szymon Przemysław Stolarczyk; Writing -review and editing: Olga Krupa and Kuba Borys Romańczuk; Visualization: Daria Rybak and Magdalena Agata Czerska; Supervision: Paulina Dorota Pietrukaniec; Project administration: Bartosz Omasta and Kinga Furtak; Receiving funding -no specific funding. All authors have read and agreed with the published version of the manuscript.

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Conflict of interest

The authors deny any conflict of interest.

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