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Impact of Intermittent Fasting on Type 1 Diabetes: A Systematic Review.

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ABSTRACT

Intermittent fasting (IF) has gained popularity as a potential therapeutic approach for various health conditions, including diabetes. While its effects on type 2 diabetes have been extensively studied, the impact on type 1 diabetes (T1D) remains less clear. This systematic review aims to evaluate the current evidence on the effects of intermittent fasting in individuals with T1D, focusing on glycemic control, metabolic parameters, and safety considerations. We analyzed studies from 2000 to 2024, including various fasting regimens such as Ramadan fasting, time-restricted eating, and prolonged fasting protocols. The review reveals mixed results, with some studies showing potential benefits in glycemic control and metabolic parameters, while others highlight risks such as hypoglycemia and diabetic ketoacidosis. The findings underscore the need for individualized approaches and close medical supervision when implementing intermittent fasting in T1D management.

Keywords: Type 1 diabetes, fasting interventions, intermittent fasting, time-restricted fasting, periodic fasting, Ramadan fasting, CGM (Continuous Glucose Monitoring).

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INTRODUCTION

Type 1 Diabetes: Pathophysiology and Management

Type 1 diabetes (T1D) is an autoimmune condition characterized by the destruction of pancreatic beta cells, leading to insulin deficiency and lifelong dependence on exogenous insulin [1]. Management of T1D requires a delicate balance of insulin administration, dietary intake, and physical activity to maintain optimal glycemic control and prevent both short-term and long-term complications [2].

In recent years, intermittent fasting (IF) has emerged as a popular dietary approach with potential health benefits, including improved insulin sensitivity, weight loss, and metabolic health [3]. While the effects of IF on type 2 diabetes have been extensively studied, its impact on T1D management remains a subject of ongoing research and debate [4].

Intermittent Fasting: Concepts and Methods

Intermittent fasting is an eating pattern that cycles between periods of fasting and eating. It doesn't specify which foods to eat but rather when to eat them. There are several different IF methods, including:

- Time-restricted eating: Limiting daily food intake to a specific time window, typically 8-12 hours.
- Alternate-day fasting: Alternating between "fasting" days (consuming 25% of normal caloric intake) and regular eating days.
- 5:2 diet: Eating normally for five days of the week and restricting calorie intake to 500-600 calories on the other two non-consecutive days.
- Periodic fasting: Fasting for 24 hours or more, typically done once or twice a month.
- Ramadan fasting: Abstaining from food and drink from dawn to sunset for approximately 29-30 days.

Mechanisms providing benefits in Intermittent fasting[Figure 1].



Figure 1: Mechanisms by which Intermittent fasting provides benefits in Type1 Diabetes

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Metabolic switching: The transition from using glucose as the primary energy source to using ketones derived from fat[5].

Autophagy: A cellular "cleaning" process that removes damaged components and may improve cellular function[6].

Hormonal changes: Alterations in growth hormone, insulin, and norepinephrine levels that may promote fat burning and cellular repair.

Reduction in oxidative stress and inflammation: Which may contribute to various health benefits [7,8,9].

Circadian rhythm alignment: Time-restricted eating, a form of IF, may help align food intake with circadian rhythms, potentially improving metabolic health [5].

Gut microbiome modulation: Although not specifically studied in T1D, IF has been shown to impact the gut microbiome, which may indirectly influence glucose metabolism and inflammation.

This systematic review aims to comprehensively evaluate the current evidence on the effects of intermittent fasting in individuals with T1D. We will examine various fasting regimens, including religious fasting (e.g., Ramadan), time-restricted eating, and other forms of IF, to assess their impact on glycemic control, metabolic parameters, and overall safety in the T1D population.

METHODOLOGY

Search Strategy

To ensure the authenticity, we registered our review in PROSPERO (CRD42024564330).We conducted a comprehensive literature search using PubMed, MEDLINE, Cochrane Library, and Google Scholar databases. The search terms included combinations of "type 1 diabetes," "intermittent fasting," "Ramadan fasting," "time-restricted eating," "prolonged fasting," "glycemic control," and "metabolic effects." We included studies published between 2000 and 2024 to capture the most recent and relevant research.

Inclusion Criteria

- Studies involving participants with diagnosed T1D
- Interventional studies, observational studies, and case reports on intermittent fasting in T1D
- Studies reporting outcomes related to glycemic control, metabolic parameters, or safety
- Full-text articles available in English

Exclusion Criteria

- Studies focusing exclusively on type 2 diabetes or gestational diabetes
- Review articles without original data
- Studies with insufficient data on fasting protocols or outcomes

Data Extraction

We extracted the following information from each included study: author(s), year of publication, study design, sample size, fasting regimen, duration of intervention, outcomes measured, and key findings.

RESULTS

Overview of Included Studies

Our search identified 15 relevant studies that met the inclusion criteria. These studies encompassed a range of fasting protocols, including Ramadan fasting (n=10), other forms of intermittent fasting (n=3), and prolonged fasting (n=2). The studies varied in design, including randomized controlled trials, observational studies, and case reports[Table 1].

Table1: Chronological Overview of Studies on Intermittent Fasting in Type 1 Diabetes and Related Metabolic Effects

Author (Year)	Sample size	Fasting regimen	Results	
Kadiri et al. (2001) [13]	n=64	Ramadan fasting	↓hypoglycemia using insulin lispro	
Salti et al.(2004) [10]	n=11,173	Ramadan fasting	holistic reported hypoglycemia (0.14	
			episodes/Ramadan vs. 0.03 episodes/other	
			months)	



Reiter et al. (2007) [26]	n=43	prolonged fasting (>25 h)	↓insulin dosage, ↑HbA1c	
Al-Khawari et al. (2010) [14]	n=28	Ramadan fasting	Can fast during Ramadan with proper precautions ↓dose of basal insulin by 10-20%	
Khalil et al. (2012) [15]	n=21	Ramadan fasting	Studied role of insulin pump therapy accompanying CGM and dose adjustment during fasting	
El-Hawary et al. (2016) [6]	n=53 (children)	Ramadan fasting	↓fructosamine, ↑Total cholesterol and LDL, ↓HbA1c	
Alfadhli (2018) [24]	n=22	Ramadan fasting	Higher rate of hyperglycemia than hypoglycemia during fasting in patients with uncontrolled T1D	
Al-Ozairi et al. (2019) [11]	n=43	Ramadan fasting	↓hypoglycemia	
Mohamed et al. (2019) [35]	n=50	Ramadan fasting	Fasting on 20 ± 9.9 days in Ramadan (7.8% broke the fast due to mild hypoglycemia)	
Fernández-Cardona et al. (2020) [25]	Case report (n=1)	IF with ketogenic diet for 9d	IF triggered ketoacidosis in a patient with stable, long-term T1D	
Hassanein et al. (2020) [23]	n(<18 y)=370 n=279(fasted) n(>18y)=1113 n=761(fasted)	Ramadan fasting	holistic reported hypoglycemia (60.7%) holistic reported hyperglycemia (44.8%)	
Bartholomew et al. (2021) [21]	n=103	Twice per week for first 4 weeks followed by once per week for 22 weeks	↓HOMA-IR (homeostatic model assessment of insulin resistance) ↓MSS (Metabolic Syndrome Score)	
Moser et al. (2021) [20]	n=20	(a) overnight fasting—12 h fasting (b) prolonged fasting—36 h fasting	↑Fat oxidation, ↓carbohydrate oxidation, ↓BMI ↓rate of hypoglycemia	
Berger et. al.(2021)[22]	n=20	7 days fasting	↓Body weight , ↓BMI, ↓LDL/HDL ratio	
Elbarbary and Ismail (2022) [12]	n=42	Ramadan fasting	↓hypoglycemia using Advanced hybrid closed loop system	

HbA1c: Glycosylated Hemoglobin, CGM: Continuous glucose monitoring, T1D: Type1 Diabetes, LDL: Low density lipoprotein, HDL: High density lipoprotein, BMI: Body mass index

Ramadan Fasting and Type 1 Diabetes

Ramadan fasting, which involves abstaining from food and drink from dawn to sunset for approximately 29-30 days, has been the most extensively studied form of intermittent fasting in T1D. Several studies have examined its effects on glycemic control and metabolic parameters:

Glycemic Control

Salti et al. conducted a large population-based study on diabetes management during Ramadan, including individuals with T1D. They reported an increased frequency of severe hypoglycemia during Ramadan compared to other months (0.14 vs. 0.03 episodes/month) [10]. However, more recent studies have shown improved outcomes with proper management strategies: Al-Ozairi et al. demonstrated that intermittent fasting could be safely achieved in people with T1D undergoing structured education and advanced glucose monitoring, with a reduction in hypoglycemic events [11]. Elbarbary and Ismail conducted a randomized controlled trial using advanced hybrid closed-loop insulin delivery systems during Ramadan fasting, showing a significant reduction in hypoglycemia compared to conventional insulin therapy [12].

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Metabolic Parameters

El-Hawary et al. studied the effects of Ramadan fasting in children with T1D and observed a decrease in fructosamine levels and HbA1c, but an increase in total cholesterol and LDL cholesterol [6]. These findings suggest potential improvements in short-term glycemic control but highlight the need for monitoring lipid profiles during fasting periods.

Insulin Management

Several studies have addressed insulin management strategies during Ramadan fasting: Kadiri et al. reported a reduction in hypoglycemia when using rapid-acting insulin analogs (insulin lispro) compared to regular human insulin during Ramadan fasting [13]. Al-Khawari et al. found that adolescents on basal-bolus insulin regimens could safely fast during Ramadan with proper precautions, including a 10-20% reduction in basal insulin doses [14]. Khalil et al. investigated the use of insulin pump therapy with continuous glucose monitoring (CGM) during Ramadan, demonstrating the potential for improved glycemic control with technological advancements [15].

Risk Stratification

Proper risk assessment is crucial when considering IF for T1D patients. Hussain et al. suggested rethinking the classification of risk for T1D patients fasting during Ramadan [16]. Ali et al. provided guidelines for managing diabetes during Ramadan [17]. Deeb et al. provided ISPAD Clinical Practice Consensus Guidelines for fasting during Ramadan by young people with diabetes [18], emphasizing the importance of age-specific considerations in risk assessment. Loh et al. conducted a systematic review and meta-analysis on the safety of Ramadan fasting in young patients with T1D [19].

Other Forms of Intermittent Fasting in Type 1 Diabetes

Time-Restricted Eating

Moser et al. conducted a crossover-controlled trial comparing the effects of overnight fasting (12 hours) and prolonged fasting (36 hours) in 20 adults with T1D. They observed: (a) Increased fat oxidation and decreased carbohydrate oxidation during fasting periods (b) Reduced BMI (c) Lower rates of hypoglycemia during fasting periods [20]. These findings suggest that short-term fasting may have metabolic benefits and potentially reduce hypoglycemia risk in some individuals with T1D.

Weekly Intermittent Fasting

Bartholomew et al. investigated the effects of once-weekly intermittent fasting in a mixed population that included individuals with T1D. Their findings showed improvements in insulin resistance (measured by HOMA-IR) and metabolic syndrome scores, suggesting potential metabolic benefits of regular, short-term fasting [21].

Prolonged Fasting

Berger et al. conducted a pilot study on 7-days fasting (Buchinger fasting) as a multimodal intervention for adults with T1D. They reported (a) decreased body weight and BMI (b) improved LDL/HDL cholesterol ratio (c) no severe adverse events during the supervised fasting period [22]. However, the authors emphasized the need for close medical supervision and individualized approaches when implementing prolonged fasting in T1D.

Safety Considerations and Adverse Events

While many studies have demonstrated the potential for safe implementation of intermittent fasting in T1D with proper management, several important safety considerations have been identified:

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Hypoglycemia

The risk of hypoglycemia remains a primary concern in IF for T1D. Hassanein et al. reported that 60.7% of individuals with T1D who fasted during Ramadan experienced hypoglycemia [23]. However, studies using advanced insulin delivery systems and CGM have shown promising results in reducing this risk [12].

Hyperglycemia and Diabetic Ketoacidosis (DKA)

Alfadhli observed a higher rate of hyperglycemia than hypoglycemia during Ramadan fasting in patients with uncontrolled T1D [24]. Additionally, Fernández-Cardona et al. reported a case of DKA triggered by intermittent fasting combined with a ketogenic diet in a patient with previously stable T1D, highlighting the potential risks of extreme dietary approaches [25].

Long-term Metabolic Effects

Reiter et al. studied the effects of prolonged fasting (>25 hours) in individuals with T1D and observed a decrease in insulin dosage but an increase in HbA1c levels [26]. This underscores the need for careful monitoring of long-term glycemic control when implementing fasting regimens.

DISCUSSION

Potential Benefits of Intermittent Fasting in T1D

The reviewed studies suggest several potential benefits of intermittent fasting for individuals with T1D:

- **Improved insulin sensitivity:** Some studies have shown reduced insulin requirements during fasting periods, which may indicate improved insulin sensitivity [14].
- **Metabolic improvements**: Several studies reported positive changes in lipid profiles, body weight, and metabolic syndrome scores [4,6,21,22,27,28,29].
- **Enhanced glucose variability:** With proper management and advanced technologies, some individuals experienced improved glucose stability during fasting periods [11, 12].
- **Potential cognitive benefits:** Xiong et al. suggested that intermittent fasting might alleviate T1D-induced cognitive dysfunction by improving frontal cortical metabolic disorders, although more research is needed in this area [30].
- **Anti-inflammatory effect:** IF diets could reduce plasma concentrations of inflammatory biomarkers [31], which may have anti-inflammatory effects contributing to improved cardiovascular health in T1D.
- **Effect on autoimmunity:** IF might have promising effects on autoimmune diseases, although specific evidence for T1D is limited [32]. While the autoimmune destruction of beta cells is typically complete by the time of T1D diagnosis, the modulation of the immune system through IF could have implications for overall health and potentially for emerging immunotherapies in T1D [33].

Challenges and Risks

Despite the potential benefits, several challenges and risks associated with intermittent fasting in T1D have been identified:

- **Hypoglycemia risk:** This remains a significant concern, particularly during prolonged fasting periods or in individuals with poor glycemic control [10,23].
- **Hyperglycemia and DKA:** The risk of hyperglycemia and ketoacidosis, especially with extreme fasting approaches, highlights the need for careful monitoring and education [24, 25].
- **Long-term glycemic control:** Some studies have reported increases in HbA1c levels with prolonged fasting, emphasizing the importance of regular monitoring of long-term glycemic markers [26].
- **Individual variability:** The reviewed studies demonstrate significant variability in responses to fasting among individuals with T1D, underscoring the need for personalized approaches.

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Management Strategies

Based on the reviewed literature, several management strategies have emerged as crucial for the safe implementation of intermittent fasting in T1D

- **Structured education:** Comprehensive diabetes education, including carbohydrate counting and insulin adjustment techniques, is essential for successful fasting [11].
- Advanced glucose monitoring: The use of continuous glucose monitoring systems has shown promise in reducing the risk of hypoglycemia during fasting periods [12].
- **Insulin regimen adjustments:** Tailoring insulin doses, particularly basal insulin reductions and the use of rapid-acting analogs, can improve glycemic control during fasting [13,14].
- **Individualized approaches:** Given the variability in responses to fasting, personalized strategies based on an individual's glycemic patterns, lifestyle, and preferences are crucial [29,34].
- **Medical supervision:** Close monitoring by healthcare providers, especially during initial fasting attempts or prolonged fasting periods, is essential for safety [22,35].

Future Research Directions

While the current body of literature provides valuable insights into the effects of intermittent fasting in T1D, several areas require further investigation:

- **Long-term studies:** Most existing studies focus on short-term outcomes. Longer-term studies are needed to assess the sustained effects of intermittent fasting on glycemic control, metabolic parameters, and diabetes-related complications in T1D.
- **Optimal fasting protocols:** Research is needed to determine the most effective and safe fasting regimens for individuals with T1D, considering factors such as duration, frequency, and timing of fasting periods.
- **Technology integration:** Further exploration of how advanced diabetes technologies (e.g., closed-loop insulin delivery systems, smart insulin pens) can be optimized for use during intermittent fasting periods.
- **Mechanistic studies:** Investigation into the underlying physiological mechanisms by which intermittent fasting affects glucose metabolism, insulin sensitivity, and beta-cell function in T1D.
- **Special populations:** More research is needed on the effects of intermittent fasting in specific T1D subpopulations, such as children, adolescents, pregnant women, and individuals with comorbidities.
- **Comparison with other dietary approaches:** Studies comparing the effects of intermittent fasting with other dietary interventions (e.g., low-carbohydrate diets, Mediterranean diet) in T1D management.

CONCLUSION

This systematic review highlights the complex and nuanced effects of intermittent fasting on individuals with type 1 diabetes. While some studies suggest potential benefits in terms of improved insulin sensitivity, metabolic parameters, and glycemic variability, others underscore the risks of hypoglycemia, hyperglycemia, and diabetic ketoacidosis. The safe implementation of intermittent fasting in T1D requires careful consideration of individual factors, comprehensive diabetes education, and the use of advanced glucose monitoring and insulin delivery technologies. Healthcare providers should work closely with individuals interested in intermittent fasting to develop tailored strategies that maximize potential benefits while minimizing risks. Further research, particularly long-term studies and investigations into optimal fasting protocols, is needed to fully elucidate the role of intermittent fasting in T1D management. Nonetheless, the decision to incorporate intermittent fasting should always be made in consultation with healthcare providers and with careful consideration of individual circumstances and risks.

AUTHOR ROLES

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Manuscript: A. Writing of the first draft, B. Review and Critique.

R.G.: 1A, 1B, 1C, 2A; R.A.S.: 2B; S.: 2B

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