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The role of intermittent fasting diet in NAFLD management: A scoping review of RCT and clinical trial studies in adult patients

Peran intermittent fasting dalam penanganan NAFLD: Tinjauan Scoping Review terhadap studi RCT dan clinical trial pada pasien dewasa

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Abstract

Non-Alcoholic Fatty Liver Disease (NAFLD) is the accumulation of fat in the liver not caused by alcohol consumption and is now a leading cause of chronic liver disease globally. Intermittent fasting has the potential to improve the metabolic parameters associated with NAFLD; however, more scientific evidence is needed to confirm this. This review aims to examine the role of intermittent fasting in the management of NAFLD based on existing research. The method used was A scoping review was conducted with a literature search through the PubMed and ScienceDirect databases, and article selection was performed using the PRISMA flow. The inclusion criteria were randomized controlled trials (RCTs) or clinical trials published between 2014 and 2024, resulting in seven articles meeting the criteria. The results showed that various IF methods, such as 5:2 fasting, Alternate-Day Fasting and Time-Restricted Eating, can reduce body weight, waist circumference, fat mass, and several biochemical parameters, such as triglycerides, LDL, total cholesterol, ALT, AST, and inflammatory markers. However, its effectiveness on biochemical parameters still requires further study due to the limited number of studies that comprehensively address these parameters. In conclusion, IF is considered safe for patients with NAFLD and may be a strategic approach to improve NAFLD.

Keywords: Intermittent Fasting, NAFLD, Scoping Review, Liver Steatosis, Metabolic syndrome, Diet Intervention

Abstrak

Non-Alcoholic Fatty Liver Disease (NAFLD) merupakan penumpukan lemak di hati tanpa disebabkan oleh konsumsi alkohol dan kini menjadi penyebab utama penyakit hati kronis global. Intermittent fasting berpotensi memperbaiki parameter metabolik terkait NAFLD, namun bukti ilmiahnya masih dibutuhkan lebih banyak untuk memastikan perannya. Artikel ini bertujuan untuk meninjau penelitian yang ada terkait peran intermittent fasting sebagai pendekatan alternatif dalam pengelolaan NAFLD. Metode yang digunakan adalah *scoping review* dengan pencarian literatur melalui basis data PubMed dan ScienceDirect, serta seleksi artikel menggunakan alur PRISMA. Kriteria inklusi mencakup desain penelitian *Randomized Controlled Trial* (RCT) atau *Clinical Trial* yang diterbitkan antara tahun 2014 hingga 2024, sehingga diperoleh 7 artikel yang memenuhi kriteria. Hasil menunjukkan bahwa berbagai metode IF seperti 5:2 fasting, Alternate Day Fasting dan Time Restricted Eating dapat menurunkan berat badan, lingkar pinggang, massa lemak, serta beberapa parameter biokimia seperti trigliserida, LDL, kolesterol total, ALT, AST, dan penanda inflamasi. Namun, efektivitasnya pada parameter biokimia masih perlu dikaji lebih lanjut karena keterbatasan jumlah studi yang mengevaluasi parameter tersebut secara menyeluruh. Dengan demikian, IF aman untuk penderita NAFLD dan dapat menjadi alternatif penanganan NAFLD.

Kata Kunci: Intermittent Fasting, NAFLD, Tinjauan Cakupan, Steatosis Hati, Sindrom Metabolik, Intervensi Diet

Introduction

Non-Alcoholic Fatty Liver Disease (NAFLD) is the accumulation of fat in the liver without alcohol consumption and is the main cause of chronic liver disease that affects 30% of the world's population (Amini-Salehi et al., 2024). NAFLD can develop gradually from steatosis, steatohepatitis, cirrhosis, and liver cancer, which can lead to the need for a liver transplant or even death (Kechagias et al., 2020). NAFLD is strongly associated with metabolic syndrome, obesity, insulin resistance, and dyslipidemia, which are considered major risk factors for the condition (Pouwels et al., 2022). The prevalence of NAFLD increases significantly in obese individuals, namely, 57% in adults and 38% in children. (Amini-Salehi et al., 2024).

The prevalence of NAFLD continues to increase annually, with the burden varying between countries and regions (Dong et al., 2024). The prevalence of NAFLD based on meta-analysis studies was found to be 32.6% in Europe, 47.8% in North America, and the highest in Africa at 56.8% (Teng et al., 2023). In Asia, the prevalence is estimated at 29%, with regional variations, with the highest in Indonesia at 51.04% and the lowest in Japan at 22.28% (Li et al., 2019). The prevalence of NAFLD is expected to increase significantly by 2030, along with increasing cases of obesity and metabolic syndrome, if not accompanied by appropriate interventions (Teng et al., 2023). To date, no specific drug has been approved by the Food and Drug Administration (FDA) or the European Medicines Agency (EMA) owing to undesirable side effects or limited clinical effectiveness. (Wei et al., 2024). Therefore, it is necessary to explore non-pharmacological approaches to suppress disease progression and improve patients' quality of life (Tacke et al., 2024)

Non-pharmacological approaches, such as weight loss, dietary modification, and increased physical activity, are key strategies for preventing and treating complications in patients with NAFLD. Weight loss of more than 5% has been shown to improve steatosis, steatohepatitis and fibrosis (Koutoukidis et al., 2021). Although weight loss can improve NAFLD, achieving this goal is difficult in the long term. Previous studies have shown that intermittent fasting (IF) improves dietary adherence, making IF an alternative to calorie restriction, with similar benefits for weight loss and chronic disease management (Zhang et al., 2022).

Intermittent fasting (IF) has been shown to reduce body weight, improve glucose metabolism, lipid profile, and insulin sensitivity, and reduce liver steatosis (Naous et al., 2023). Systematic review studies showed an average reduction of 4.3% in BMI and waist circumference in overweight or obese individuals (Welton et al., 2020). IF also plays a role in suppressing inflammation and oxidative stress by regulating macrophages, hormones, and gene expression (He et al., 2023). Although several previous studies have demonstrated the benefits of IF in weight loss and improved metabolic parameters, understanding its mechanisms of action and clinical implementation in the context of NAFLD remains limited. Several systematic reviews have been conducted on the role of IF in the management of NAFLD; however, these are limited in number, and some have not specifically synthesized evidence from RCTs. Therefore, this study aimed to comprehensively review the literature and current scientific evidence regarding the role of IF in the management of NAFLD.

Methods

This study used a six-stage scoping review design based on the Preferred Reporting Items for Systematic Review and Meta-analysis Extension for Scoping Reviews (PRISMA-ScR) guidelines. Researchers used the Population, Intervention, Comparison, Outcome, Study Design (PICOS) approach to formulate questions, identify key concepts, and establish the inclusion and exclusion criteria.

a. Population: Patients with NAFLD
b. Intervention: IF and its various methods (alternate-day fasting, time-restricted eating, 5:2 fasting)
c. Comparison: Other dietary intervention groups, or no intervention at all
d. Outcomes: Improvements in anthropometric parameters, biochemistry, and liver function.
e. Study Design: RCT and Clinical Trial

Inclusion Criteria
(1) Patients diagnosed with Non-Alcoholic Fatty Liver Disease
(2) Providing IF dietary interventions and various methods (alternate-day fasting, time-restricted eating, 5:2 fasting) along with macronutrient composition
(3) Providing comparison information with a control group, other interventions, or no intervention at all
(4) Providing outcome information in the form of metabolic, anthropometric, and biochemical changes
(5) Research design in the form of an RCT or clinical trial
(6) Research published within the last 10 years

Exclusion Criteria
(1) Animal studies
(2) Study protocols or research that only present the research plan without including the results
(3) Articles cannot be accessed in full text

The initial search strategy used several keywords based on MeSH, namely "Intermittent Fasting" OR "Alternate-day fasting" OR "Time-restricted eating" AND "Non-Alcoholic Fatty Liver Disease". In the extraction stage, researchers entered selected studies into a table with data on authors, year, methods, interventions, and macronutrient composition. Seven articles that met the inclusion criteria through the PRISMA method were assessed for quality using the JBI Critical Appraisal Tool. All articles were RCT and met 13 quality criteria according to the JBI checklist. The journal identification and screening processes were carried out using Excel 2021 software, and bibliographies were compiled using Mendeley software.

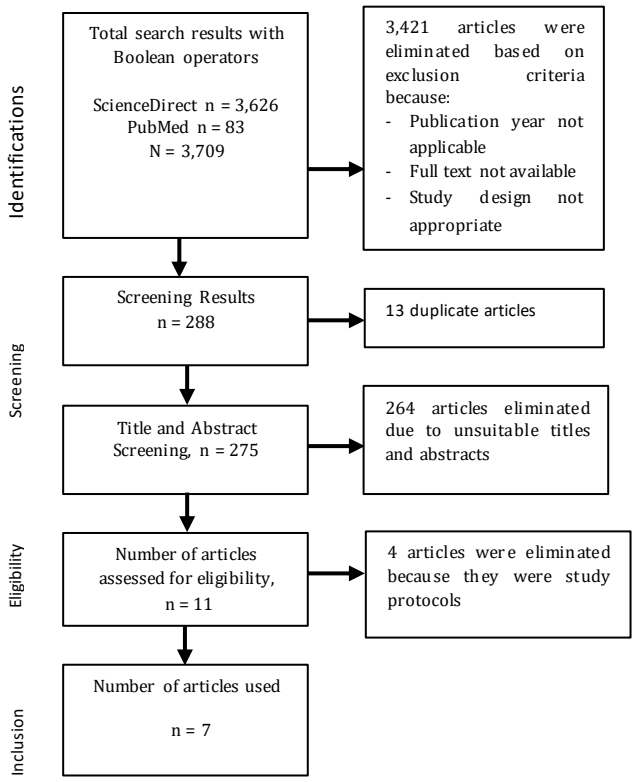

Figure 1. Search method based on PRISMA flowchart

Result and Discussion

As shown in Table 1, of the 3709 articles found in ScienceDirect (3626) and PubMed (83), 288 articles remained after the initial screening. Based on the inclusion criteria, seven articles were selected that discussed the role of IF in NAFLD using time-restricted eating, alternate day fasting, and 5:2 fasting methods. The reported outcomes included improvements in anthropometry, biochemistry, and the combination of IF with other methods in the management of NAFL.

Table 1. Characteristics of scoping review articles

Author, Year	Method	Intervention and Macronutrient Composition	Result	Conclusion
Lindqvist et al. (2023)	RCT, 12 Weeks	LCHF Intervention Energy (Women): 1600 kcal/day, Energy (Men): 1900 kcal/day, Carbohydrate: 5-10% TEE, Fat: 50-80% TEE, Protein: 15-40% TEE Intervention 5: 2	Group 5: 2 fasting days Decreased: Weight, BMI, HbA1c, HOMA-IR, Total Cholesterol, LDL-C, TG No change: HDL LCHF group Decreased: Weight, BMI,	Improvement in Body Composition and Metabolic Function (Both diet methods (LCHF and 5:2) resulted in

		Fasting Periods 2 Fasting Days Energy (Women): 500 kcal/day, Energy (Men): 600 kcal/day For 5 days Energy (Women): 1600 kcal/day, Energy (Men): 1900 kcal/day, Carbohydrate: 48% TEE, Fat: 32% TEE, Protein: 20% TEE SoC Group Standard of care for NAFLD by a hepatologist	HbA1c, HOMA-IR, TG Increased: HDL No change: Total Cholesterol, LDL-C SoC group Decreased: Weight, BMI	improvements in various parameters related to body composition and metabolic function, regardless of the type of diet used)
Holmer et.al. (2021)	RCT, 12 weeks	Group 5: 2 2-Day Fasting Energy: 500 kcal/day (Women) Energy: 600 kcal/day (Men) For 5 days Energy: 1600 kcal, max 2000 kcal (Women), Energy: 1900 kcal, max 2400 kcal (Men), Carbohydrate: 45-60% TEE, Fat: 25% TEE, Protein: 10-20% TEE LCHF Group Energy: 1600 kcal (Women), Energy: 1900 kcal (Men), Carbohydrate: 5-10% TEE, Fat: 50-80% TEE, Protein: 15-40% TEE SOC Group Standard care for NAFLD by a hepatologist	Group 5: 2 fasting days Decreased: Weight, BMI, Steatosis Score, Liver Stiffness, HbA1c, HOMA-IR, ALT, Total Cholesterol, LDL, TG No change: HDL, AST LCHF Group Decreased: Weight, BMI, Steatosis Score, HbA1c, HOMA-IR, ALT, TG Increased: HDL No change: Liver Stiffness, AST, Total Cholesterol, LDL-C SoC Group Decreased: Weight, BMI, Liver Stiffness, ALT, AST	The LCHF and 5:2 diets were more significant in reducing liver fat accumulation and body weight in NAFLD patients compared to standard care, indicating that dietary recommendations can be tailored to individual preferences.
Ezpeleta et. al. (2023)	RCT, 12 weeks	ADF and Combination Groups 2-day fasting Energy: 600 kcal (2500 kJ), Fat: 30% TEE, Carbohydrate: 55% TEE, Protein: 15% TEE 5-day fasting No calorie restriction Exercise-only and Control Groups No special dietary or	ADF + Exercise Group Reduction in: weight, fat mass, waist circumference, fasting insulin, HOMA-IR No change in: lean muscle mass, visceral fat, BMI, GDP, HbA1c, total cholesterol, HDL, LDL, triglycerides, ALT, AST ADF Only Group Reduction in: weight, fat mass, waist circumference,	The combination of ADF with exercise is effective in reducing hepatic steatosis in patients with NAFLD, but may not provide additional benefit compared with ADF alone.

		food interventions were given and they were asked to maintain their normal eating habits.	fasting insulin, HOMA-IR No change in: lean muscle mass, visceral fat, BMI, GDP, HbA1c, total cholesterol, HDL, LDL, triglycerides, ALT, AST Exercise Only Group Reduction in: waist circumference, fasting insulin, HOMA-IR No change in: weight, fat mass, lean muscle mass, visceral fat, BMI, GDP, HbA1c, total cholesterol, LDL, HDL, triglycerides, fetuin-A, FGF21, selenoprotein	
Kord et. al. (2023)	RCT, 12 months	Energy was calculated using the Mifflin-St Jeor formula. Fat: 30% TEE Protein: 15% TEE KH: 55% TEE With 9 servings of fruits and vegetables for both groups. Free sugar intake was limited to less than 3% of daily calories in the intervention group.	TRE Group Reduction in: Weight, BMI, waist circumference, fat mass, fibrosis, steatosis score, ALT, AST, TG, Total cholesterol, LDL, CRP, CK-18 No change in: HDL, GDS, Insulin, HOMA-IR, TAC Non-Intervention Group No change in: Weight, BMI, waist circumference, fat mass, fibrosis, steatosis score, ALT, AST, TG, CRP, CK-18	TRE with a low-sugar diet can reduce adiposity and improve liver, lipid, and inflammatory markers in NAFLD patients.
Cai et. al. (2019)	RCT, 12 months	Intervention and Control Groups Energy requirements using the Mifflin-St. Jeor formula American Heart Association (AHA) Guidelines Fat: 30% TEE Protein: 15% TEE KH: 55% TEE	ADF Group Reduction: Weight, fat mass, waist circumference, total cholesterol, triglycerides No change: fat-free mass, HDL, LDL, fasting insulin, FBG, systolic BP, diastolic BP TRE Group Reduction: Weight, fat mass, triglycerides No change: fat-free mass, total cholesterol, HDL, LDL, fasting insulin, FBG, systolic BP, diastolic BP Control Group No change: total cholesterol, HDL, LDL, fasting insulin, FBG, systolic BP, diastolic BP	ADF appears to be an effective dietary therapy for individuals with NAFLD that can achieve weight loss and improvement in dyslipidemia in a relatively short period of time (4 to 12 weeks).
Kord et al. (2022)	RCT, 12 months	Energy requirements were determined using the Mifflin-St. Jeor	Group 5: 2 Reduction in: Weight, BMI, waist circumference, fat mass, triglycerides, fibrosis	The 5:2 IF diet can reduce weight loss and

		formula for each respondent. On fasting days, patients received 25% of their recommended calorie intake for two hours, from 12:00 PM to 2:00 PM. The calorie target was divided into 30% calories from fat, 15% calories from protein, and 55% calories from carbohydrates.	score, steatosis score, ALT, AST, hs-CRP, CK-18 No change in: HDL, LDL, total cholesterol, GDP, insulin, HOMA-IR Control Group No change in: Weight, BMI, waist circumference, fat mass, triglycerides, HDL, LDL, total cholesterol, fibrosis score, steatosis score, ALT, AST, GDP, insulin, HOMA-IR	related parameters (fat mass and anthropometric indicators of obesity), as well as hepatic steatosis, liver enzymes, triglycerides, and inflammatory biomarkers in NAFLD patients.
Wei et. al (2023)	RCT, 12 months	TRE Group Men: 1500–1800 kcal Women: 1200–1500 kcal Macronutrient Composition: Carbohydrate: 40–55% TEE Protein: 15–20% TEE Fat: 20–30% TEE	TRE Group Decreased: weight, waist circumference, body fat percentage, fat mass, muscle mass, visceral fat, subcutaneous fat, visceral to subcutaneous fat ratio, cholesterol, triglycerides, LDL, FBG, HbA1c, HOMA-IR, ALT, AST, IHTG, liver stiffness Increased: HDL DCR Group Decreased: weight, waist circumference, body fat percentage, fat mass, muscle mass, total abdominal fat, subcutaneous fat, visceral fat, visceral to subcutaneous fat ratio, total cholesterol, LDL, FBG, HbA1c, HOMA-IR, ALT, AST, IHTG, liver stiffness Increased: HDL	Both the TRE and DCR methods produced similar reductions in IHTG, liver stiffness, and improvements in NAFLD. There were no significant differences between the two methods in liver fat reduction or other health parameters. The TRE diet was significantly more effective in reducing insulin resistance than the DCR diet.

Intermittent Fasting Method

IF is a non-pharmacological approach to managing obesity and metabolic syndrome through fasting from caloric food and beverages (Lavallee et al., 2022). Here are some IF methods:

a) Time-restricted eating (this is a diet) limits eating to a 4–10 h period per day, followed by a 14–20 h fast. TRE can be performed daily with an energy composition of 15% protein, 55% carbohydrates, and 30% fat (Brocchi et al., 2022).
b) Alternate day fasting, this is a fasting pattern that alternates between fasting days and free-eating days. During fasting, energy consumption is limited to 0–10% of body weight, and water consumption is maintained. On free-eating days, the standard diet is 15% protein, 55% carbohydrates, and 30% fat (Fanti et al., 2021)
c) 5 : 2 fasting, a fasting method involves fasting for two days a week and eating unrestrictedly on the remaining five days. On fasting days, the intake is limited to approximately 500–700 kcal (approximately 25% of energy needs), with no specific meal timings. Fasting days can be consecutive or separate. The other five days followed a free-range diet with a nutritional composition of

15% protein, 55% carbohydrates, and 30% fat (Fanti et al., 2021).

The Role of Intermittent Fasting in NAFLD Conditions

Anthropometric Improvement

Measurement of body weight, BMI, waist circumference, fat mass, and fat-free mass is important in patients with NAFLD because obesity is a high-risk condition that is closely associated with metabolic syndrome, such as insulin resistance, hypertension, and dyslipidemia. Weight loss is a key intervention for NAFLD, as it can reduce liver fat, inflammation, and fibrosis. The primary goal is a loss of ≥5% body weight, with a focus on reducing fat mass without reducing the lean body mass (Deng et al., 2024).

Of the seven studies reviewed, the most consistent anthropometric changes were weight loss and waist circumference reduction, which were almost always reported by all the studies. Fat mass measurements were conducted using different methods, with some studies measuring total fat mass and others specifically measuring visceral and subcutaneous fat. Of these seven studies, five showed a decrease in total fat mass, while the other two did not measure total fat mass but evaluated visceral and subcutaneous fat mass, both of which also showed a decrease. This is consistent with the study by Lindqvist et al. (2023), in which weight loss was directly related to a decrease in total fat mass, visceral fat, and subcutaneous fat.

According to Cai et al. (2019), ADF resulted in slightly greater body fat loss than TRE, with the fat-free mass remaining stable. The higher effectiveness of ADF is likely due to naturally occurring calorie restriction, whereas in TRE, participants are not required to restrict calorie intake. Furthermore, weight loss in the TRE method in this study was <5%, so the effect of TRE on NAFLD patients requires further investigation. However, this study is inconsistent with that of Wei et al. (2023), who reported that the TRE method can reduce body weight by >5% within 3 months. However, this study did not compare it with the ADF method and only compared it with the control group.

The 5:2 method, according to Lindqvist et al. (2023), showed significant weight loss of >5% compared to the control group. This finding aligns with that of Holmer et al. (2021), who reported clinically significant weight loss. However, that study also compared another method, the LCHF, which is equally effective for weight loss. However, implementing LCHF is considered less straightforward because of ongoing debates regarding its long-term risks. Therefore, dietary choices should be tailored to individual needs and preferences.

Biochemical Improvement

NAFLD is associated with lipid metabolism disorders, characterized primarily by dysfunction of hepatic lipid and glucose metabolism, which can increase cardiovascular risk, including insulin resistance, high triglyceride levels, and elevated LDL-C levels (Malinowski et al., 2019). The primary goal of NAFLD treatment is to improve liver-specific conditions (steatosis, fibrosis, and liver enzymes), with other benefits, such as improvements in lipid and metabolic profiles, considered additional beneficial effects (Tacke et al., 2024).

However, most of the seven articles reviewed evaluated lipid profiles rather than specific aspects of liver disease, such as steatosis score, fibrosis score, or liver enzyme levels. Steatosis and fibrosis scores were measured in only three studies, all of which showed a decrease in the scores. Liver enzyme measurements were performed in four studies, all of which showed improvement, but one study did not show a decrease in aspartate aminotransferase (AST) levels. ALT and AST are markers of liver function that are elevated in liver disease and can worsen the condition (Kalas et al., 2021). The TRE method, compared with the control group, can help reduce ALT and AST levels (Wei et al., 2023).

In addition, the TRE method combined with a low-sugar diet also decreased ALT and AST liver enzyme levels compared to an isocaloric control diet. This reflects improved liver function and a potential reduction in liver damage in patients with NAFLD. The 5:2 fasting method also decreased ALT and AST levels compared to the control diet (Kord Varkaneh et al., 2022). Decreased ALT and AST levels are associated with reduced visceral fat and hepatic steatosis, respectively. Excess fat accumulation in the liver can trigger inflammation and cell damage, so improving these conditions contributes to a decrease in previously elevated liver enzyme levels (Johari et al., 2019)

Based on lipid profile improvements from the seven reviewed studies, six studies reported a decrease in triglyceride (TG) levels, and four studies noted a decrease in LDL and total cholesterol levels. Cai et al. (2019) used the ADF method to improve total cholesterol and triglyceride levels, but LDL levels remained unchanged. Holmer et al. (2021) used the 5:2 method and showed a decrease in triglycerides, total cholesterol, and LDL, but not in HDL. Kord Varkaneh's (2022) study using the 5:2 method showed a decrease in triglycerides, but no significant changes in total cholesterol, LDL, or HDL. The TRE method can reduce total cholesterol, LDL, and triglyceride levels (Wei et al., 2023). Various fasting methods can improve lipid profiles through a metabolic shift from glucose to ketones, which triggers the expression of PPARα and PGC-1α, increases fatty acid oxidation, and decreases apolipoprotein B, liver triglycerides, VLDL, and LDL-C (Ahmed et al., 2021). Fasting also decreases the expression of the cholesterol ester transfer protein, which is associated with reduced fat mass, and suppresses the expression of SREPB-2, thereby reducing the activity of the cholesterol synthesis enzyme (Santos & Macedo, 2018).

However, the other six studies showed no significant changes in HDL levels. According to Cai et al. (2019), the lack of HDL increase was due to the participants' initial HDL levels being sufficiently high, thus maintaining the absence of changes in HDL levels. However, Wei et al. (2023) using the TRE method did help increase HDL, but not significantly compared to the calorie reduction method used in the comparison. Furthermore, of the seven studies, only two evaluated inflammatory markers, such as hs-CRP and CK-18, but both reported a decrease in inflammation levels. NAFLD is closely associated with an increased risk of cardiovascular disease. High hs-CRP levels are commonly found in NAFLD sufferers in response to inflammation caused by fat accumulation in the liver. CK-18 is a biomarker of oxidative stress and liver cell death, which are relevant to the pathogenesis of NAFLD (Zhu et al., 2021). Therefore, decreased hs-CRP and CK-18 levels may indicate the potential of IF in reducing the risk of systemic inflammation and cardiometabolic complications in patients with NAFLD.

Combination of Intermittent Fasting and Aerobic Exercise

Innovations in non-pharmacological treatments are needed to address NAFLD, with healthy lifestyle interventions that combine diet and exercise having a greater impact on reducing fatty liver disease (Mantovani & Dalbeni, 2021). Physical activity can reduce hepatic steatosis, inflammation, oxidative stress, and apoptosis, and improve insulin sensitivity, thereby slowing the progression of NAFLD and reducing the risk of cardiovascular disease (Farzanegi et al., 2019). Although exercise is beneficial, NAFLD treatment guidelines recommend a combination of physical activity and a weight-loss diet as an effective non-pharmacological therapy (Ando & Jou, 2021). Ezpeleta et al. (2023) compared a combination of aerobic exercise and ADF, ADF alone, aerobic exercise alone, and a control group. The results showed that the combination of ADF and aerobic exercise significantly reduced intrahepatic triglyceride (IHTG) levels and improved body weight, fat mass, waist circumference, ALT levels, and insulin sensitivity. Physical exercise increases fat burning through increased β-oxidation and the TCA cycle in skeletal muscle, which helps regulate hepatic lipid metabolism by increasing fatty acid oxidation and reducing lipogenesis through the modification of enzymes such as acetyl-CoA carboxylase (ACC) and fatty acid synthase (FAS) phosphorylation (Farzanegi et al., 2019).

Combination of Intermittent Fasting and Low Sugar Diet

The TRF method combined with a low-sugar diet can reduce adiposity and improve liver, lipid, and inflammatory markers in patients with NAFLD (Kord-Varkaneh et al., 2023). Diet composition influences body fat distribution, where high-fat intake can decrease hepatic glucose production and de novo lipogenesis, whereas high-carbohydrate intake can maintain fat mass due to the lipogenic effect of insulin (Lundsgaard et al., 2019). Excessive consumption of refined carbohydrates, such as fructose and glucose, can trigger long-term fatty liver disease by providing excess substrates for enzymes involved in hepatic de novo lipogenesis, the formation of new fat in the liver. This process can trigger insulin resistance, liver inflammation, and elevated blood triglyceride (TGs) levels, leading to chronic NAFLD and

various related clinical problems (Softic et al., 2016).

Potential Obstacles and Challenges in IF Implementation

All seven studies reported that IF is a safe dietary strategy for people with NAFLD because it has few side effects. Although IF is relatively safe, it is unsuitable for all individuals. IF should not be used in pregnant women because the evidence is conflicting, and the long-term effects are unclear. In individuals with type 2 diabetes, IF is relatively safe but still requires close monitoring, especially for those taking glucose-lowering medications. Furthermore, patients should be informed about the side effects of IF, such as decreased energy, headache, presyncope, impaired concentration, mood changes, constipation, and bad breath (Lavallee et al., 2022).

This study has limitations, as most studies were short-term and lacked statistical analysis. Therefore, strong conclusions cannot be drawn regarding the effectiveness of IF on NAFLD clinical parameters. Further research is needed with a more robust design, longer duration, and more robust statistical analysis, focusing on improving steatosis and liver enzymes as the primary therapeutic targets. Further robust studies are needed to assess its effects on lipid profiles.

Conclusion

Intermittent fasting (IF) can help manage obesity and Non-Alcoholic Fatty Liver Disease (NAFLD) through various methods, such as Time-Restricted Eating (TRE), alternate-day fasting (ADF), and 5:2 fasting. IF can improve anthropometric parameters, including weight loss and fat mass. Furthermore, IF has the potential to reduce triglyceride, LDL, cholesterol, liver enzyme, and inflammatory marker levels, such as hs-CRP and CK-18.

However, further studies are needed because of the limited number of studies that have comprehensively evaluated these parameters. Combining IF with aerobic exercise or a low-sugar diet reduces liver enzymes, increases insulin sensitivity, and improves inflammation. Therefore, IF is considered safe for patients with NAFLD and can be an alternative strategy for improving NAFLD.

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