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EFFECTS OF INTERMITTENT FASTING ON METABOLISM IN INDIVIDUALS WITH TYPE II DIABETES MELLITUS

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Abstract:

Background: *For obese people, intermittent fasting (IF) has been suggested as a weight-loss method with extra cardiometabolic advantages. It's still unknown how IF affects people with type 2 diabetes (T2DM), despite its increasing popularity.* ***Aim :****In order to assess the metabolic effects of IF in relation to the conventional diet in individuals with type 2 diabetes, we carried out a systematic review and meta-analysis.* ***Method:*** *Between 1950 and August 12, 2020, randomised, diet-controlled trials assessing any IF intervention in individuals with T2DM were sought after using Embase, PubMed, and clinicaltrials.gov. Using a random-effects model to calculate pooled estimates of the absolute changes in body weight and glycated hemoglobin A1c (HbA1c) compared to a control group, we investigated the effects of IF on weight reduction and glucose-lowering.* ***Results:*** *Our inclusion criteria were met by seven studies (n = 338 participants; mean baseline HbA1c 8.8%, mean body mass index [BMI] 35.65). Compared to a conventional diet, IF caused a larger drop in body weight of -1.89 kg (95% CI, -2.91 to -0.86 kg), with no discernible between-study heterogeneity (I2 21.0%, P =.28). Studies with a heavier population (BMI > 36) showed a significant extra weight reduction as did studies with a shorter duration (≤ 4 months) .When compared to a conventional diet, IF did not result in a higher decrease in HbA1c* ***Conclusion:*** *According to available data, individuals with type 2 diabetes may lose more weight when following an IF diet as opposed to a conventional diet, while also experiencing comparable improvements in glycemic control.*

Key words: *Glycated hemoglobin, body weight, type 2 diabetes, and intermittent fasting*

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BACKGROUND:

Type 2 diabetes mellitus (T2DM) accounts for 61% to 79% of cases (1); obesity adds to the morbidity of the disease because higher body mass index (BMI) has been associated with a worse cardiovascular risk profile and higher mortality in this patient population (2–5). While lifestyle modifications are a crucial component of diabetes care, it can be challenging to maintain weight loss and achieve long-term glycemic control without the use of medications (6).

Recent research has focused on intermittent fasting (IF), which is defined as a period of time during which energy consumption is deliberately and regularly interrupted or drastically reduced. IF has been advocated as a weight-loss method with added cardiometabolic benefits for persons who are overweight or obese. These other advantages include lowering blood pressure and total cholesterol. (7-12). Time-restricted feeding (TRF), in which feeding is permitted for only a window of 4 to 8 hours per day with 16 to 20 hours of fasting (13–16), and intermittent or short-term energy restriction through very-low calorie diets (VLCDs), in which caloric consumption remains between 300 and 600 kcal/day (17) are common regimens for intermittent fasting (IF).

There has been little study done on T2DM patients, despite IF's rising appeal in the general public (18). According to earlier research on people with type 2 diabetes, IF therapies may cause weight loss and glycated hemoglobin A1c (HbA1c) reductions comparable to those achieved with conventional dietary guidelines (19–23). Nevertheless, the limited sample sizes hinder drawing firm conclusions from these isolated investigations, emphasizing the necessity for a thorough and methodical assessment of the impact of IF in type 2 diabetes. Therefore, the goal of this meta-analysis and comprehensive review is to assess how IF treatments affect patients with type 2 diabetes in terms of metabolism.

METHOD:

Data sources and searches

I choose pertinent research that was released between August 12, 2020, and 1950. We utilised the following combined text and Medical Subject Heading (MeSH) phrases to search clinicaltrials.gov, Embase, and PubMed: "intermittent fasting," "time-restricted feeding," "very low-calorie diet," and "type 2 diabetes." Here is what the full PubMed search looked like: ((((time-restricted feeding [Text Word] OR relatively low calorie diet [Text Word]) OR)) AND ("diabetes mellitus, type 2" [MeSH Terms] OR type 2 diabetes mellitus [Text Word]). Review eligibility was extended to all potentially eligible research, irrespective of language or primary outcome. Additionally, we manually searched utilizing the references of important English-language publications.

Study selection

Studies could be included if they met three criteria: (1) they were interventional studies; these could be crossover trials or randomized parallel-arm trials with adults with type 2 diabetes; (2) they compared the effects of any IF intervention to a standard diet that included either a normal caloric intake (control group) or a healthy pattern dietary recommendation with a caloric deficit; and (3) they reported changes in body weight or HbA1c. The exclusion criteria included observational studies, retrospective studies, and studies without a control group. We included the data pertaining to the primary outcome of a study if it was reported in several publications.

Examining the intervention and measuring the results

Any IF intervention, comprising of (i) intermittent restricted energy intake (25 percent total calorie intake), (ii) 24-hour complete fasting, and (iii) TRF (feeding permitted for just a window of 4 to 8 hours daily with 16 to 20 hours of fasting), was assessed. The IF intervention was compared to a typical dietary prescription that included regular eating hours. It might be performed on alternate days, twice weekly, or for an extended period of time. The main results were the average variations in body weight and HbA1c from the beginning to the completion of the intervention. Changes in fasting blood sugar, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, and systolic and diastolic blood pressure were evaluated as secondary outcomes.

Extraction of data and evaluation of quality

The study titles and abstracts were assessed by E.B. and C.K.K., two independent investigators. Research that met the requirements for inclusion were retrieved and examined in full. The agreement value (k) of the studies that both investigators chose for review was 98.3%; differences were settled by a third investigator (J.M.).

The following information was taken out of each study: mean changes in body weight (mean [SD]), mean changes in HbA1c (mean [SD]), mean changes in other metabolic parameters (mean changes in secondary outcomes listed earlier), age, percentage of male participants, total number of participants, duration of intervention, baseline BMI, baseline

HbA1c. The PRISMA guidelines (24) were followed in the evaluation of the risk of bias.

RESULTS:

Study characteristics

Fifty studies were found, 34 of which had their titles and abstracts removed. After sixteen papers were located for a thorough evaluation, nine of them were eliminated—five because they had extra publications from included trials and four because they lacked a control group. Our inclusion criteria were met by seven studies (21-23, 26, 29-31) containing data from 338 people; six of these studies were randomized parallel-arm trials, while one study was a randomized crossover trial (26). The included studies had a median study duration of 24 weeks (range, 19-260 weeks) and were published between 1991 and 2018. The patients were primarily obese with poor glycemic control; their mean age was 56.3 years (range, 51.2-65 years), 24.2% to 54% of them were male, and their mean baseline BMI was 35.65 (range, 32.4-37.9). They also had a mean baseline HbA1c of 8.8% (range, 7.2%-10.4%). The length of diabetes was documented in two investigations (mean duration of 8.0 years). Data on background diabetes therapy were published in five trials (21, 23, 26, 29, 30). Of the patients, 75%–100% were either on diet or oral antidiabetic medicines (21, 23, 29, 30), and 20%–25% were also taking insulin (21, 23, 29, 30).

These studies used different types of IF interventions: two evaluated intermittent energy restriction (21, 22), four evaluated short-term energy restriction by VLCD (23, 29–31), and one evaluated TRF (26). Three studies (22, 23, 30) about physical activity advised individuals to raise their level of physical activity without further evaluating adherence to this recommendation. Using a pedometer, Kahleova et al. (26) assessed physical activity and found no differences between the intervention arms.

Impact of intermittent fasting on weight loss

Six studies compared the body weight differences between the IF and the regular diet (21-23, 26, 29, 31). Combining the data from these trials revealed that the body weight of the IF arm was 1.89 kg lower than that of the control group, and there was no significant between-study heterogeneity.

Impact of intermittent fasting on glycemic control

There was no significant between-study heterogeneity and a nonsignificant drop of -0.11% in the IF arm compared to control in the pooled analysis of the six trials (21-23, 26, 29, 31). Understanding that decreases in HbA1c are more noticeable over a few months and that IF treatments may impact people differently who have greater baseline HbA1c. As with the pooled analysis, no significant between-study heterogeneity was found and no subgroup differences in the HBA1c reduction resulting from IF treatments relative to conventional diet were found.

Impact on additional metabolic parameters:

In order to examine the metabolic effects of IF therapies in comparison to a conventional diet, we combined the data from many studies that measured variations in blood pressure, waist circumference, lipid profile, and fasting glucose. When compared to a typical diet, IF did not show any additional beneficial effects on any of these parameters.

DISCUSSION:

According to our data, persons with T2DM who are primarily obese and have poor glycemic control may benefit from IF in terms of weight loss (around 1.9 kg) and equivalent improvements in HbA1c, lipid profile, and blood pressure as compared to a regular diet. The beneficial effects of IF on weight loss were more noticeable in shorter-term studies and in patient populations with higher body masses.

While losing weight is essential for treating type 2 diabetes mellitus linked to obesity (32), nonpharmacological approaches have not been as successful in treating adults with T2DM when they have not followed guidelines for physical exercise and maintaining a balanced diet (33).

Our findings showed that IF might be a therapeutic substitute since, in comparison to a conventional diet, this intervention dramatically reduced body weight; this effect was shown regardless of the subjects' initial BMI or length of research. Reiterating the findings of our analysis, Carter et al. (21) reported a –6.8-kg weight loss in the IF arm compared to –5.0 kg in the control group, with a HbA1c reduction of –0.5% vs. –0.2%, respectively, in the longest trial testing IF in T2DM (12 months' duration). Carter and colleagues (21) showed that the IF arm had a similar reduction in fat-free mass to the control group, despite the IF arm having a greater impact on weight loss.

Interestingly, the extra weight loss brought on by IF was negligible when compared to the research population's baseline BMI of 35.6; yet, this extra weight loss might help achieve the overall objective of a 5% decrease in total body weight in obese people with type 2 diabetes (32, 34–41).

Our results show that IF therapies had a neutral effect on HbA1c decrease, even when they cause a greater amount of weight loss. In addition to a significant decrease in BMI, a prior meta-analysis (42) assessing the effects of IF in the general population (n = 545 individuals) showed a small reduction in fasting glucose of –4.16 mg/dL. However, it should be highlighted that even though IF did not statistically outperform a typical diet for glycemic management in people with T2DM, there may still be important clinical implications

After a 20-week intervention, Williams et al. (22) reported no difference in HbA1c levels between the IF and regular diet arms; however, more participants in the IF group than in the control group achieved the goal HbA1c (22). The concurrent usage of antidiabetic medicines is an additional factor to take into account. Wing and colleagues observed that, one year after the intervention, 45% of participants in the IF arm and 69% of participants in the control arm took glucose-lowering medications, despite similar reductions in HbA1c among study arms) (23). This finding suggests that IF may represent another lifestyle option to optimize diabetes care, reducing the requirement of antidiabetic medications.
The study has documented potential advantages of intermittent fasting (IF) beyond weight loss and glycemic control. This may be the result of IF's capacity to switch glucose's primary metabolic target from glycogenolysis to fatty acids and the ketones derived from them. Specifically, a metabolic pathway independent of pancreatic insulin secretion produces fatty acids and glycerol through increased lipolysis that takes place during an extended fasting phase when hepatocyte glycogen stores are depleted (43). By causing this shift, IF may promote beneficial metabolic changes even in the absence of weight loss.

Limitations:

Our study are limited by the variability of the IF procedures. IF protocols are now defined in the literature as dietary plans with extremely low calorie intake, such as 400–500 kcal per day, along with full fasting (18, 45). The quantity of calories permitted per day, the length and timing of the fasting window, the number of fasting days per week, and the duration of the intervention have all varied throughout fasting initiatives, resulting in a lack of standardization in IF interventions. Nevertheless, it is unlikely to have an impact on our findings because fasting and extremely low-calorie diets both cause a ketogenetic state that is marked by a rise in free fatty acids and the ketone bodies acetoacetate and β-hydroxybutyrate, which is the key

Due to the fact that most of the included trials had durations of one to twenty-four weeks, another drawback is the uncertainty surrounding long-term adherence to IF. Furthermore, it is not clear how the caloric deficit in these experiments was attained in detail. Lastly, it was not able to assess the safety of IF in T2DM in our analysis, which is especially important for patients who are on insulin. According to findings from a prior study, rates of hypoglycemia in T2DM patients receiving IF for two consecutive or nonconsecutive days are manageable and can be lowered with appropriate education and antidiabetic drug titration (20).

CONCLUSION:

Considering the past difficulties with nonpharmacological treatment of type 2 diabetes, our findings bolster the idea that IF is a non-inferior weight-loss alternative. Our findings underscore the need for more research in this area and show the therapeutic potential of IF as a weight-reduction tactic in T2DM. Trials evaluating the various IF protocols with extended follow-up periods and in-depth phenotyping of the clinical and metabolic consequences of this intervention in T2DM patients are specifically needed.

REFERENCES:

1. Janssen I . The public health burden of obesity in Canada. Can J Diabetes.2013;37(2):90-96.
2. Kramer CK , Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions? A systematic review and meta-analysis. Ann Intern Med.2013;159(11):758-769.
3. Khalangot M , Tronko M, Kravchenko V, Kulchinska J, Hu G. Body mass index and the risk of total and cardiovascular mortality among patients with type 2 diabetes: a large prospective study in Ukraine. Heart.2009;95(6):454-460.
4. McEwen LN , Kim C, Karter AJ, et al. Risk factors for mortality among patients with diabetes: the Translating Research Into Action for Diabetes (TRIAD) Study. Diabetes Care.2007;30(7):1736-1741.
5. Zhao W , Katzmarzyk PT, Horswell R, et al. Body mass index and the risk of all-cause mortality among patients with type 2 diabetes mellitus. Circulation.2014;130(24):2143-2151.
6. Franz MJ , Boucher JL, Rutten-Ramos S, VanWormer JJ. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review

and meta-analysis of randomized clinical trials. J Acad Nutr Diet.2015;115(9):1447-1463.
7. Tinsley GM , La Bounty PM. Effects of intermittent fasting on body composition and clinical health markers in humans. Nutr Rev.2015;73(10):661-674.
8. Heilbronn LK , Civitarese AE, Bogacka I, Smith SR, Hulver M, Ravussin E. Glucose tolerance and skeletal muscle gene expression in response to alternate day fasting. Obes Res.2005;13(3):574-581.
9. Varady KA , Bhutani S, Church EC, Klempel MC. Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults. Am J Clin Nutr.2009;90(5):1138-1143.
10. Bhutani S , Klempel MC, Berger RA, Varady KA. Improvements in coronary heart disease risk indicators by alternate-day fasting involve adipose tissue modulations. Obesity (Silver Spring).2010;18(11):2152-2159.
11. Varady KA , Bhutani S, Klempel MC, Lamarche B. Improvements in LDL particle size and distribution by short-term alternate day modified fasting in obese adults. Br J Nutr.2011;105(4): 580-583.
12. Klempel MC , Kroeger CM, Varady KA. Alternate day fasting increases LDL particle size independently of dietary fat content in obese humans. Eur J Clin Nutr.2013;67(7):783-785.
13. Klempel MC , Kroeger CM, Bhutani S, Trepanowski JF, Varady KA. Intermittent fasting combined with calorie restriction is effective for weight loss and cardio-protection in obese women. Nutr J.2012;11:98.
14. Carlson O , Martin B, Stote KS, et al. Impact of reduced meal frequency without caloric restriction on glucose regulation in healthy, normal-weight middle-aged men and women. Metabolism.2007;56(12):1729-1734.
15. Stote KS , Baer DJ, Spears K, et al. A controlled trial of reduced meal frequency without caloric restriction in healthy, normal-weight, middle-aged adults. Am J Clin Nutr.2007;85(4):981-988.
16. Tinsley GM , Forsse JS, Butler NK, et al. Time-restricted feeding in young men performing resistance training: a randomized controlled trial. Eur J Sport Sci.2017;17(2):200-207.
17. Tsai AG , Wadden TA. The evolution of very-low-calorie diets: an update and meta-analysis. Obesity (Silver Spring).2006;14(8):1283-1293.
18. Horne BD , Grajower MM, Anderson JL. Limited evidence for the health effects and safety of intermittent fasting among patients with type 2 diabetes. Jama.2020;324(4):341-342.
19. Furmli S , Elmasry R, Ramos M, Fung J. Therapeutic use of intermittent fasting for people with type 2 diabetes as an alternative to insulin. BMJ Case Rep.2018;2018:bcr2017221854.
20. Corley BT , Carroll RW, Hall RM, Weatherall M, Parry-Strong A, Krebs JD. Intermittent fasting in type 2 diabetes mellitus and the risk of hypoglycaemia: a randomized controlled trial. Diabet Med.2018;35(5):588-594.
21. Carter S , Clifton PM, Keogh JB. Effect of intermittent compared with continuous energy restricted diet on glycemic control in patients with type 2 diabetes: a randomized noninferiority trial. JAMA Netw Open.2018;1(3):e180756.
22. Williams KV , Mullen ML, Kelley DE, Wing RR. The effect of short periods of caloric restriction on weight loss and glycemic control in type 2 diabetes. Diabetes Care.1998;21(1):2-8.
23. Wing RR , Blair E, Marcus M, Epstein LH, Harvey J. Year-long weight loss treatment for obese patients with type II diabetes: does including an intermittent very-low-calorie diet improve outcome?Am J Med.1994;97(4):354-362.
24. Moher D , Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. Ann Intern Med.2009;151(4):264-269, W64.
25. Higgins JP , Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med.2002;21(11):1539-1558.
26. Kahleova H , Belinova L, Malinska H, et al. Eating two larger meals a day (breakfast and lunch) is more effective than six smaller meals in a reduced-energy regimen for patients with type 2 diabetes: a randomised crossover study. Diabetologia.2014;57(8):1552-1560.
27. Begg CB , Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics.1994;50(4):1088-1101.

Google ScholarCrossrefPubMedWorldCat

28. Duval S , Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics.2000;56(2):455-463.
29. Wing RR , Marcus MD, Salata R, Epstein LH, Miaskiewicz S, Blair EH. Effects of a very-low-calorie diet on long-term glycemic control in obese type 2 diabetic subjects. Arch Intern Med.1991;151(7):1334-1340.
30. Paisey RB , Frost J, Harvey P, et al. Five year results of a prospective very low calorie diet or

conventional weight loss programme in type 2 diabetes. J Hum Nutr Diet.2002;15(2):121-127.
31. Li C , Sadraie B, Steckhan N, et al. Effects of a one-week fasting therapy in patients with type-2 diabetes mellitus and metabolic syndrome—a randomized controlled explorative study. Exp Clin Endocrinol Diabetes.2017;125(9):618-624.
32. Pi-Sunyer X , Blackburn G, Brancati FL, et al. ; Look AHEAD Research Group. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. Diabetes Care.2007;30(6):1374-1383.
33. Nagelkerk J , Reick K, Meengs L. Perceived barriers and effective strategies to diabetes self-management. J Adv Nurs.2006;54(2):151-158.
34. Jonker JT , Snel M, Hammer S, et al. Sustained cardiac remodeling after a short-term very low calorie diet in type 2 diabetes mellitus patients. Int J Cardiovasc Imaging.2014;30(1):121-127.
35. Snel M , Jonker JT, Hammer S, et al. Long-term beneficial effect of a 16-week very low calorie diet on pericardial fat in obese type 2 diabetes mellitus patients. Obesity (Silver Spring).2012;20(8):1572-1576.
36. Teeuwisse WM , Widya RL, Paulides M, et al. Short-term caloric restriction normalizes hypothalamic neuronal responsiveness to glucose ingestion in patients with type 2 diabetes. Diabetes.2012;61(12):3255-3259.
37. Steven S , Hollingsworth KG, Al-Mrabeh A, et al. Very low-calorie diet and 6 months of weight stability in type 2 diabetes: pathophysiological changes in responders and nonresponders. Diabetes Care.2016;39(5):808-815.
38. Berk KA , Mulder MT, Verhoeven AJ, et al. Predictors of diet-induced weight loss in overweight adults with type 2 diabetes. PLoS One.2016;11(8):e0160774.
39. Hammer S , Snel M, Lamb HJ, et al. Prolonged caloric restriction in obese patients with type 2 diabetes mellitus decreases myocardial triglyceride content and improves myocardial function. J Am Coll Cardiol.2008;52(12):1006-1012.
40. Wang Y , Snel M, Jonker JT, et al. Prolonged caloric restriction in obese patients with type 2 diabetes mellitus decreases plasma CETP and increases apolipoprotein AI levels without improving the cholesterol efflux properties of HDL. Diabetes Care.2011;34(12):2576-2580.
41. Dhindsa P , Scott AR, Donnelly R. Metabolic and cardiovascular effects of very-low-calorie diet therapy in obese patients with type 2 diabetes in secondary failure: outcomes after 1 year. Diabet Med.2003;20(4):319-324.
42. Capstick F , Brooks BA, Burns CM, Zilkens RR, Steinbeck KS, Yue DK. Very low calorie diet (VLCD): a useful alternative in the treatment of the obese NIDDM patient. Diabetes Res Clin Pract.1997;36(2):105-111.
43. Anton SD , Moehl K, Donahoo WT, et al. Flipping the metabolic switch: understanding and applying the health benefits of fasting. Obesity (Silver Spring).2018;26(2):254-268.
44. Sutton EF , Beyl R, Early KS, Cefalu WT, Ravussin E, Peterson CM. Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes. Cell Metab.2018;27(6):1212-1221.e3.
45. de Cabo R , Mattson MP. Effects of intermittent fasting on health, aging, and disease. N Engl J Med.2019;381(26):2541-2551.