Intermittent fasting vs daily calorie restriction for type 2 diabetes prevention: a review of human findings

ADRIENNE R. BARNOSKY, KRISTIN K. HODDY, TERRY G. UNTERMAN, and KRISTA A. VARADY

CHICAGO, ILL

Intermittent fasting (IF) regimens have gained considerable popularity in recent years, as some people find these diets easier to follow than traditional calorie restriction (CR) approaches. IF involves restricting energy intake on 1–3 d/wk, and eating freely on the nonrestriction days. Alternate day fasting (ADF) is a subclass of IF, which consists of a "fast day" (75% energy restriction) alternating with a "feed day" (ad libitum food consumption). Recent findings suggest that IF and ADF are equally as effective as CR for weight loss and cardioprotection. What remains unclear, however, is whether IF/ADF elicits comparable improvements in diabetes risk indicators, when compared with CR. Accordingly, the goal of this review was to compare the effects of IF and ADF with daily CR on body weight, fasting glucose, fasting insulin, and insulin sensitivity in overweight and obese adults. Results reveal superior decreases in body weight by CR vs IF/ADF regimens, yet comparable reductions in visceral fat mass, fasting insulin, and insulin resistance. None of the interventions produced clinically meaningful reductions in glucose concentrations. Taken together, these preliminary findings show promise for the use of IF and ADF as alternatives to CR for weight loss and type 2 diabetes risk reduction in overweight and obese populations, but more research is required before solid conclusions can be reached. (Translational Research 2014;164:302–311)

Abbreviations: ADF = Alternate day fasting; BMI = Body mass index; CR = Calorie restriction; HOMA-IR = Homeostatic model assessment-insulin resistance; IF = Intermittent fasting

INTRODUCTION

At present, 35% of adults older than 20 years in the United States have prediabetes.[1] If no lifestyle changes are made to improve health, 15%–30% of these individuals will develop type 2 diabetes within 5 years.[1] A key strategy to prevent the progression of prediabetes to type 2 diabetes is weight loss.[2] Accumulating evidence suggests that even modest weight loss (5%–7% of initial weight) helps to improve several diabetes risk parameters, including fasting glucose, insulin, and insulin sensitivity.[3,4]

Daily calorie restriction (CR) regimens are still the most common diet strategies implemented for weight loss.[5] CR regimens involve reducing energy intake every day by 20%–50% of needs.[5] Although CR is effective for weight loss in some individuals, many people find this type of dieting difficult, as it requires vigilant calorie counting on a daily basis.[6] People also grow frustrated with this diet, as they are never able to eat freely throughout the day. In light of these issues with CR, another approach termed intermittent fasting (IF) has shown promise in achieving weight loss goals.[7] IF differs from CR, in that it only requires an individual to restrict energy 1–3 d/wk, and allows for ad libitum

From the Division of Endocrinology, Department of Medicine, University of Illinois at Chicago, Chicago, Ill; Department of Kinesiology and Nutrition, University of Illinois at Chicago, Chicago, Ill.

Submitted for publication January 15, 2014; revision submitted May 5, 2014; accepted for publication May 8, 2014.

Reprint requests: Krista A. Varady, Department of Kinesiology and Nutrition, University of Illinois at Chicago, 1919 West Taylor Street, Room 506F, Chicago, IL 60612; e-mail: varady@uic.edu.

1931-5244/$ - see front matter

http://dx.doi.org/10.1016/j.trsl.2014.05.013

food consumption on the nonrestriction days.[7] Alternate day fasting (ADF) is a subclass of IF, which consists of a "fast day" (75% energy restriction) alternating with a "feed day" (ad libitum food consumption). Recent reviews suggest that IF and ADF are equally as effective as CR for weight loss cardioprotection.[7,8] What has yet to be elucidated, however, is whether IF and ADF elicit comparable improvements in diabetes risk indicators, when compared with CR. Accordingly, the goal of this review was to compare the effects of IF and ADF with daily CR on body weight, fasting glucose, fasting insulin, and insulin sensitivity in overweight and obese adults.

METHODS

We performed a systematic search in MEDLINE PubMed using the following search strings: (1) "intermittent fasting and weight loss," (2) "alternate day fasting and weight" or "alternate day calorie restriction," (3) "calorie restriction and weight loss and insulin," (4) "caloric restriction and weight loss and obesity," and (5) "calorie restriction and metabolic syndrome." Two reviewers (A.B. and K.H.) separately screened the abstracts for inclusion and exclusion. Full text articles were retrieved from all abstracts that were potentially relevant and were reviewed independently by the 2 researchers. The comprehensive literature search revealed 108 articles under the umbrella category of IF and 4945 articles in the category of CR. Articles that were excluded if they did not meet the inclusion criteria, were review articles, editorials, letters, comments, or conferences proceedings. References of the retrieved articles were also screened for additional studies. Inclusion criteria were as follows: (1) randomized control trials and nonrandomized trials, (2) total sample size $\geq$8 subjects, (3) primary endpoints of body weight and one or more relevant diabetes risk parameter, (4) average daily energy restriction $<$50% (to exclude very low calorie diets that result in muscle wasting[9]), (5) trial duration between 3 and 24 weeks, (6) male and female subjects, (7) age between 25 and 75 years, (8) body mass index (BMI) between 25 and 40 kg/m^2, (9) nonsmokers (because of the effects of smoking on lipid metabolism),[10] (10) sedentary or moderately active individuals, and (11) articles published after 2003. We chose 2003 as a cutoff date because all the IF studies found were published within this time frame, and we wanted to use the same time frame for CR studies. Exclusion criteria were as follows: (1) cohort and observational studies; (2) trials that combined CR/IF with supplements, pharmacologic substances, or exercise; (3) diabetic; and (4) very active individuals or athletes. Ten CR trials and 9 IF trials were found that matched these criteria. None of the papers retrieved implemented intention to treat analyses.

BODY WEIGHT AND VISCERAL FAT MASS

Obesity is a well-established risk factor for the development of type 2 diabetes. Findings from the Nurses' Health Study demonstrate a 100-fold increase in diabetes risk over 14 years in those with a BMI $>$35 kg/m^2 compared with normal weight individuals.[11] At least one contributing factor to insulin resistance that occurs in obesity is the decrease in insulin-mediated peripheral glucose uptake.[12] Weight loss results in substantial reductions in insulin resistance, with every 1 kg lost associated with a 16% reduction in estimated risk of developing diabetes.[2]

The distribution of excess fat mass also contributes to the risk for metabolic derangements.[13] In 1947, the concept of regional fat distribution having different physiological and metabolic effects was first introduced by Vague.[14] Over the subsequent decades, it has been shown that visceral obesity has a stronger correlation with a risk for the development of diabetes, hypertension, hyperlipidemia, hepatic steatosis, and coronary artery disease compared with that of a gluteoemoral fat distribution.[13] The presence of visceral obesity has also been shown to have a strong inverse relationship with insulin sensitivity.[13] Evaluation of glucose disposal rates by euglycemic insulin clamps and visceral adipose tissue by the computed tomography technique, illustrated an inverse association.[15] Thus a higher visceral fat content is correlated with lower insulin sensitivity.[15] Weight loss has been shown to decrease both visceral fat and improve markers of insulin sensitivity.[16]

IF: effects on body weight and visceral fat mass. Body weight changes were assessed in 2 IF studies[17,18] and 7 ADF studies[19-25] (Table I). Findings from these trials demonstrate 3%–8% reductions in body weight after 3–24 weeks of treatment. Providing food to subjects on the fast day appears to be a key factor in determining greatest weight loss. For instance, the most pronounced weight loss was seen in a study performed by Johnson et al,[21] where ADF subjects were provided with a 320–380 kcal meal replacement shake on each fast day. After 8 weeks of treatment, subjects lost 8% of body weight.[21] Comparable decreases in body weight (6%–7%) were also noted in the other 8-week ADF studies that provided food on the fast day.[22,23,25] An exception to this rule is the ADF study by Bhutani et al.[24] In this 12-week trial, fast day food was provided, but only a 4% weight loss was observed.[24] This limited weight loss may be explained by the fact that food was only provided for the first 4 weeks of the study,[24] and not for the entire duration of trial. Another