

Role of Intermittent Energy Restriction (IER) in Weight Loss and Metabolic Parameters of Overweight/Obese Patients

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Abstract. Currently, obesity became a prevalence concern in terms of its scale and health-related impact among the global. Medical comprehensive intervention among dietary pattern and living manners are recommended by guidelines as foundation of obesity treatment. Identifying alternative dietary weight loss strategies become a common and safe choice for many obsess people's medical consolors and clinical doctors. Many positive impacts of Intermittent Energy Restriction (IER) have been suggested by preliminary study, but it still lacks well-powered intervention studies. This passage objects at clarify the metabolic parameters, summarized evidence of preclinical studies of IER's role in used as a weight loss strategy compared to other common strategies the guideline recommended, for instance, continuous energy restriction (CER), etc. Specifically, the randomized studies last 8-26 weeks performing in overweight and obsess adults. The result is compared in a paradigm of IER with CER, suggesting the outcome of weight loss and change in biomarkers of metabolic parameters. The evidence suggests that IER produce positive impact on weight loss and some positive but indirect effect on metabolic diseases.

Keywords: Weight Loss, Obesity, Overweight, Intermittent Fasting, Metabolism

1. Introduction

The World Health Organization (WHO) recently suggested the worldwide overweight (using BMI scale is between 24-27.9) and obesity (using BMI scale is ≥ 28) population as follows: in 2016, over 1.8 billion adults were considered as overweight, and over 650 million of the examined population were obese. Among the population, 39% were overweight and 12% were obese. From 1975 to 2016, the global obesity prevalence increased nearly threefold [1].

The current treatment guidelines of overweight/obess residents suggested that moderate energy restriction(ER) with a comprehensive medical intervention of life manner is an effective approach. Intermittent Energy Restriction(IER) is a succedaneous method to achieve loss in weight by restricting intake of energy [2], which consist fast days (20%-30% energy deficit) and fed days (no intentional restriction). Even though its role has been recognized by much evidence in preclinical study, the relationship between its impact on metabolic parameters, body weight, safety and tolerability lack a systemically study to demonstrate its values. This article analyzes their associations and provides insights into the advantages, disadvantages, and applications of IER.

2. The prevalence and harm of overweight/obesity

Overweight is concerned as being weigh more than is normal or necessary, which is having more body weight than what is considered as healthy for individual's age or body [3]. Overweight in adults can be measured by body mass index (BMI), the calculation method is dividing individual's weight (kg) by the square of height (m), a scale of 24-27.9 is concerned as overweight.

Obesity refers to excessive total fat content in organism and/or excessive partial fat content or abnormal distribution, which is a chronic metabolic disease influencing by factors from genetic, environmental dimensions and etc. According to BMI, a scale ≥ 28 is concerned as obesity.

With the rapid improvement of social economy residents' lives, the prevalence of overweight/obesity in China has shown an obvious upward trend. In 2016, more than 1.9 billion adults over the age of 18 worldwide are overweight, and more than 0.6 billion of the population are diagnosed as obesity. Also, it shows a trend of getting younger over time as the overweight/obesity rate of juveniles are 19% and 10.4% [2]. Currently, overweight/obesity has become a crucial public health-related issue which is seriously affecting people's physical and mental health. According to the latest national survey report, by 2020, the overweight/obesity rates of Chinese adults are 34.3% and 16.4%, 11.1% and 7.9% of juveniles of age 6 to 17, and 6.8% and 3.6% of juveniles under 6 years old, respectively [3]. Recently published studies predicted that by 2030, the overweight/obess Chinese adults will reach 65.3% and in juveniles is 31%. In preschool children (≤ 6 years old) will be 15.6 percent [4].

Obesity/overweight is believed by WHO as being associated with a greater risk of early expired and increases individual mortality. As a subject to the mass effect of excess adipose tissue and direct metabolic effect it brought, it is also associated with the development of various chronic disease, including diabetes mellitus, stroke, coronary artery disease, hypertension, respiratory disease, obstructive sleep apnea, osteoarthritis, gallstones and even tumors [5]. This can be shown by the study of Nutrition and chronic Diseases in China, the Chinese population who have chronic diseases is expanding, and shows sign of increasing, and proportion of death due to chronic diseases will also continue to increase.

Furthermore, according to many studies, it is known that obesity may have adverse psychological and social consequences for individual [3].

3. Overview of medical weight loss interventions

As the increasing number of overweight and obesity population, better management of a disease depends on effective prevention and treatment, and education management is one of the effective measures to prevent the occurrence of overweight and obesity. In today's era of rapid development of science and technology, education management can be carried out from individual, community, and policy levels in a variety of occasions in a variety of forms. For example, online small programs can be used to understand population status and carry out nutrition education courses. Carry out offline diet and nutrition consultation, skills learning courses, etc. One study showed significant reductions in BMI, body fat content, and blood sugar levels through a 3-month multimedia, interactive, and self-disinclined intervention [6]. Another study showed that BMI, total cholesterol, apolipoprotein, LDL, and TG levels were significantly improved in both the traditional management group and the NuTRI-Expert management system (an electronic nutrition education system), but the latter group had greatly higher dietary knowledge test scales comparing to the traditional management group [7].

Holistic lifestyle management refers to the simultaneous implementation of multiple lifestyle intervention strategies for overweight/obesity patients, including three main components: diet management, physical exercise, and behavioral intervention. Medical nutrition therapy is the basis of obesity treatment and dietary intervention, and is an indispensable measure to prevent and control obesity at any stage in its natural course.

4. Background and definition of IER

Dietary caloric restriction is the keystone in decades of efforts of weight loss, as being the main form of weight loss diet control. However, maintaining a constant caloric restriction to approach reduction

in weight it is hard for many individuals. Intermittent energy restriction (IER) is another dietary restriction method that has become popular in recent years for weight loss. In 2014, the concept of light fasting (also known as intermittent energy control) was introduced by British author Michael. Moseley, M.D., first proposed. Unlike continuous energy control, intermittent energy restriction (IER) could be considered as a pattern limiting calories intake over a specified period of time [8]. Then several studies have suggested that IER is effective supporting weight loss, but also plays a significant role in reducing metabolic diseases.

IER is a dietary pattern fasting or intaking limited calories over a standardized period of time following with certain standards. The commonly used IER methods including alternate day fasting (every 24 hours), 4:3 or 2:5 IER (fasting for 2-3 days every week on consecutive/nonconsecutive days). In the fasting period of IER, usually has an energy deficit of 20%-30% in fast day. In the group operating IER, it is suggested that body weight, body mass and body fat content were tremendously reduced, and even waist circumference was greatly reduced.

5. Preclinical studies of IER providing evidence

A set of weight loss IER-related studies performed in overweight and obesity (according to BMI) patients ≥ 18 years' old has been reviewed (See TABLE 1). In this all studies, IER is defined as IEF. It's because there always a major problem of lacking standard to define the term to describing various intermittent energy restriction methods. A group of expertise have considered intermittent fasting as the term to define "Periodical fasting in energy intake and periodical ordinary energy intake, the duration usually last long as a dietary pattern" [9]. The IMF describes fasting periods of short-term lasting from 2-21 days [9].

Table 1. Random clinical studies on weight loss in duration of 8-26 weeks in overweight/obese individuals with comparing IMF method with IER method.

Reference	Participants	Age(years)	BMI(kg/mm ²)	Duration	Interventions
Harvie et al., 2011 [10]	107 Female 0 Male 107 in total	30-45	30-45	26 weeks	IFM:25% calories restriction on 2 consecutive days every week; no restriction in the rest 5 days IER:25% restriction in 7 consecutive days every week
Schübel et al., 2018 [11]	75 Female 75 Male 150 in total	35-46	35-46	12 weeks	IFM: 80% energy restriction 2 non-consecutive days every weekday; no restriction in the rest 5 days IER: Continuous energy restriction at 80% Control No energy restriction
Catenacci et al., 2016 [12]	18 Female 8 Male 26 in total	18-55	≥ 30	8 weeks	IER 100% calories restriction on 2 non-consecutive fasting day; ad libitum on 5 fed days.

In general, the three studies last 8-26 weeks, and the IMF group standardized $\geq 60\%$ calories limitation on food restriction period, on intake time period is ordinary dietary pattern with intake at or above ordinary calories demands per day. All of them indicated the form used in IMF diet (25% of energy intake (EI) or specific calorie goals on 2 restricted days per week, with no restriction on rest the days) (TABLE 1) [10, 11].

A few preclinical studies didn't indicate the appropriate amount of exercise during the intervention. However, according to Chinese overweight/obesity medical treatment guideline (2021), the exercise recommendation of participants should maintain in physical activity levels [12]. Only the study of Harvie et al. indicated the recommended amount of exercise, by slowing gaining the strength [10].

Among those enrolled participants, their daily life lacks physical activity reaching underscore of healthy recommendation. These research show an inclination on female participants which most were pre-menopausal women, only few were older male war veterans. However, no suggestion indicates that attempts were made to account for the potentially confounding effects of phases of the menstrual cycle [9].

Table 2. IMR Method compared to IER group in weight loss and attrition in body fat.

Reference	Weight loss	Body fat
Harvie et al., 2011[10]	IFM: -6.4 ± 11.2 kg e	IFM: -20.8%
	CER: -5.6 ± 9.2 kg e	IER: -13%
Schübel et al., 2018[11]	IFM: $-7.1 \pm 0.7\%$ d	IFM: -4.1%
	IER: $-5.2 \pm 0.6\%$ d	IER: -6.1%
Catenacci et al., 2016 [12]	IFM: $-8.8 \pm 3.7\%$ e	IFM: 6.7%
	IER: $-6.2 \pm 3.1\%$	IER: 14.3%

Among the three studies, the difference in body fat loss shows no significant difference, except the Harvie's study (TABLE 2). The study showed a great success in weight loss by using IER [10]. The specific way of intervention is 2DW IER. Regimen which obligated low carbohydrates intake of 70% energy restriction and 40g carbohydrates, or obligated intake of libitum protein and monounsaturated fatty acid. Meanwhile, the other two groups, the Schübel and the Catenacci design the study differently [9, 12]. The Schübel et al. required only 75% energy deficit in 2 days fasting (fast day) and five regular days (fed day) [11]. And the Catenacci et al. required a standardized total nutrient complement (50% carbohydrate, 20% protein, and 30% fat) in two group, no matter during fasting or in regular day [12]. The Catenacci et al. has a more specific caloric distribution than other two groups, which is 20% breakfast, 30% lunch, 40% dinner, and 10% snack (only on fed day) [12].

6. Effect of IER on weight loss and lipid metabolism in overweight/obese individuals

Obesity is the expression of excessive fat in the body, which is intimately relating to disorder of lipid metabolism. Hyperinsulinemia and insulin resistance are not only the result of obesity, but also the main cause of lipid metabolism disorder in obese patients.

One study showed that IER reduced weight, body fat, and waist circumference in obese patients [13]. Meng's systematic review found that IER significantly reduced TC, LDL-C and TG levels compared with non-dietary control, and had beneficial effects on lipid metabolism, which may be related to the reduction of carbohydrate intake. CER is more effective than IER in reducing TC and TG levels, and the two diets can reduce LDL-C to the corresponding range. Subgroup analysis showed significant decreasing in TC and LDL-C levels among participants who consumed more than 50% of their daily calories requirements, but more stringent energy restriction did not further reduce these levels. In this study, it was found that IER had no significant change in HDL-C concentration compared with CER, but IER was better than CER in improving insulin resistance in the short term [14].

7. Effect of IER on glucose metabolism in overweight/obese patients

In addition to storing and utilizing energy, adipose tissue also secretes some bioactive mediators that regulate metabolism. Adipose tissue dysfunction is a key factor of obesity, associating to metabolic consequences. Inflammation and insulin resistance are considered as markers of adipose tissue dysfunction. Dysfunctional obese adipose tissue over releases FFAs, ROS, and PR inflammatory cytokines, thereby inducing an insulin-resistant environment, and the disruption of islet sensitivity and glucose homeostasis further increases systemic FFAs and lipid deposition [15]. Another study showed that IER caused weight loss and attrition of fat tissue, but no effect on fasting blood glucose and glycosylated hemoglobin was observed [13].

In nondiabetic overweight/obese individuals, IER can improve insulin resistance and insulin sensitivity, but its effect on blood glucose is uncertain. According to TABLE 2, it is showed that IER can improve insulin resistance and insulin sensitivity.

A systematic review by Cho assessing the effort of IER on BMI reduction and glucose metabolism in nondiabetic subjects suggested the IER method had improved glucose and insulin resistance compared with baseline values [16].

8. Details of preclinical studies

The three studies are operated under a well-rounded intervention containing intense performance aid in enrolled participants, which are given by an experienced interventionist. The recommendation of treating guidelines indicates intervention in life manner including intense performance aid provided in participants by experienced interventionist one to one [17].

9. Safety and compliance of IER in overweight/obese individuals

Studies indicates that IER strategies are harmless and easy-compliant, at the meanwhile weight loss of 3–8% is generated in overweight/obese adults with. Although, the three studies cannot sufficiently prove having equal values in weight loss or outcomes of chronic disease. The longest study lasted 26 weeks in duration but did not meet follow-up period, causing following concerns in whether how long and effective IER can last as a weight loss approach over time period.

The safety of tolerable is universally supported. Another study on the elderly population showed that the incidence of IER adverse events was low and most elderly people could tolerate it [18, 19]. Jebeile et al. conducted a study on IER intervention in obese adolescents (12-17 years old) for 26 weeks, which showed that TG level and adipose tissue content were significantly decreased after intervention compared with baseline data, and carotid intermedia thickness and vascular dilatation were also improved compared with baseline, indicating that IER is a possible and high-efficiency intervention among juveniles. However, there is still a lack of RCT studies with high evidence level on the effectiveness of IER in children [20]. Jospe et al. conducted an observational study on diet choice, compliance, and weight loss effect, including 250 subjects. 54.4% of subjects chose IF, 27.2% of subjects chose Mediterranean diet, 18.4% of subjects chose Paleo diet. At 12 months, only 54% of the IMF group, 57% of the Mediterranean diet group and 35% of the Paleo diet group were keeping to the diet [21]. This study showed that the adherence to IER diet was poor, and nutrition managers should strengthen the management of IER intervention population to improve the adherence.

10. Conclusion

In this passage, current studies have been summarized as evidence of IER as treatment for overweight and obesity. Specific medical treatment and interventions have been clarified. However, current studies could continue intentional behavioral aid and frequent records in weight loss and pathological outcomes after the interventional duration is over, in order to determine whether improvement in outcome is long-lasting. As a form of effective and safety dietary structure and medical dietary intervention, IER has sufficiency potential in reduce the burden of energy limitation, and help individuals achieving the goal of weight-losing, according to the studies shows its mentalism and physical outcomes of preclinical studies. The mechanism by which IER improves insulin resistance has not been clearly studied. In addition, the compliance of obese people with this model is poor. How to improve the compliance of patients is also the focus of future research of nutrition managers.

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