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Review

Timing of food intake: Sounding the alarm about metabolic impairments? A systematic review

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ABSTRACT

Growing evidence points to an association between timing of food intake and obesity in humans, raising the question if when to eat matters as much as what and how much to eat. Based on the new definition of obesity as a chronobiological disease, an unusual or late meal timing represent a circadian chronodisruption, leading to metabolic impairments.

Preliminary data from cross-sectional and experimental studies suggest that changes in meal timing can influence obesity and success of weight loss therapy, independently from total energy intake, dietary composition and estimated energy expenditure.

A systematic review of observational and experimental studies in humans was conducted to explore the link between time of food ingestion, obesity and metabolic alterations. Results confirm that eating time is relevant for obesity and metabolism: observational and experimental studies found an association between meal timing, weight gain, hyperglycemia and diabetes mellitus with benefits deriving from an early intake of food in the day in a wide range of individuals. Herein clinical, future perspectives of chronoprevention and chronotherapy of obesity and type 2 diabetes are also provided.

In conclusion, meal timing appears as a new potential target in weight control strategies, and therapeutic strategies should consider this contributor in the prevention of obesity.

Contents

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1. Introduction

In the last decade, a new relevant question has arisen: when to eat [1–3]. In addition to what and how much to eat, food timing represents a novel issue in our 24-h modern society, characterized by more exposure to artificial light, later food intake and bedtimes. Food is a major synchronizer of peripheral circadian clocks, and delayed feeding due to prolonged night-time wakefulness leads to desynchrony between central circadian and peripheral clocks [4].

Growing evidence points to an association between timing of food intake and obesity in humans, suggesting that changes in meal timing can influence obesity and success of weight loss therapy [1]. Also in animals, weight regulation is affected by the timing of food ingestion [5,6].

On this basis, obesity could now represent a "chronobiological disease" [7]. Differently from the time-restricted feeding pattern unintentionally practiced by our ancestors for thousands of years, the current trend is to shift most of the caloric intake later in the day [8]. In a few cross-sectional studies, an increased risk of overweight and obesity was found when a greater daily caloric intake was consumed in the evening [9–12], while a reduced risk was observed when consuming a larger proportion of calories at lunch or breakfast [9,11,13].

Even though the association between evening eating and body weight was not confirmed in a prospective US cohort, it was present in specific subgroups (smoking men, physically active men, inactive women) [14]. Another prospective study showed that late-night eaters had an increased coronary heart disease risk [15].

The clinical relevance of meal timing appears to be supported by its role in weight loss strategies. In a 20-week intervention study, as compared with early lunch eaters, late lunch eaters lost less weight independently from self-reported 24-h caloric intakes [16]. In overweight and obese women with metabolic syndrome, a 12-week weight-loss program with high caloric breakfast was more effective in reducing weight and waist circumference than an isocaloric diet with high caloric intake at dinner [17].

Aside from body composition and weight regulation, timing of food intake seems to have a negative impact also on metabolism. Eating lunch later in the day was associated with poorer insulin sensitivity assessed by HOMA-IR (Homeostasis-Model Assessment-Insulin Resistance) index [16]. Experimental studies showed a higher decrease in HOMA-IR after a high caloric breakfast *vs* dinner in women with metabolic syndrome [17] and polycystic ovary syndrome [18]. Late lunch eating was associated with decreased pre-meal resting energy expenditure, lower pre-meal carbohydrate utilization, and decreased glucose tolerance after mixed-meal test [19]. In another study exploring food-induced thermogenesis in the morning and evening, the same meal consumed in the evening determined a lower after-meal resting metabolic rate and increased, delayed concentrations of glucose and insulin [20].

These preliminary data suggest that consuming a larger proportion of total daily energy in the morning, as opposed to later in the day, might be more beneficial for weight loss.

The aim of this study was to perform a systematic review of observational and experimental studies comparing the effect of different food timing on body weight and metabolic outcomes in adults. The possibility to undertake a meta-analysis of the effects of the interventions on at least some of the outcomes was evaluated too.

2. Material and methods

This article is structured according to the preferred items for Systematic Reviews and Meta-Analyses (PRISMA) guideline [21].

2.1. Literature search strategy

The following electronic databases were queried using a combination of search terms: PubMed (National Library of Medicine), Trip database and The Cochrane Library, until 01 March 2017. The construction of the search strategy was performed using database specific subject headings and keywords. The search terms included combinations of "timing meal" or "timing meals" or "timing of food" or "food timing"; and Body Mass Index (BMI); obesity; weight; hyperglycemia; glycemia; insulin; insulin-resistance and type 2 diabetes mellitus (free-term and MESH as possible) (Appendix A).

These search strategies were supplemented by hand searching the bibliographies of all the included studies. Searches were limited to randomized controlled trials, parallel or cross-over, and observational studies in healthy volunteers or patients (e.g. individuals with obesity/overweight, polycystic ovary syndrome, metabolic diseases or other underlying diseases). We excluded studies performed in children.

2.2. Study selection

We included studies reporting comparisons of different timing meal interventions or habits (early eaters/late eaters or different timing of daily energy intake distribution) to reduce weight, insulinemic and glycemic areas-under-the-curve values and other metabolic variables.

Two review authors (SB, CM) independently scanned the abstract, title, or both, of every record retrieved, to determine which studies should be assessed further. All potentially relevant articles were investigated as full text. Any discrepancy about inclusion was resolved by discussing with a third review author (GB).

2.3. Data collection and extraction

For the trials that fulfilled the inclusion criteria, two authors independently abstracted key participant characteristics and reported data on efficacy outcomes using standard data extraction templates.

From each included study, information was extracted on:

- Characteristics of study participants (type of population, age, BMI);
- Type of intervention;
- Outcomes:
- Anthropometric variables (BMI, weight, waist circumference, total body fat, etc.);
- Metabolic variables (blood glucose values, triglycerides, total cholesterol, HDL and LDL-cholesterol, etc.);