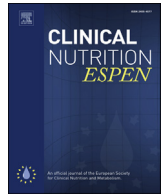




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Original article

Effect of whey protein supplementation on long and short term appetite: A meta-analysis of randomized controlled trials

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ABSTRACT

Specific components of dairy, such as whey proteins may have beneficial effects on body composition by suppressing appetite, although the findings of existing studies have been inconsistent. Therefore, a meta-analysis of randomized controlled trials was performed to investigate effect of whey protein supplementation on long and short term appetite. A systematic search was conducted to identify eligible publications. Means and SDs for hunger, fullness, satiety, desire to eat and prospective consumption of food, before and after intervention, were extracted and then composite appetite score (CAS) calculated. To pool data, either a fixed-effects model or a random-effects model and for assessing heterogeneity, Cochran's Q and I^2 tests were used. Eight publications met inclusion criteria that 5 records were on short term and 3 records on long term appetite. The meta-analysis showed a significant reduction in long term appetite by 4.13 mm in combined appetite score (CAS) (95% Confidence interval (CI): $-6.57, -1.96$; $p = 0.001$). No significant reduction in short term appetite was also seen (Mean difference (MD) = -0.39 95% CI = $-2.07, 1.30$; $p = 0.653$). Subgroup analyses by time showed that compared with carbohydrate, the reduction in appetite following consumption of whey consumption was not significant (MD = -0.39 , 95% CI = $-2.07, 1.3$, $p = 0.65$, $I^2 = 0.0\%$). A significant reduction in prospective food consumption was seen (MD = -2.17 , 95% CI = $-3.86, -0.48$). The results of our meta-analysis showed that whey protein may reduce the long and short term appetite, but our finding did not show any significant difference in appetite reduction between whey protein and carbohydrate in short duration.

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Introduction

Compared to 850 million underweight people in the world, about 1 billion are overweight or obese [1]. There are a continuing growth of obesity and diabetes in both sexes, all ages, races and educational levels [2]. Because of the strong association between overweight and obesity and several chronic disease such as diabetes, cardiovascular disease and certain cancers and the high economic burden of overweight and obesity on healthcare system and society, reversing the obesity epidemic is an urgent matter [1–3]. The maintenance of a reduced weight is very challenging due to the natural augmentation in the motivation to eat and reduction

of lean body mass and subsequently reduction in basal metabolic rate (BMR), as a result of a weight loss diet [4,5].

There are several studies that show dietary composition specially protein, affects appetite sensation, body composition and basal energy expenditure [6]. Whey protein is naturally formed during the production of cheese and accounts for 20% of the all protein in bovine milk. Several studies have shown that administration of this substance may lead to reduce several risk factors for metabolic diseases such as reduction in appetite sensation, food intake, hypertension, insulin resistance and oxidative stress [7].

Recent studies have shown that whey protein can suppress appetite and improve satiety at a subsequent meal (short-term appetite) [8–11]. It is suggested that whey protein is rapidly digested and increases level of amino acids in blood rapidly which, in turn suppress the food intake [12]. Moreover, whey protein releases several gut peptides such as cholecystokinin [13] and glucagon-like peptide 1 [14] which involve in satiety. However,

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some studies have examined its effect on long-term appetite (a few days or weeks after supplement therapy) [15–17]. Results of previous studies have been inconsistent and it is not clear if whey protein in compared with carbohydrate changes short- and long-term appetite. Then, the aim of this study is to investigate the effect of whey protein on some aspects of short and long term appetite including fullness, satiety, hunger, and desire to eat.

Methods

Search strategy and study selection

The present meta-analysis was registered in PROSPERO (International prospective register of systemic reviews, <http://www.crd.york.ac.uk/prospero>; CRD42016032575) and attempted to follow

$$CAS = \frac{\text{hunger} + \text{desire to eat} + (100 - \text{fullness}) + \text{prospective food consumption}}{4}$$

the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines in writing of this meta-analysis [18].

Literature search was conducted in MEDLINE and EMBASE databases from inception to November 3, 2015 for original human research articles. The following search terms were used: Whey protein (MeSH term) OR Whey (title/abstract) AND appetite (MeSH term) OR Satiation (MeSH term) OR Satiety (title/abstract) OR appetite (title/abstract) OR Fullness (title/abstract). The search was limited to English language, as well as the reference lists of studies that included into our meta-analysis, were searched.

Study selection and inclusion/exclusion criteria

Studies were eligible for inclusion if they fulfilled the following criteria: (1) were published articles, (2) applied clinical trial design on supplementation with whey protein, (3) recruited apparently healthy subjects in 18 years old or higher, (4) reported the scores of fullness, desire to eat, hunger, prospective consumption of food or combined appetite score, (5) administered carbohydrate as placebo for short term studies (for long-term we had no restriction for control group), (6) used visual analogue scale questionnaire (VAS) for assessing different aspects of appetite.

Exclusion criteria: (1) studies with combined supplementation of whey protein and dietary or lifestyle change and (2) studies on co-supplementation of whey protein and any other substance.

Data extraction and quality assessment

After searching the databases, two investigators (MM and MR) separately reviewed the publications by title and abstracts and then compared the outcome and resolved their disagreements by consulting a third researcher (SS-b).

The following characteristics were extracted from each included publication: study first author, year of publication, country that study has conducted in that, journal name, study design, characteristics of study population (for example sex, mean age, mean body mass index (BMI)), number of participants, dose and type of administrated whey protein and placebo, duration (for long-term studies), means and standard deviations (SD) of hunger, fullness, satiety, desire to eat, prospective consumption of food and combined appetite score, before and after intervention. Studies that had more than one stratum were considered as several studies. The

quality of publications was assessed by Jadad scales that assigns scores for randomized controlled trials [19].

Data synthesis and statistical analyzing

Within-subject comparison in appetite is more valuable than between-subject comparison then we used within-subject data for analysis [20].

For long term appetite

Means and SDs of hunger, fullness, satiety, desire to eat, prospective consumption of food, before and after intervention, were extracted and then composite appetite score (CAS) calculated by following equation [21]:

For within subject analyzing we used CAS at the baseline and after intervention in our analysis. Since VAS questionnaires usually are a 100-mm (mm) or 10-cm (cm) horizontal lines, and subjects placed a vertical mark on each horizontal line to indicate the intensity of each sensation felt [22], in this meta-analysis the unit of appetite changes is mm. In cases that appetite scores reported in cm, numbers were converted to mm.

If a standard error (SE) was reported in place of SD, we converted it to SD. for analyses by following equation [23]:

$$SD = SE * \sqrt{N}$$

In cases where data were not available in the published articles we contacted authors for additional information. Weighted mean difference (MD) for within changes in appetite was the primary outcome for analyzing the effects of whey protein on long term appetite. For short term appetite, MD was performed between intervention group and placebo group (carbohydrate). The Q test at the $p < 0.10$ level of significance for estimating existence of heterogeneity and I^2 test for quantifying the percent of heterogeneity were used. In the presence of significant heterogeneity, we used the random-effect model (the DerSimonian-Laird method) to calculate the pooled effect size. To investigate the effect of time of whey protein consumption on CAS, a subgroup analyses by time was conducted.

Results

Search result and study selection

The flowchart of literature search is shown in Fig. 1. Of 195 identified publications, after removing duplicated, 141 records remained for screening by title and abstract. A total of 102 records excluded because they were animal studies, reviews, observational studies. Some studies which administered whey protein with co-supplementation of another substance or with changing in diet or lifestyle also were excluded. 39 records were assessed for eligibility by reviewing full texts and 28 records excluded because of the age of participants (age of participants was under 18 years old), not eligible placebo groups and timing of studies (some studies assessed neither long term nor short term appetite, for example whey protein had administered before sleep and appetite had

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