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Probiotics for weight loss: a systematic review and meta-analysis☆

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ABSTRACT

The intestinal microbiota has been reported to be one of the potential determinants of obesity in recent human and animal studies. Probiotics may affect the gut microbiota to modulate obesity. This systematic review aims to summarize and critically evaluate the evidence from clinical trials that have tested the effectiveness of probiotics or foods containing probiotics as a treatment for weight loss. Literature searches of electronic databases such as PubMed, Cochrane Library, and EMBASE were conducted. Methodological quality was assessed using body weight and body mass index (BMI). Initial searches yielded 368 articles. Of these, only 9 met the selection criteria. Because of insufficient data, only 4 of the studies were randomized controlled trials (RCTs) that compared the therapeutic efficacy of probiotics with placebo. The meta-analysis of these data showed no significant effect of probiotics on body weight and BMI (body weight, n = 196; mean difference, –1.77; 95% confidence interval, –4.84 to 1.29; $P = .26$; BMI, n = 154; mean difference, 0.77; 95% confidence interval, –0.24 to 1.78; $P = .14$). However, the total number of RCTs included in the analysis, the total sample size, and the methodological quality of the primary studies were too low to draw definitive conclusions. Thus, more rigorously designed RCTs are necessary to examine the effect of probiotics on body weight in greater detail. Collectively, the RCTs examined in this meta-analysis indicated that probiotics have limited efficacy in terms of decreasing body weight and BMI and were not effective for weight loss.

1. Introduction

The prevalence of obesity has continuously increased worldwide over the last few decades. Obesity is a problem not only in terms of appearance but also as a trigger for development of metabolic diseases such as type 2 diabetes, cardiovascular diseases, osteoarthritis, and certain cancers [1]. Obesity is mainly associated with an impaired energy balance, the difference between energy intake and energy expenditure. However, changes in energy balance alone cannot explain the increased incidence of obesity [2]. Recent human and animal studies have shown the intestinal microbiota to be a potential determinant of obesity [3,4].

The intestinal microbiota plays an important role in physiologic regulation of metabolic functions in the host [3,5]. Some members of the intestinal microbiota affect

Abbreviations: BMI, body mass index; LPS, lipopolysaccharide; RCT, randomized controlled trial; WHR, waist-and-hip ratio.

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metabolic diseases, including obesity as confirmed by animal and human studies [5,6]. Gut microbial composition is strongly influenced by diet and in turn influences gut function [6]. Diet-induced weight loss and bariatric surgery result in significant changes in the gut microbial composition and can affect the success of weight control in the long term [7-9]. Recently, Le Chatelier et al [10] reported that obese subjects exhibited qualitative changes in the gut microbiota, namely, an increase in the phyla *Proteobacteria* and *Bacteroidetes*; a decrease in *Akkermansia muciniphila* (antiinflammatory bacteria); and an increase in pathogens, such as *Campylobacter* and *Shigella* [10]. These changes in the gut microbiota reduce the production of butyrate to decrease intestinal barrier integrity and increase mucus degradation and oxidative stress [10]. The increased levels of *Bacteroides fragilis*, *Clostridium leptum*, and *Bifidobacterium catenulatum* and decreased levels of *Clostridium coccoides*, *Lactobacillus*, and *Bifidobacterium* after dietary interventions are strongly associated with a significant weight loss, independent of total food intake [6,10]. Thus, changes in the microbiota play a crucial role in ensuring the efficacy of obesity treatments.

Probiotics are defined by the Food and Agricultural Organization and the World Health Organization as "live microorganisms, which when administered in adequate amounts, confer a beneficial health effect on the host." The genera *Lactobacillus* and *Bifidobacterium* have been reported to exert multiple beneficial effects on metabolic syndrome, such as weight loss, reduced visceral fat, and improved glucose tolerance in most animal studies and some in humans [11,12]. However, some studies have reported that probiotics do not exert beneficial effects and that prebiotics, "chemicals that induce the growth and/or activity of commensal microorganisms", are more useful, as the consumption of probiotics may not alter the gut microbiota in humans [13]. Two studies have suggested that beneficial species of the gut microbiota have important effects on modulating adiposity [14,15]. Although these studies suggested a potentially beneficial effect of probiotics on the changes of body weight and adiposity, the results are far from conclusive. However, probiotics have been advertised for lowering body weight. Therefore, a systemic review is necessary to more fully examine the clinical effects of probiotics on body weight and adiposity. No systematic review or meta-analysis has provided critical evidence regarding the potential benefits of probiotics in weight loss. Therefore, this systematic review aims to summarize and critically evaluate the evidence from clinical trials that have tested the effectiveness of probiotics or foods containing probiotics as a treatment for weight loss, either alone or in combination with other weight loss interventions, compared with no probiotics.

2. Methods and materials

2.1. *Search strategy, inclusion criteria, and selection of studies for the meta-analysis*

The selected studies were checked and reviewed independently by 2 researchers (SP and JHB). Any disagreement between the investigators in data abstraction was resolved by discussion. The following information about eligible articles was collected: probiotics used, study design, duration of intervention, sample size, subjects' characteristics, age dose of probiotics or their fermented dairy products, and results of the intervention in terms of body weight and body mass index (BMI). The full text of all studies was assessed for eligibility against the inclusion criteria. The search was limited to human studies but not restricted to any particular language. Eligibility criteria for considering studies for this review were as follows:

- Type of study: randomized controlled trial.
- Type of intervention: probiotics supplementation without restrictions regarding dose, route of administration, or dosage interval. The control was no probiotic supplementation or placebo.
- Type of outcome measure: BMI and body weight.

We designed the search strategy and performed independent, comprehensive searches of the PubMed, Cochrane Library, and EMBASE databases from their inception through December 28, 2014, using various combinations of probiotics and obesity as the search terms. MESH terms used were "probiotics" and "obesity," "weight control," or "weight loss." We included randomized controlled trials (RCTs) that compared the effects of probiotics (regardless of type, dose, and duration of treatment) with placebo in patients with obesity. Studies were included only if the 2 groups were treated equally except for the provision of the probiotic to the treatment group. Studies not meeting this criterion were excluded. We excluded studies involving pregnant females and infants. The review was carried out in accordance with the recommendations of the Quality of Reporting of Meta-Analyses (QUOROM) statement [16]. Data were also extracted on the number of participants, age, diagnostic criteria used for obesity, study subgroups, type and dose of probiotics, duration of treatment, and the relevant outcome measures used. The data included the type of study and funding, the characteristics of the population, intervention, outcomes, assessment of risk of bias, and statistical data. According to recommendations outlined in the Cochrane Handbook [17], we used the following criteria for assessing the risk of bias in randomized studies: inadequate sequence generation, inadequate allocation concealment, lack of blinding of participants and practitioners, incomplete of outcome data, selective outcome reporting, and other potential bias. The potential for bias in each study was judged as high, low, or unclear risk.

2.2. *Statistical analyses*

2.2.1. *Effect size*

The analysis was performed using Review Manager, version 5.3.3 (The Cochrane Collaboration, 2014, Nordic Cochrane Center, Copenhagen, Denmark). For continuous outcomes, mean difference (MD) and 95% confidence interval (CI) were calculated as summary statistics for the statistical analysis, and a fixed-effects model with the Mantel-Haenszel method was used based on the heterogeneity in outcomes across studies [18]. Studies that investigated the effects of probiotics on the body weight and BMI of subjects were selected, and articles were selected for meta-analysis if they fulfilled the following criteria: the study design comprised a double-blind study in which participants and