Probiotics in Metabolic Syndrome

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The aim of this systematic review is to evaluate whether the use of probiotics has any effect on the components of metabolic syndrome (MetS) before patients develop type 2 diabetes. A qualitative systematic review, following the Cochrane methodology, and a comprehensive literature search of randomized controlled trials (RCTs) were conducted in PubMed and Scopus from inception until 4 July 2019. According to our inclusion criteria, nine clinical studies were finally analyzed, corresponding to six RCTs. Probiotics intake in patients with MetS resulted in improvements in body mass index, blood pressure, glucose metabolism, and lipid profile in some studies. Regarding inflammatory biomarkers, probiotics also positively affected the soluble vascular cell adhesion molecule 1 (sVCAM-1), interleukine-6 (IL-6), tumor necrosis factor α (TNF-α), vascular endothelial growth factor (VEGF), and thrombomodulin. Despite the diversity of the published studies, the intake of probiotics for patients with MetS may offer a discrete improvement in some of the clinical characteristics of the MetS and a decrease in inflammatory biomarkers. Nevertheless, these beneficial effects seem to be marginal compared to drug therapy and a healthy lifestyle and clinically non-relevant.

Metabolic syndrome Obesity Probiotics

1. Introduction

Obesity is increasing worldwide and is associated with the development of metabolic syndrome (MetS), which is a cluster of cardio-metabolic risk factors and comorbidities conveying high risk of both cardiovascular disease (CVD) and type 2 diabetes. MetS is characterized by increased white adipose tissue and insulin resistance, which leads to an expanded risk of CVD. According to the International Diabetes Federation (IDF), MetS is defined by the presence of central obesity plus any two of the following four factors: Raised triacylglycerols (>150 mg/dL) or specific treatment for this lipid abnormality; reduced high-density lipoprotein cholesterol (HDLc) (<40 mg/dL in males, <50 mg/dL in females) or specific treatment for this lipid abnormality; raised blood pressure (BP) (systolic BP > 130 mm Hg or diastolic BP > 85 mm Hg) or specific treatment for previously diagnosed hypertension; raised fasting plasma glucose (FPG > 100 mg/dL) or prediabetes.

In recent years, it has become apparent that the alteration of the gastrointestinal microbiota composition can contribute to the development of insulin resistance associated with obesity. The gastrointestinal microbiota constitutes the set of microorganisms that reside in the gastrointestinal tract. The vast majority of microbes that exist in the human gastrointestinal tract live in the colon. More than 90% of all bacterial phylogenetic types belong to only two of the 70 divisions known (phyla) in the bacterial domain: Bacteroidetes and Firmicutes.

In this regard, a decreased ratio of Bacteroidetes/Firmicutes has been described in obese compared to lean subjects. However, there is a lack of consistency among studies. It has been recently hypothesized that low microbial gene richness is a good marker for MetS. Also, an aberrant gut microbiota can promote subacute systemic inflammation, resistance to insulin, and increased risk of CVD, due to mechanisms' exposure to bacterial products, namely bacterial lipopolysaccharide (LPS).

Furthermore, it has been proposed that probiotic intake may ameliorate some of the clinical components of MetS. The term probiotic is currently used to describe bacteria associated with beneficial effects for humans and animals [FAO/WHO Expert Consultation 2001]. The most accepted definition of probiotics is "live microorganisms, which when consumed in adequate amounts, confer a health effect on the host". However, discrepant data regarding the health benefits of probiotics on metabolic diseases have been described. Some of the studies have found a beneficial effect in some of the components of MetS (BP and lipid profile), whereas contradictory results have been described on their effect on BMI in adult population. These differences can be partially explained because of different study designs and the use of different probiotic strains, dose, and administration form.

For this reason, and to summarize the current status of the available evidence, our group has performed a systematic review of randomized controlled trials (RCTs) in MetS. This review aimed to answer the question: "Does the use of probiotics have any effect on the components of MetS as defined by the IDF before the development of type 2 diabetes?"

2. Role of Probiotics in Metabolic Syndrome

According to the available data, most of the analyzed articles describe that the addition of probiotics to the treatment of patients with MetS may offer a discrete advantage to the current medical treatment in terms of improvement of some, but not all, of the clinical characteristics of the MetS and related inflammatory biomarkers. Although we cannot conclude that probiotics exert beneficial effects, they may have some positive effects that are marginal compared to drug therapy and a healthy lifestyle, and probably dose- and strain-specific. Also, the duration of the interventions may have not been long enough to prove the decrease in MetS associated complications.

For this reason, there is a need for better RCTs in humans with MetS able to fully elucidate if probiotics can be actually used as a coadjuvant therapy for this pathology. In this sense, we suggest following these recommendations when designing RCTs: (1) A crossover design is a more appropriate approach to determine the health benefits of clinical interventions than a parallel design. (2) RCTs should be designed with a more appropriate estimation of the size and statistical power, duration, type of strain, dose, and mode of delivery. (3) Finally, special caution should be taken in the interpretation of results so as to not confound statistical significance with biological relevance or strength of evidence.