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The Role of Microbioma in the Weight Control

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Abstract

Obesity is an evolutionary, chronic and relapsing medical condition, which consists of a pathological accumulation of adipose tissue, in absolute and percentage values, in relation to lean mass, to an extent that negatively affects the state of health. It is a real metabolic disease, which compromises the regulation of appetite and energy metabolism. Obesity is spreading among adults and children and is the leading cause of preventable death worldwide - one of the most serious public health problems of the 21st century. Overweight and obesity cause physical disability and reduced working capacity and predispose to the onset of numerous chronic diseases related to the metabolic syndrome, of which obesity is a constituent part. The consequences of obesity fall into two broad categories: pathologies attributable to the effects of increased body fat mass (such as osteoarthritis, obstructive sleep apnea or social stigmatization) and those due to the numerical increase in adipose cells (diabetes, dyslipidemia, cancer, cardiovascular disease, non-alcoholic fatty liver disease).

This "global epidemic" affecting 50% of the adult population of industrialized civilizations. According to data provided by the WHO, the number of obese people in the world has almost tripled since 1975; in 2016, over 1.9 billion adults, aged 18 and over, were overweight; of these over 650 million are obese. In addition, 41 million children under the age of 5 are overweight or obese. This led the European Association for the Study of Diabetes (EASD) to recognize the importance of obesity prevention and treatment, considered "the most important public health problem in the world".

Today, a new thought is emerging, born from innovative and recent scientific discoveries, which attribute to the intestinal microbiota a direct responsibility for the management of body weight. In fact, more and more numerous studies show that the balance of the microbiota is a crucial element in ensuring the correct intestinal absorption of macronutrients by the human body.

Below we report a possible relationship between microbiota and weight control.

Keywords: *diet, microbiota, overweight, obesity*

Introduction

Obesity is a condition characterized by an excessive accumulation of body fat, generally due to incorrect nutrition and a sedentary life, which can adversely affect both the quality and life expectancy. In recent years, awareness has grown that a balanced weight is a necessary condition for good physical and mental health. On a psychological level, in fact, obesity can completely upset a person's life: those who are obese are often isolated and can run into anxiety and depression. In particular, overweight children tend to develop a difficult relationship with their body and with their peers, with consequent isolation which often results in further sedentary habits. Obesity can also be the result of genetic risk factors and, although studies are still preliminary, given the multifactorial nature of obesity, it is likely that there are combined genetic factors capable of promoting or not the ability to lose weight and keep it low [1,2].

Other health problems associated with excess body weight are: hypertension, hypercholesterolemia, sleep apnea and respiratory problems, asthma, increased surgical risk, complications in pregnancy, hirsutism and menstrual irregularities. A particularly serious problem is that of the onset of obesity among children and adolescents, exposed since childhood to respiratory difficulties, joint problems, reduced mobility, but also digestive and psychological disorders. Those who are obese in childhood are often obese as adults: the risk of developing cardiovascular risk factors (hypertension, coronary heart disease, tendency to heart attack) and conditions of impaired metabolism, such as type 2 diabetes or hypercholesterolemia [3,4].

The main treatment is prevention: in order to control the weight, we need to adopt healthy lifestyles, i.e. proper nutrition and adequate physical activity. In the diagnosis of obesity and especially in all subsequent therapies and dietary treatments, it is necessary to avoid self-diagnosis, but to rely on a specialist. The treatment consists in reducing body weight, under close medical supervision and in specialized centers and in maintaining a weight appropriate to one's height [5,6]. Alongside the diet, which must be studied on the individual, physical activity (appropriate to the type of patient) and possibly also behavioral therapy must be combined. Furthermore, according to American guidelines, in more complex cases, drug therapy can also be combined for periods ranging from 6 months to one year. The use of surgical interventions is instead recommended only in extreme cases, for those patients who present acute obesity (with BMI> 35-40) and other associated pathologies, which are at high risk of mortality, or who do not respond to other treatments [7].

However, long-term treatment is very problematic and requires an integrated approach, which uses the tools available in a complementary way, making use of different professional skills, which share the same therapeutic objective [8]. It is now an established and commonly accepted opinion for many years that, in order to face the obesity epidemic, it is necessary to resort to various therapies (nutritional, cognitive-behavioral, pharmacological and surgical), differently combined in the individual patient [8]. The clinical goal must be to reduce body weight sufficient to significantly improve the risks associated with obesity, especially cardiovascular ones. However, when this first strategy is insufficient or completely ineffective, it is possible to resort to drug therapy, taking into account that a chronic disease such as obesity must be managed flexibly and that the treatment must be as much adapted as possible to the individual patient, as underlined by the new guidelines 2016-1017 of the Italian Obesity Society (SIO) and of the Italian Association of Dietetic and Clinical Nutrition (ADI) [8].

Methods and Results

Today, in addition to these causes widely demonstrated over the years by scientific studies, a new thought is emerging from innovative and recent scientific discoveries, which attribute to the intestinal microbiota a direct responsibility for the management of body weight. In fact, more and more numerous studies show that the balance of the microbiota is a decisive element in ensuring the correct intestinal absorption of macronutrients by the human body. But what is the intestinal microbiota and why is it so important? It is the set of microorganisms (bacteria, viruses, fungi and

protozoa) that populate the digestive tract with different densities and "demographics". The ability to metabolize substrates that affect digestive processes and immunological mechanisms makes this community a factor capable of influencing not only intestinal pathophysiology, but also that of all other systems of the body.

Metagenomic studies in obese patients have made it possible to highlight how obesity is associated with an imbalance of the bacterial flora, with the proliferation of potentially pathogenic bacteria. The alteration of the microbiota, in fact, can affect the metabolism and energy homeostasis of the host, being also involved in the control of body weight through the extraction of an additional amount of calories from ingested food [9]. Among the mechanisms that can explain what has been observed there is that linked to the extraction of energy from food components such as polysaccharides (cellulose, hemicellulose, non-digestible starch, pectins, gums) which are processed by bacterial enzymes with the production of monosaccharides (subsequently absorbed) and short-chain fatty acids (SCFA, mainly acetate, butyrate and propionate) that participate in the breakdown of fats in the liver, through the expression of some key enzymes such as acetyl-CoA carboxylase (ACC) and fatty acid synthase (FAS). The conversion of fermentable dietary fibers into SCFAs therefore provides additional energy for the host, suggesting the possibility of being able to promote obesity in this way [10].

In the context of digestive processes we can make a rough distinction between fermentative flora able to digest starch and other polysaccharides, and putrefactive flora involved, in fact, in the process of putrefaction, anaerobic metabolization of peptides and proteins (elastin and collagen from food sources, pancreatic enzymes, exfoliated epithelial cells and lysed bacteria) which determines the production of SCFA but also of potentially toxic substances including: ammonia, amines, phenols, thiols and indoles [9]. The intestinal epithelium is covered in all its extension by a double layer of mucus, internal and external, secreted by the goblet cells and filled with mucins. These are glycosylated proteins that allow the intestinal mucus to perform a lubricating, trophic and protective action against the epithelial cells of the mucosa itself. Its concentration strictly depends on a dynamic and delicate balance between synthesis, secretion and degradation of the mucins that constitute it.

Akkermansia muciniphila (Phylum Verrucomicrobia) plays a fundamental role in this equilibrium: Gram-negative, anaerobic, non-motile, non-spore-forming and oval-shaped bacterium, is able to use gastric mucins as the only source of carbon and nitrogen and it represents 1-5% of the intestinal microbiota. A recent study has defined the protective role of Akkermansia muciniphila against the development of metabolic diseases [11]. The abundance of this muco-degrading bacterium is inversely related to body weight in both humans and rodents [11], while it is negatively associated with both Type 1 [12] and Type 2 diabetes [13].

Literature data have shown that the administration of prebiotics, such as FOS, and probiotics, such as Bifidobacterium Animalis ssp. lactis LMG P-28149, are able to determine an increase in Akkermansia Muciniphila [14], with consequent improvement of the metabolic profile, reduction of fat mass, metabolic endotoxemia, adipose tissue, inflammation of the tissue adipose and insulin resistance. These studies explain why patients often assimilate foods with a different efficiency and therefore develop a different body composition on the same diet. This can happen both in the case of a classic Mediterranean diet and during low-calorie diets, slowing down or preventing the entry into ketosis and therefore weight loss. Enterococcus, lining the intestinal mucosa, creates a barrier against various pathogens (eg Clostridium) by inhibiting their growth through a numerical overwhelming mechanism, acidifying the environment and producing bacteriostatic and bactericidal substances.

Enterococcus Faecium causes an increase in the immunization capacity of the intestine and improves the multiplication of beneficial flora. It is combined with Bifidobacterium with known probiotic properties able to restore eubiosis. When proteins act as growth factors for some species of bacteria with a mechanism strictly dependent on the amino

acid composition, thus confirming the important role played by the quality of the protein [15,16]. Vitamins and minerals are an important support for many metabolic processes and also support the immune system. Studies show how Lactobacillus Gasseri strain LG050, Lactobacillus Reuteri strain PBS072 and Lactobacillus Acidophilus strain LA001 intervene on the metabolism of lipids and carbohydrates, reducing the concentration of lipase, HMG-Co A reductase, α amylase and α glycosidase. The effect is to have a lower absorption of sugars, a stimulus to the oxidation of carbohydrates and an improvement in glucose tolerance. Furthermore, the specific formulation allows to keep blood cholesterol levels under control, reducing the markers of hyperlipidemia and hypercholesterolemia and the volume of abdominal and subcutaneous white adipose tissue. Probiotic supplements are an enhancer of the typical symptoms associated with obesity and systematic inflammation such as constipation and abdominal bloating.

Conclusions

The use of probiotic supplements containing prebiotic components that targets the microbiota is emerging as a promising intervention in the global nutritional approach to reduce obesity. Weight loss resulting from low-carb, high-protein diets can be significant but has also been linked to potentially negative health effects due to increased bacterial fermentation of undigested protein in the colon and subsequent changes in microbiota composition. intestinal. Probably a dysbiosis situation to be corrected. This was verified by a placebo-controlled clinical intervention study evaluating the effects of a synbiotic supplement on the composition, richness and diversity of the gut microbiota and the associations of microbial species with body composition parameters and biomarkers of obesity in 20 participants in a weight loss program (10 with supplement, 10 checks). The probiotic component of the synbiotic used in the study contained Lactobacillus acidophilus, Bifidobacterium lactis, Bifidobacterium longum, and Bifidobacterium bifidum, and the prebiotic component was a mixture of galactooligosaccharide.

Results showed no statistically significant differences in body composition (body mass index, BMI, body fat mass, body fat percentage, lean body mass and bone mineral content) between the placebo group and the group with the integrator at the end of the clinical trial (3 months). Symbiotic supplementation increased the abundance of gut bacteria associated with positive health effects, particularly Bifidobacterium and Lactobacillus, and also increased gut microbiota richness. At the end of the trial, a decreasing trend in gut microbiota diversity was observed between the placebo group and the synbiotics, which may imply the effect of the high-protein, low-carbohydrate diet used in the weight loss program. Regression analysis performed to correlate species abundance after supplementation with body composition parameters and obesity biomarkers found an association between a decrease in blood glucose over time and an increase in Lactobacillus abundance, in particularly in the synbiotic group. Decreases in body mass, BMI, waist circumference and fat mass over time have been associated with a decrease in Bifidobacterium abundance. The results obtained support the conclusion that the symbiotic supplement used in this clinical study modulates the human gut microbiota by increasing the abundance of potentially beneficial microbes [17].

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