Intestinal Dysbiosis in Adult Women: How to Prevent?

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Abstract

Changes in the intestinal microbiota have been associated with inflamatory diseases, leaky-gut, obesity, Cardio-metabolic diseases, breast câncer, polycystic ovary syndrome and stress-related disorders, mainly depression, anxiety, attention deficit and irritable bowel syndrome. From the balance of the microbiome, it is possible to achieve an immunological and metabolic balance and, consequently, there will be, in a practical way, the control of microbial proliferation, mainly of pathogenic bacteria. Intestinal modulation can stimulate the immune system, regulate the absorption and digestion of nutrients, produce compounds necessary for tissue renewal, in addition to minimizing metabolic, autoimmune and behavioral diseases.

Intestinal Microbiome and Intestinal Dysbiosis

The intestinal microbiome is defined as the collective genomes of microorganisms that inhabit the intestinal tract [1]. The intestinal microbiota can cause changes that may be related to the brain, thyroid, lung, stomach, intestine, kidneys, liver, heart, skin, adipose tissue, metabolic changes or even autoimmune diseases [2].

Bacteroidetes, Firmicutes, Actinobacteria and, to a lesser extent, Proteobacteria, are part of the human microbiota, and in other organs, in order to maintain the proper functioning of the intestinal microbiota, a balance between the species of bacteria that compose it is necessary. Large changes in the proportion between these phyla or the expansion of new bacterial groups lead to a disease-promoting imbalance, also known as dysbiosis [3]. A reduction in the diversity and bacterial growth of Proteobacteria are characteristic of dysbiosis. Dysbiosis can be a trigger for inflammatory diseases, for low-grade intestinal inflammation or even for the so-called Leaky Gut.

Diseases Associated with Intestinal Dysbiosis

Obesity

Dysbiosis may be related to the occurrence of metabolic diseases such as obesity. Crusell MK, et al. (2018) [4] demonstrated a reduction in the survival rate of Akkermancia muciniphila associated with obesity. In addition, the same study proves that the occurrence of type 2 diabetes associated with a qualitative dysbiosis, especially in pregnant women, can generate metabolic consequences, such as a reduction in the production of short-chain fatty acids [4].

Cardio-metabolic Diseases

When there is a higher survival rate of microorganisms that decarboxylate amino acids, the individual will have a greater exposure to trimethylamine, which is a metabolite derived from the decarboxylation of carnitine or from degradation of choline [5]. Trimethylamine, when absorbed and reaches the liver, is converted by a liver enzyme called flavin monooxygenase that transforms trimethylamine into trimethylamine oxide, decreasing the reverse transport of cholesterol and may be involved in the cause of cardiovascular diseases, more mainly related to arteriosclerosis [6].

Cardiac impairment can also occur due to changes in the microbiota, leading to a reduction in mucin production and rupture in tight junctions, which would promote a permeability to the lipopolysaccharide (LPS) of pathogens, also called molecular patterns associated with microorganisms [7]. This exposure to LPS causes a connection to occur in receivers called *Toll Like Receptor* (TLR) [8]. Specifically, LPS has an affinity for TLR4 which promotes an activation of MYD88 which in turn stimulates NF-κB, stimulating pro-inflammatory cytokines, with low-grade inflammation and a greater likelihood of obesity, diabetes, cancer and cardiovascular diseases [9].

The Impact of Dysbiosis on Breast Cancer

Breast cancer is a carcinoma characterized by atypical cell proliferation with loss of cell differentiation [10]. In 2018, it corresponded to approximately eleven percent of new cancer cases per year in the world, in both sexes and at all ages, proving the importance of studies related to this neoplasm [11].

There are several risk factors for the development of breast cancer, such as age, endocrine and metabolic factors, obstetric gynecological history, behavioral, environmental and genetic factors [12]. Women over 50 years of age, who were exposed to estrogenic stimulus-endogenous, by early menarche and late menopause, or exogenous, by the use of oral contraceptives-, who ingest alcoholic beverages, smokers, overweight in the post- menopause and who have been exposed to ionizing rays, are especially favorable to this evolution.

According to National Cancer Institute (2020), genetic factors are associated with the mutation of the BRCA1 and BRCA2 genes, representing only five to ten percent of total breast cancer cases. In contrast, physical activities, successful pregnancies and lactation are protective factors for this neoplasm. The microbiota has an extreme influence on carcinogenic progression, due to metabolic effects and its action on neutrophils. The symbiosis provided by the intestinal microbiome and the other systems of the human body is a protective factor for the development of cancer, and dysbiosis is a factor that induces the progression of breast cancer through the loss of homeostasis [13]. In addition, in the breast tissue, the microbiota is also dependent on food and genetic factors, being an important modulator of the risk and development of breast cancer [14,15].

Microbiota and Polycystic Ovary Syndrome

Tremellen K, et al. (2012) [16] already hypothesized that microbiota dysbiosis may have an effect as a causal agent of polycystic ovary syndrome. The diet high in fat and sugar and low in fiber can lead to dysbiosis promoting a condition of leaky gut, thus having a greater permeability to LPS triggering an inflammatory effect which initiates a mechanism of resistance to insulin [17]. This condition activates the whole cascade of reactions that lead to Polycystic Ovary Syndrome (PCOS) [18]. Dysbiosis correlates with metabolic disorders, more specifically with insulin resistance, and with hyperandrogenism stimulated by the hypothalamic-pituitary and gonad (HPG) axis [19]. Treatment options involve a balanced diet, prebiotics, probiotics and symbiotics. In GALT (gut-associated lymphoid tissue) ILC3 stimulates IL-22 which causes more antimicrobial peptide to go into the intestinal lumen, causing a greater defense of this intestinal epithelium, in addition, beta glucans stimulate the production of defensins that ensures homeostasis of the intestinal epithelium and stimulates defense [20,21, and 22].

Intestinal Microbiota Versus Mental Health

It is known that some factors can influence mental health, including the intestinal microbiota. According to Inserra A, et al. (2018) [23], there is a way of interaction between the intestine and the brain that operates in both directions, these interactions occur through several mechanisms, mainly through the vagus nerve, immune system and the metabolism of resident bacteria. The effects of this communication network are combined, so the psychiatric pathophysiology and the maintenance of this network can undoubtedly contribute to satisfactory effects of mental health, since the composition of the intestinal microbiome influences behavioral responses and stimuli of stress, anxiety, depression, among other psychocognitive situations [24].

The Central Nervous System (CNS) and the various branches that compose it are influenced and regulated by the gut-brain axis, so when the microbiota is healthy, the axis is kept stable, the relationship between the microorganisms of the flora and the host occurs benefiting both. However, any problem in this relationship leads to dysregulation of the metabolism, generating negative consequences, among which are

the metabolic and neural endocrine disorders, in the latter, triggering factors for mental disorders are present [25]. According to Wiley NC, et al. (2017) [26], the physiological mechanisms of the human organism are affected when there is no necessary balance in the gut-brain axis, which concerns the intercommunication between the gastrointestinal tract and the central nervous system, so psychiatric illnesses can be developed from undue responses of the immune system, which increase the amount of inflammatory mediators inappropriately [26].

The hormonal, immunological and physiological relations existing between the brain and the intestine have been known for more than three decades and the concept of microbiota-intestine-brain axis has been polished over the years, with the contribution of several areas of science, which try to understand this phenomenon. The knowledge about the influence of the Central Nervous System on the intestine, such as the regulation of mucus and hormone production, in addition to the control of smooth muscle motility and immune role, has been put in place for longer, already the answer offered by the System Enteric Nervousness (ENS), given this influence, is more recent [27]. The ENS has the ability to modulate the CNS, as it is modulated by it, occurring a set of interconnected factors: the peripheral neural network of the gastrointestinal system, the microbiota that resides in it and the metabolites or compounds produced by the system and the microorganisms. Beneficial bacteria, inhabitants of the intestines, are able to metabolize important compounds, which have a regulatory role, such as neurotransmitters, such as serotonin and gamma-aminobutyric acid (GABA), which are essential in balancing mood and depressive and anxiety disorders [26].

Changes in the intestinal microbiota have been associated with stress-related disorders, mainly depression, anxiety, attention deficit and irritable bowel syndrome [28]. Liang S, et al. (2015) [29] suggest that the use of *Lactobacillus helveticus* and *Bifidobacterium longum* is associated with the relief of feelings of anguish, depression, anger and anxiety. Corroborating with these data, Costa et al described that the use of Lactobacillus casei helps to improve mood and anxiety symptoms [30]. In addition, Maehata H, et al. (2019) [31] demonstrated that the use of *Lactobacillus plantarum* reduces the symptoms of depression.

Forms of Prevention

It is essential to have a nutritional strategy, with the greatest possible diversity, avoiding ultra-processed foods and giving a large supply of prebiotics, which in turn will promote the health of the microbiota with the growth of beneficial bacteria, promoting a diversity of the microbiota and consequently greater production of short-chain fatty acids that act on receptors called GPR-43 that promote in L cells (enteroendocrine cells) the increase of PYY and GLP-1 peptides and consequently improve the biochemical marker [32].

There is a change in the metabolic profile from this adaptation of the microbiota from a more adequate diet. Through the Mediterranean or Plant Based Diet or even a diet based on raw foods, rich in fiber, it is possible to reestablish the origin of food and escape the main cause of metabolic changes in the modern world that is derived from a Western standard diet or from fast food diet [33]. If you have a western standard diet, the individual evacuates less and this causes a change in the substrates that are metabolized by this microbiota and this can cause a change in metabolism [2].

There are changes that can be made in the gastrointestinal tract, with the use of multi-strain probiotics, through food choices that will cause us to have less insulin resistance, less inflammatory diseases,

more short-chain fatty acids. And when there is a Western standard diet, there is a whole change in insulin sensitivity, as well as an increase in the inflammatory process [34].

The balance in metabolism and immune diseases is achieved with a change in lifestyle. This is the gear that has to change, so that the microbiota changes, and potentiates the metabolism and blocks inflammatory and autoimmune diseases. Therefore, it is important to consider all the changes that will be necessary regarding the indiscriminate use of industrialized food, regarding urbanization, regarding water quality, regarding the use of antibiotics indiscriminately, or even with family life [35].

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