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Review Article

Age in Older Adults Alters Intestinal Microbiota

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Abstract

Aging is related to changes in the intestinal microbiota that are associated with physiological modifications of the gastrointestinal tract and changes in dietary patterns, together with a deterioration in cognitive and immune function, contributing to the frailty of the elderly.

We carry out a comprehensive analysis, where the physiological bases that occur to generate countless alterations are observed, which can, if not be completely removed, if minimized, so that these human beings, who have almost always left something positive to the Society, they are reimbursed, at least, a little of the much they gave.

Basic concepts about the Intestinal Microbiota are determined, which is the organ of shock in these patients, as well as its frequent dysbiosis, as a preponderant factor of the changes that occur.

Intestinal Microbiota Transplantation is approached as an accepted procedure in not only the management of Clostridiodes *difficile*, but also of a good number of pathologies.

Keywords: *Elderly (E); Intestinal Microbiota (IM); Microbiota (M); Fecal Microbiota Transplantation (FMT); Intestinal Microbiota Transplantation (IMT)*

Introduction

The health problem that older people is immense, so we must be well informed, to reduce the different conditions that occur in them, more than anything, as an obligation, for what they have contributed beneficially to society, during his lifetime. We include in the present work the population known as Young Older Adults, which includes people between 60 and 74 years old; The elderly (E) from 75 to 84 years. To long-lived older Adults from 85 to 99 years old. To the centenarians, those who exceed the age of 100 years. Although the United Nations calls them as Older Adults when they begin to live in their 60s and old or E at the beginning of 75 years and after 90 years, great old or long-lived [1].

It is time to act, as huge changes will be seen, as only people over 60 years will double before 2050 [2].

Not all patients should be treated the same, but it will depend on the comorbidities they present, as well as their health status. What if we are going to analyze as a whole, are the different stages of the Microbiota (M), especially the Intestinal, due to the enormous impact it has on these characters, by generating alterations in the digestive, immunological and cognitive systems [3].

Once we have delved into the analysis of the M, we will address dysbiosis, due to the enormous relationship it has with the E and we will look for what to do so that this alteration affects to a lesser degree in these patients and not only in the respiratory system [4].

We will delve into the analysis of Fecal Microbiota Transplantation (FMT), as well as its indications, methodology, the experience that exists in E, in which conditions it is useful and what its future will possibly be [5]. The same is carried out with probiotics, prebiotics and symbiotics, as well as postbiotics and paraprobiotics [6,7].

We conclude with 5 points, really relevant.

Intestinal microbiota (IM): Set of microorganisms: bacteria, eukaryotes, viruses and archaea present in a defined environment. The one that is located in the intestine, is called Intestinal Microbiota [8].

The composition of IM will depend on several factors, first of all the conditions that occur, which can be: Irritable Bowel Syndrome, Obesity, Inflammatory Bowel Disease, as well as the degree of inflammation [9]. Generally, the *Bacteroides* phylum is the most abundant, followed by the *Firmicutes* phylum, with *Clostridium* appearing in abundance [10]. *Proteobacteria* and *Actinobacteria* can be found. The M of each person constitutes a unique and unrepeatable profile [11]. It weighs about four pounds and in addition to bacteria it is made up of viruses and fungi, within the latter the genus *Candida* predominates [12]. High-throughput amplicon pyro-sequencing is the method of choice for determining microbial phylotypes. The M is known as a "second genome" because it includes microorganisms, genomic DNA, proteins, and metabolites. IM in the elderly is related to decades ago, since in the baby it stabilizes around 6 to 36 months. From then on it changes to a more complex adult pattern, which remains stable for a long time, until reaching old age, where extreme variability of the super-organ appears [13]. These intense changes will appear depending on the environment, lifestyle, genetics, ethnicity, the administration of medications, especially antibiotics and diet [14].

IM is affected by various diseases, as well as health problems [15].

Long-term diet changes, surgery, inflammation, and old age also play a role. It is not clear whether changes in the M are a consequence or cause of aging. We must not forget the bidirectional communication between the IM and the brain, through the gut-brain axis, which plays a significant role in brain activity and the gastrointestinal tract [16,17]. With aging, IM produces significant imbalances in major phyla, such as the anaerobes *Firmicutes* and *Bacteroidetes*, as well as in a diverse range of facultative organisms, resulting in impaired immune responses [18]. The diversity of IM and commensals: *Bacteroides*, *Bifidobacteria* and *Lactobacilli* decreases, while the opportunistic: *Enterobacteria*, *C. perfringens* and *C. difficile* increase [19].

To strengthen the intestinal microbiota and reduce the risk of disease, it must be strengthened throughout life, administering an adequate diet; exercise according to age and add probiotics, prebiotics, and symbiotics, as well as postbiotics and paraprobiotics [20-22].

We must establish strategies to improve the health in the E. For this, it is necessary to conserve the M, which would delay or prevent various diseases. The use of metagenomic tools and high-throughput sequencing will be the bases in the immediate future to understand the role of microorganisms in disease and health [23]. This will give us the bases to know which microorganism is doing what, how and why, anticipating the presence of diseases, in order to have a healthy aging and answer questions that we ask ourselves today: How is it possible to delay aging?; By modulating IM, using and better understanding the gut-brain axis, will we help with the various health status? Etc. [24].

Dysbiosis: It is the imbalance between pathogens and commensals and is present in the disease [25]. These changes in resident commensal communities are very frequent in the E [26]. This evidences the participation of IM, as an inflammatory process, due to the presence of T cells, which even translate into alterations in neurological behavior.

Why do these alterations appear in the old man more frequently? It is because diversity decreases, intestinal permeability and inflammation increase, and metabolism decreases, as well as, a greater number of pathogens appear [27].

All of the above generates a myriad of Diseases, among which are: Parkinson's Disease and Alzheimer's Disease, as well as intestinal disorders, colorectal cancer, various infections. High blood pressure, cardiovascular disease, stress, and dementia [28]. Autoimmune and other diseases also occur [29].

Now, how is the impact of dysbiosis minimized in older people? The slopes that are used to reduce the appearance of diseases in the old are different. Among them are [30-33]:

- Diet rich in fiber and low in carbohydrates and fat
- Administration of probiotics, prebiotics and symbiotics
- Administration of postbiotics and paraprobiotics
- Microbiota transplantation.

Intestinal microbiota transplantation (IMT): Being a second genome and by including proteins, genomic DNA and metabolites, it has real efficiency, in multiple diseases, especially the multi-mentioned *Clostridiodes difficile* [34,35], which also usually affects older people.

The indications for IMT are as follows [36-39]:

- *C. difficile* infection
- Initial or recurrent *C. difficile* infection that does not yield to antibiotics
- Severe *C. difficile* infection, complicated or refractory to therapy
- Severe anxiety
- Rheumatoid arthritis with severe complications
- Colorectal cancer
- Hepatocellular cancer
- Breast cancer
- Chronic nonspecific ulcerative colitis
- Major depression
- Type 2 diabetes mellitus, with severe complications

- Alzheimer´s disease
- Crohn's disease
- Parkinson's disease
- High impact multiple sclerosis
- Fatty liver Grade II-III
- Severe osteoporosis
- Idiopathic thrombocytopenic purpura
- Severe sarcopenia
- Chronic fatigue syndrome, with severe comorbidities
- Long-lasting irritable bowel syndrome and maximum impact
- Metabolic syndrome, severe.

In the future, we must ensure that the inherent risks of transplantation are minimized, based on regulations and good practices, such as through standardization of samples, including the determination of resistance to antibiotics [40].

Probiotics: Live microorganisms that, after ingestion in specific amounts, exert health benefits beyond those of inherent basic nutrition. Its use has been shown to alleviate gastrointestinal disorders in the E, using *Saccharomyces boulardii*, *Lactobacillus acidophilus*, *paracasei* and *reuteri* [41].

Probiotics are used in which disease? Although they are frequently used in allergic diseases, necrotizing enterocolitis, irritable bowel syndrome, constipation and prevention of respiratory infections, as well as hepatic encephalopathy in children and adults [42]. In older people its use turns out to be beneficial in *Clostridiodes difficile*, constipation, irritable bowel syndrome, inflammatory bowel disease and cancer prevention. Positive effect that is achieved through immune stimulation; improving resistance to colonization and reducing fecal enzymes [43].

In the future, the morbid processes caused by *Fusobacterium nucleatum* and *Sutterela* will be determined [44]. And the effectiveness of probiotics in the E will be demonstrated, knowing the entire mechanism of action of these substances [45].

Prebiotics: Glenn Gibson and Marcel Roberfroid define the prebiotic as "Non-digestible food ingredient, which beneficially affects the host by selectively stimulating the activity or growth of a limited number of bacteria, thereby improving their health" [46]. A few years later, at the Sixth Meeting of ISAPP, the International Scientific Association of Probiotics and Prebiotics, they were defined as: "Selectively fermented ingredients that produce specific changes in the activity or composition of the Intestinal Microbiota and thus cause changes in the host health" [47]. The prebiotics can be: Galacto-oligosaccharides (GOS), fructo-oligosaccharides (FOS) and transgalacto-oligosaccharides (TOS) [48].

Below we list interesting results from different authors, which give rise to future research: *Lactobacillus rhamnosus* and *Bifidobacterium Lactis* plus inulin could reduce the risk of colorectal cancer [49]. The prebiotics arabinoxylan and arabinose can improve general

cognition, decreasing the process of accumulation of glial fibrillar acid protein, related to dementia in mice [50]. Oligofructose could improve mood [51]. GOS mixed polydextrose reduces anxiety in mice [52]. Prebiotics can reduce the risk of Brain Vascular Disease by reducing inflammatory elements [53]. After administration of *Bifidobacterium infantis*, corticosterone and ACTH have normal levels [54].

Consumption of GOS increases the level of cortisol in saliva and improves its concentration [55]. Galacto-oligosaccharides correct changes in the Gut Microbiota and improve the immune status associated with old age [56].

Symbiotic: They are a mixture of probiotics and prebiotics, administered simultaneously, which usually benefit the Intestinal Microbiota [57]. They are consumed as raw fruits or vegetables, fermented dairy products or pickles, or as pharmaceutical formulas [58]. Its effect on metabolic health is linked to the mixture: probiotic-prebiotic [59]. The most commonly used combination is that of *Bifidobacterium* or *Lactobacillus* with fructo-oligosaccharides [60]. They can generate reduced concentrations of undesirable metabolites, and inactivation of carcinogens and nitrosamines [61].

Symbiotics are used in the same processes as probiotics, only it is referred to have a better effect. For example, it has been shown as a significant fact that they produce an increase in HDL, lowering blood glucose [62].

What are the best symbiotics? Undoubtedly, the first thing that must be taken into account to answer this question is that they have greater resistance to pathogens. Among them, the *Bifidobacterium bifidum*, *Saccharomyces boulardii*, *Lactobacillus plantarum* and *rhamnosus* stand out, mixed with prebiotics (oligosaccharides, fructo-oligosaccharides, galacto-oligosaccharides, xyloseoligosaccharides and inulin) [63].

The symbiotic positively influences the host by improving its survival and implantation of live microbial dietary supplements in the gastrointestinal tract; stimulating growth and activating the metabolism of health promoting bacteria. The future of symbiotics will be based on larger and more consistent research. Because this product is more beneficial than the same probiotics and prebiotics, used alone. They will soon be used by many pathologies [64].

Postbiotics: Functional bioactive compounds, generated in a matrix during fermentation, that can be used to promote health. They can be considered as a general term for all synonyms and components of microbial fermentation. They include short-chain fatty acids, metabolites, functional proteins, microbial cell fractions, and extracellular polysaccharides [65].

It is a new term in the field of "biotics". They alleviate ailments such as infant colic and atopic dermatitis. We believe that their investigation in older people is worthwhile, since they also have immunomodulatory effects [66].

Paraprobiotics: The area of biotics is increased by the introduction of paraprobiotics which are non-viable microbes, which could produce health benefits, similar to those generated by live probiotics [67].

Conclusion:

1. The alteration of the functions is associated with the change in the intestinal microbiota linked to the gut-brain axis.
2. Aging is related to changes in the Gut Microbiota.
3. To strengthen the IM and reduce the risk of disease in the E, it must be strengthened by means of an adequate diet, exercise according to age, probiotics, prebiotics and symbiotics, as well as postbiotics and paraprobiotics.
4. Parkinson's disease and Alzheimer's disease, as well as intestinal disorders, colorectal cancer, various infections. High blood pressure, cardiovascular diseases, stress and dementia are the most frequent conditions in the elderly.

5. Microbiota Transplantation reduces the impact of diseases in the elderly.

Conflicts of Interest

The authors declare that do NOT have affiliation or participation in organizations with financial interests.

Ethical Approval

This report does not contain any study with human or animal subjects carried out by the authors.

Informed Consent

The authors obtained informed written consent from the patients, in order to develop this article.

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