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Review Article

Intestinal Microbiota Transplantation in Children

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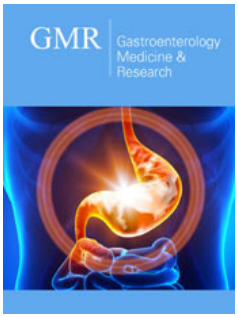

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Summary

It is concluded that Intestinal Microbiota Transplantation can be beneficial in numerous childhood ailments, considering in the application, the recommendations of the FDA, due to the current crisis of COVID-19.

Abbreviations: IM: Intestinal Microbiota; IMT: Intestinal Microbiota Transplantation; FDA: Food & Drugs administration

Introduction

The use of excellent donors makes the transplanted microbiota have a higher incidence in children [1]. We must not forget that COVID-19 infection forces us to follow the recommendations of the FDA [2]. Likewise, the use of probiotics, prebiotics and symbiotics and a special diet can improve various childhood disorders [3]. Next, a good number of topics - not all - will be addressed that will undoubtedly expand knowledge about children, their diseases and their management.

Microbiome

The microbiome refers to the total number of microorganisms and their genetic material [4]. It has been called the invisible organ of the body [5]. The last human organ under investigation [6]. As a new systemic organ [7]; the last human organ [8], as well as the super-organ or super-organism [9]. Or the forgotten organ [10]. So many nominations make us see the importance of this organ. And above all we are surprised by the name of "Forgotten Organ", since it has so much potential. The Microbiome was mentioned until 2001, with few previous references, without determining its name. Fortunately, the number of articles currently has exceeded all expectations, and the example is the 500 articles reported in one review [11]. And the enormous existence on the Internet.

Microbiota

Are there microorganisms present in the different ecosystems of the body [12]. Our Microbiome is made up of all the existing Microbiota in our human being. The most frequent are in the gut and, therefore, the most important is in the large intestine, where is greater abundance: Bacteroidetes, Firmicutes, Actinobacteria and Protobacteria [13]. The entire Microbiota Contains 100 billion bacteria: ten times higher than body cells [14]. There are more than 3 million microbial genes in our Intestinal Microbiota (IM), and there are 150 times more genes than in the human genome [15]. We must not forget the Hippocratic saying, the father of Medicine (460-377 BC), who points out: "All diseases begin in the gut" [16]. The rest of the Microbiota are located in the skin, the oral cavity, the vagina; ears, nose and throat, respiratory and urinary tracts [17-22]. The oral Microbiota is inhabited by more than 700 species and is the second most important Microbiota.

Microbiota and parasites

The microbiota of children is more unstable and variable than that of adults and depends on multiple factors, among which are: the type of birth (natural birth or cesarean section),

the life cycle, nutrition, the use of antibiotics, the type of milk administered, as well as the probiotics administered [23]. The fact of having found viruses in the amniotic fluid is transcendent, although contradictory, since it is not located in all the samples [24]. On the other hand, there is one who in one study suggests that the primary colonization may be in the womb [25]. Those born by caesarean section have a lower microbiota diversity and a lower Th1 response, so there is the possibility of developing allergic and inflammatory processes [26]. Variants of their Microbiota are usually found in the various stages of child development [27]. In the newborn, if there are postpartum sleep disturbances, dissatisfaction of dietary needs, and neurological disorders, commensal bacteria within the body can be disrupted and communication between the gut and brain can be disrupted [28].

There are various circumstances that produce a benefit to the newborn's Microbiota, among them feeding stands out, where children born by caesarean section start their maternal diet much earlier, helping themselves substantially with breast milk [29]. The maternal Microbiota influences the development of its offspring, by providing essential substrates and metabolites [30]. The fetus must tolerate autoantigens, through the elimination of autoreactive T-cell clones in the thymus, which prevents autoimmune disease [31]. And finally, what happens to the Microbiome of children, by the administration of antibiotics? Obviously, the first impact of the administration of antibiotics is Dysbiosis [32], with all the consequences that this represents: loss of key taxa, changes in metabolic capacity, loss in diversity and production of pathogens. Despite this, there are still a third of unnecessary prescriptions [33].

Microorganisms found in the children´s microbiota

It has already been mentioned that some authors find Microbiota in the fetus. They did this through comparative genome wide shotgun metagenomic studies, based on 16S ribosomal DNA, comparative and found: Firmicutes, Tenericutes (Mollicutis), Proteobacteria, Bacteroidetes and Fusobacteria phyla [34]. Babies have been found to incorporate Microbiota before birth, receiving a significant amount of maternal microorganisms [35]. The following microorganisms are detected fundamentally at birth: Actinobacteria, Firmicutis, Bacteroidetes, Proteobacteria, Fusobacteria and others [36]. Babies born naturally are contacted by the mother's fecal and vaginal microbiota, colonizing Lactobacillus and Prevotella [37]. Proteobacteria and Firmicutes are the main phyla that appear during the first days of life, and Actinobacteria are observed in the fecal samples of babies born by caesarean [38]. During childhood Firmicutes such as Clostridia, Bacteroidetes, and especially Bifidobacteria, as well as Escherichia and Enterococcus are included [39]. Bifidobacteria comprise the largest group within the Infant Microbiome [40].

Toddler and childhood

At this age, IM is modified by numerous factors: diet, sex, environment, medications, antibiotics, genetics, comorbidities, trauma, inflammation, metabolites, socioeconomic status, for which there is no pattern of existence of IM at this age [41].

Microbiota and parasites

Both interact with each other, in addition to competing [42]. The effects that protozoan parasites (Giardia intestinalis, Blastocystis spp, Cryptosporidium spp, Entamoeba spp. Etc.) Or metazoan (roundworms, and hookworms) have been neglected when talking about IM, given the importance it has, the latter [43]. However, parasites are also important, as they have been used for treatment in inflammatory bowel disease [44]. Likewise, the presence of parasites in the intestine, notably alters the intestinal ecosystem and, consequently, the habitat of the Microbiota [45]. Currently, many questions remain in studies investigating parasite microbiota interactions [46]. Due to the above, you should continue digging into what happens in this interaction [47]. Recent work suggests that interactions between parasites and Gut Microbiota are an important link in the evolution of the host immune system [48]. Intestinal Microbiota seems to determine the control of host susceptibility to various pathogens, and perhaps, in the coinfection by different pathogens, through similar pathways, influenced by the Microbiome [49]. Blastocystis, by increasing the number of Firmicutes and bacterial diversity, have anti-inflammatory activity [50]. The immunoregulatory effect of IM in colonization by protozoa is centered on the presence of Entamoeba histolytica, Giardia duodenales, Toxoplasma gondii, Blastocystis spp and Cryptosporidium parvum [51]. Both Microbiota and the parasites help in inflammatory processes and in immunity, a significant fact in the health process [52]. The coexistence between the Microbiota, the parasites and the host generate coevolution of these three elements, which indicates that all three are needed [53]. The IM has an area of approximately 400 m2, being the second largest surface in the body, after the respiratory tract. Through it, it offers diverse immunological mechanisms and with this, it defends the human being [54].

Metagenomic analysis

The term metagenomics, genomic analysis of a population of microorganisms, was coined by Handelsman J [55,56]. This new method generates the analysis of invisible bacterial diversity and, with this, we can enter the genetic potential of microorganisms, in order to achieve products of enormous biotechnological value [57]. Metagenomics can also be applied to solve practical challenges in the medical field, such as Type 1 Diabetes Mellitus, Ulcerative Colitis and Crohn's Disease [58]. In Greek, meta means "transcendent" [59]. Genomics: Study of the genome [60]. Now, some of the most important concepts are defined below, in the subject at hand:

Genomics and proteomics

Sciences that are in charge of the global analysis of genes and proteins, respectively.

Metabolomics

Study the set of metabolites present in a biological system.

Metagenomics

It seeks to obtain sequences of the genome of the different microorganisms, from a community, extracting and analyzing their DNA globally.

Metaproteomics

It is the study of all protein samples recovered directly from environmental sources.

Metatranscriptomics

It tries to describe the transcriptome of a group of organisms, coming from an environmental sample.

Transcriptome

The totality of messenger RNA expressed in a genome. Based on the above, specific studies have been carried out, such as this metagenomic analysis, which provides a broad understanding of microorganisms and differences between health and disease [61]. Also, based on them, changes in the composition of the microbiome could be determined [62]. This study demonstrated that there are many exogenous and intrinsic factors, correlated with the functionality and composition of the microbiome, that could be manipulated to improve health, related to it. Analysis of 16S ribosomal RNA gene sequences obtained from 20 different sites on healthy human skin showed that physiologically comparable sites harbor similar bacterial communities [63].

Dysbiosis

There are various definitions of it. Thus we see that it can be defined as: Any change in the composition of the resident diner communities, in relation to the community, found in healthy individuals [64]; A condition in which the normal structure of the microbiome population is altered, through external pressures, such as disease states or medications [65]; or alterations in the microbiota [dysbacteriosis], due to excess chemotherapy, diets that change their pattern, or antibiotics [66]. The most important thing in humans is to maintain a state of Eubiosis, which turns out to be "The balance of the intestinal microbial ecosystem" [67]. Dysbiosis (Dysbacteriosis) generates many illnesses, some of them include: Inflammatory Bowel Diseases [68]. Irritable Bowel Syndrome [69], Celiac Disease [70]; colorectal cancer [71]. As well as metabolic diseases [72]. Indiscriminate use of antibiotics [73]; Mycosis [74], allergies [75]. Rheumatoid arthritis, ankylosing spondylitis [76], and even caesarean sections [77]. As we see, there are many diseases that dysbiosis causes, so the first thing to do is ensure that dysbiosis does not develop and, if the conditions should occur anyway, we must have: Prebiotics, probiotics and symbiotics [78-80], Mediterranean diet, or resort, with all caution, given the presence of COVID-19, to Intestinal Microbiota Transplantation [IMT] [81-83]. Of course, if we have super donors, the IMT will be more beneficial [84]. Finally, we must remember that this procedure has its greatest incidence in C. difficile co-infection [85-87]. It should not be forgotten, that there are also other children's disorders, where dysbiosis is present, and in which we have a lot to do, among them the following stand out: Metabolic disorders such as Obesity and Type 1 Diabetes Mellitus [88]. Immunological Disorders such as asthma, eczema, atopic dermatitis, eosinophilia of the digestive tract and duodenal dyspepsia [89]. As well as Neuropsychiatric Diseases. Anxiety and Depression and Autism Spectrum Disorders [90]. And finally, hepatocellular carcinoma, liver cirrhosis and nonalcoholic liver steatosis, with their complications. Without overlooking chronic liver and kidney disorders [91,92].

Axes and microbiome

Without a doubt, the most important axis in the relationship of the microbiome with other organs is the intestine-brain axis, in which both the enteric nervous system, the sympathetic branches, the neuro-immune system and the parasympathetic system are considered, and act through bidirectional communication. However, there is an important variety of axes, which have special characteristics and which are the skin, the liver, the thyroid, the kidney, the heart, the lungs, the bones, the cartilage, bone marrow and even estrogen, and others [93,94].

Conclusion

A. We must try to reduce the administration of antibiotics in children.

B. It´s convenient to regulate the abuse of caesarean sections.

C. Probiotics along with prebiotics and symbiotics, usually improve moderate allergies and other conditions in children.

D. The Microbiota in children is unstable. From the age of 10 it stabilizes. In this age, children are excellent Microbiota donors.

E. Intestinal Microbiota Transplantation, following the FDA recommendations for Covid-19, can improve severe allergies and other conditions in children.

Conflicts of Interest

The authors declare don'ts 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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