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Mini Review

What is Required to have Super Donors of Microbiota?

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Abstract

The subject has been discussed, although not extensively, having, as in all cases, those who defend the process and its detractors.

Fortunately, they are more the first and this article, which is on the side of those who believe in super donors, is a review of how we should act with donors so that they reach the superlative degree of super donors and, with this, guarantee a better response. In the health of those who are undoubtedly more and more sick every day.

We analyze the diverse terminology, which is the basis for a better understanding not only of the super donors but also of the modulation of the microbiome, which ultimately is the most significant, in the different pathologies, that the alteration of the intestinal microbiota generates.

Let's take advantage of the fact that the microbiota is an environmental inheritance and that if we improve it, we will improve our health. A fact that should never be forgotten.

Keywords: *Super Donors (SD); Microbiome (Mic); Intestinal microbiota (IM); Modulation of the Microbiome (MM); Fecal Microbiota Transplantation (FMT); Probiotics (Prob)*

Introduction

The diverse terminology helps us to better understand the different processes, especially if we highlight the definitions, many of which have been accepted, which further guide the transcendent and current topic of microbiome modulation.

Within these concepts we have the following [1]:

- **Microbiota:** Communities of living microorganisms residing in a defined ecological niche.
- **Microbiome:** Set of genes of microorganisms (genome), their proteins (proteome) and their metabolites (metabolome).
- **Metagenomics:** Analysis that is usually carried out using state-of-the-art sequencing techniques, of the genetic material of microorganisms obtained from a sample of the medium that is being studied, for example feces to profile the fecal microbiota.
- **Dysbiosis:** Alteration in the structure of the microbiota, with negative implications for microbial metabolism and host physiology.

The intestinal microbiota (IM) ecosystem of microorganisms in the intestine, which exceeds those existing in soils and oceans. It is the most significant due to its diversity and density and lies mainly in the Colon [2].

The terms microbiota, microbiome, metagenomics and dysbiosis stand out. Without forgetting probiotics and their decisive impact as support therapy.

Olesen SW [3] and his group reiterate that fecal microbiota transplantation (FMT) should be recommended for recurrent Clostridioides difficile infection, with the strong potential to be useful in inflammatory bowel disease. Incidence that is achieved, thanks to the clinical efficacy of selected donors. The fact that the microbiota is an environmental inheritance gives us the enormous possibility that we can influence it throughout our lives and by improving it, we consequently improve our health [4].

Although abundant clinical trials are surely required to detect the effects of microbiota donors, we enunciate the decalogue, which seeks to improve the performance of donors and being pretentious to make them reach the denomination of super donor.

Decalogue of the super donor of microbiota

1. Make the donor participate in everything related to the patient that he will help, respecting his privacy, as well as his own [5].
2. That the donor be part of the emolument obtained, in a reasonable percentage.
3. Carry out a metagenome in the donor, in order to rule out Intestinal Dysbiosis (DI)
4. Take a complete clinical history. The interrogation must include a search for: Inflammatory bowel disease, irritable bowel syndrome, colonic polyps and consider that the donor exercises.
5. The donor must be under 25 years of age, a healthy volunteer, regardless of gender, not diabetic, obese, without gastrointestinal surgeries and not having taken antibiotics, anti-inflammatories or corticosteroids in the last 6 months.
6. Perform analysis that includes: Nasopharyngeal PCR for Covid-19. *Entamoeba histolytica; Giardia lamblia; Blastocystis hominis; Dientamoeba fragilis* (Included in the Metagenome). Stool culture Rotavirus and Adenovirus antigen in feces. *Clostridium difficile* (Toxin A and B). Luetic reactions (VDRL). Hepatitis A, B and C profile. Human immunodeficiency virus (HIV). Presumptive test. Anti-Cytomegalovirus IgG antibodies. Epstein-Barr IgG antibodies. Immunoglobulin profile.
7. Others to consider: Human leukemia virus, John Cunningham (JC) virus. Glutamate dehydrogenase (GDH). Rotavirus, *Listeria*, Vibrio, Norovirus, *E. coli* O157, *Strongyloides stercoralis, Helicobacter pylori, Schistosoma*, vancomycin-resistant Enterococci, and methicillin-resistant *Staphylococcus*. Tests for inflammation and resistance to antibiotics.
8. Preferably use only one donor per patient [6].
9. Carry out the transplant with recently acquired feces (fresh) [7].
10. Seek microbial diversity and excellent composition of donor feces [8].

Comments

Undoubtedly, the selection of the donor is decisive in the success obtained in the FMT. For this reason, Physicians dedicated to this therapy will have to design specific hypotheses and determine clinical trials that guide this process [9].

OpenBiome, the first stool bank in the world, has developed a document, where they specify a series of recommendations for the TMF to be successful. They include donors, the bank itself (it would be extrapolated to other banks); associated doctors and hospitals; finally, the patients [10].

The retention of possible donors is not easy, for example, in the study by Bénard MV and his group, they initially excluded 22.5% of potential donors, with parasitological screening another 61.5%, leaving only 10% of 393 donors potentials [11].

The results of the transplant not only depend on the ecology of the patients, but also on the interactions between the microbiomes. Being able to predict success, in the absence of specific pathological microorganisms, detected in the metagenomic study [12]. Without a doubt, the repair of the affected intestinal ecosystem is useful, through bile acids and producers of Short Chain Fatty Acids.

What Leo Tolstoy said in Anna Karenina is a principle in animal microbiomes: "The microbiological changes induced by many perturbations are stochastic (subject to chance and subject to statistical analysis) and therefore lead to transitions from stable to unstable".

This means that in dysbiotic individuals the composition of the microbial community varies more than in healthy individuals [13].

Although it is not yet known how donor microorganisms affect the efficacy of FMT, two enterotypes dominated by Enterobacteriaceae and Bacteroides (RCPT/E and RCPT/B) have consistently been found, data that guides us towards the process we are looking for: success [14].

Something that cannot be set aside are bioethical and social issues, which can be summarized as informed consent, ownership, privacy, risks, and benefit sharing [15].

Although in the literature the age of the fecal microbiota donor varies, even including cases in the sixth decade of life [16]. We prefer patients up to 25 years old, because in older patients co-morbidities are another factor to take care of, as well as the age of the microbiota, since it decreases after 65 years; age at which frailty syndrome usually appears, generated by a chronic inflammatory process [17]. And we do not perform the procedure with donors under 18 years of age, for medical-legal reasons [18]. It must be remembered that children have dynamic microbiomes and adults have already stabilized it [19]. Not forgetting that in adults there could be early markers of diseases, which should be considered [20].

Much has been insisted on donated feces being fresh, with which we agree [21]. Since the success obtained has been greater when recent dejections are used. Although there are detractors in this regard, who support the Microbiota Banks. The use of a donor is convenient, and there are interesting studies such as that of Ren R, and his group [22]. Where they treat patients with a single donor and occupy it on several occasions, with good results. The Hamilton Scale (Depression Scale), also known as HDRS and Ham-D, is the most widely used physician-administered depression assessment scale. It should be around 0 to 7, considered normal [23].

Undoubtedly, a correct choice of donor, good collection and management of feces, as well as adequate preparation and consistent administration help in the search for microbial diversity and excellent composition of the feces [24].

Although the most significant is the support of bioinformaticians, experts, who help in reading Metagenomics [25].

Conclusion

Undoubtedly, we still do not have all the tools to have Super Donors, but every day we get closer to this procedure. What we currently know, although it is not enough, does help in the FMT and consequently in its success.

As final considerations we propose the following:

- The integral participation of the donor is a fundamental element in the success of the FMT.
- A metagenome carried out on the donor one month before the procedure is essential.
- A good clinical history oriented to intestinal dysbiosis or directed surveys are essential for
- the search for super donors.
- Oriented analytics is essential.
- The use of one or several donors does not seem to influence the results.
- Fresh feces is preferable. Leaving the frozen ones for Microbiota Banks.
- The Hamilton Scale helps us in knowing the depression that the donor may have.
- The support of bioinformaticians is very significant in the successful results.

Conflicts of Interest

The authors declare that they 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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