

Interactions between the intestinal microbiota and colonization by multiresistant microorganisms

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Abstract

The intestinal microbiota has been the subject of study since multiple researchers revealed its importance in the balance and maintenance of health. The objective of this paper is to analyze the relationships between the intestinal microbiota and the colonization of multiresistant bacteria with the consequent impact on human health. To acquire bibliography, a search was carried out in SciELO, PubMed and repositories of doctoral theses, for articles in English and Spanish, published in the last 12 years (2012-2024). Priority was given to high-impact journal articles, review and research articles. Search terms included "gut microbiota," "colonization of multidrug-resistant bacteria," "functions of gut microbiota," "role of microbiota in health," "antibiotic resistance mechanisms," "fecal transplant." The intestinal microbiota is a topic of continuous study and updating, to offer results that the scientific community can use in future projects and experimental studies.

Keywords: intestinal microbiota; antimicrobial resistance; bacterial colonization; multiresistant bacteria

Introduction

Interactions between the intestinal microbiota and colonization by multiresistant microorganisms together of dissimilar organisms, the human microbiome, or community of microbes and collection of genomes found in and on the human body, is now the subject of renewed, intense study. Relman, D. A. (2012)

The intestinal microbiota has a large and complex community of resident commensal bacteria. The microbial community of the intestine participates in a series of beneficial effects for digestion, nutrient production, detoxification, protection against pathogens and in the regulation of the immune system. Guillot, (2022)

In the intestine alone, hundreds of bacterial strains and more than 9 million genes have been characterized, comprising more than 3 billion of cells. This represents approximately 0.5-2 kg of the total body weight of any individual. Moreno del Castillo et al (2018), Condori (2023)

The process of implantation and colonization of the intestinal microbiota is dynamic and progressive from the newborn stage, with significant differences at one month and six months of age, followed by gradual transformations in the first year of life until reaching stability between two to three years of age, influenced by factors related to the mode of delivery (vaginal or cesarean section), gestation time (normal or prematurity), breastfeeding (breastfeeding or artificial milk), time of introduction of solid foods and exposure to antibiotics (prenatal or postnatal). Guillot, (2022)

The mature microbiome of an adult is acquired around 3 years of age and varies throughout life depending on a series of factors such as sex, body mass index, consumption of fiber found in fruits and some vegetables, as well as the level of physical activity. Moreno del Castillo et al (2018)

The changes that occur in our body, related to an imbalance in the composition of the microbial community existing in the intestine of a healthy subject, are known as dysbiosis. In the intestine, commensal, non-pathogenic bacteria normally predominate, but when the microbiome is damaged, there is a decrease in the microbial population with a reduction in the capacity to resist colonization, which allows the appearance of opportunistic bacteria and their colonization in ecological niches. with the consequent impact on the microbiota, an increase in inflammatory cells at the mucosal level, capable of triggering low-grade inflammation and damage to intestinal permeability, events that favor bacterial translocation and the passage of metabolites from this origin into the circulation. Guillot, (2022)

Antimicrobial resistance (AMR) is a serious public health problem. The World Health Organization (WHO) has estimated that by 2050 all antibiotics will be ineffective. The main reason is the rapid, early and wide dissemination of ADR 1 genes. Colonization with drug-resistant bacteria is a great health risk, due to the potential transfer of resistance genes to pathogenic bacteria and their easy dissemination. between individuals. The

gut microbiota has been reported to be one of the main sources of urinary, respiratory and blood tract infections. Gonzales et al (2023)

The intestinal microbiota has been the subject of study since multiple researchers revealed its importance in the balance and maintenance of health. Extensive research has been carried out to know its composition, its functions, its characteristics, etc. One of its functions is to create conditions that allow the human body to deal with infections caused by bacteria. Which leads us to ask ourselves several questions: ¿What are the mechanisms of action that come into operation in the intestinal microbiota when it is colonized by multiresistant bacteria? ¿Will we be able to find other alternatives to modify the microbiota in humans that allow them to fight infections when antibiotics are not effective?

From everything mentioned above, the need arises to train a professional who puts the clinical method into practice, who has extensive knowledge of infectious diseases, critical and investigative thinking, and who stays updated regarding this topic and its impact in society.

The objective of this paper is to analyze the relationships between the intestinal microbiota and the colonization of multiresistant bacteria with the consequent impact on human health.

Functions of the microbiota

The normal microbiota fulfills multiple functions, such as endocrine functions, neurological signaling, modification of bone mineral density, maturation of the immune system, inhibition of pathogens, synthesis of vitamins (K, B12 and folate), metabolism of bile salts and modulation of some drugs. The microbiota can be considered an organ with a level of production and purification activity comparable to that of the liver. There are different mechanisms that have been described, among which are reduction, hydrolysis, denitration, decarboxylation, deconjugation, removal of succinate and formation of amino groups, among others.

It is known that certain intestinal microorganisms produce antibiotics with important effects at the level of their bacterial ecosystem. For example, *S. mutans*, a natural commensal of the oral mucosa flora, secretes mutanobactins, non-ribosomal peptides that prevent the invasion of *C. Albicans*, by stopping its conversion to hyphae. In turn, the use of antibiotics affects the microbiota, changing the bacterial populations present and generating metabolic products that can have counterproductive effects. Moreno del Castillo et al (2018).

Effects of antibiotic use on the microbiota

Antimicrobials have revolutionized the medical environment, becoming indispensable in medical practice, saving millions of lives, since they were first used to treat bacterial infections in 1941. Their discovery, made by Fleming in 1928, has brought numerous benefits: reduction in mortality from sepsis, a potentially fatal disease. Antimicrobials are designed to eliminate or attenuate the growth of microorganisms; their impact has been widely investigated in terms of the damage they cause to the intestinal microbiota and gastrointestinal epithelium. However, antimicrobials administered to attack a specific pathogen can cause collateral damage to the patient's microbial population.

Reducing or eliminating commensal species that provide protection against external pathogens, increasing the risk of subsequently suffering from infections by other microorganisms. This selective pressure, induced by antibiotics, can cause excessive overgrowth of pathogens with pre-existing resistance in the microbiota, leading to infections that are difficult to treat. Calderon (2023)

A concept that encompasses the resistance of bacterial strains is called "Resistoma", and is defined as the compilation of all those genes that contribute directly and indirectly to bacterial resistance, and therefore to the resistance of bacteria to antimicrobials. Singh (2019)

The problem of resistance is caused by several factors, including: antibiotics, which generate a selection of those bacteria capable of surviving their action, and the genetic determinants of resistance presented by the selected bacteria. Below we will mention four main mechanisms of antibiotic resistance:

Overexpression of efflux pumps: Efflux pumps are ubiquitous transmembrane proteins in this domain. These pumps expel the antibiotics out of the bacteria, therefore, by significantly reducing their intracytoplasmic and periplasmic concentration, they confer antimicrobial resistance.

Modification of the targets of action: This mechanism prevents or hinders the action of the antibiotic. It can be completed with alterations at the level of DNA gyrase, 23S rRNA and enzymes that are penicillin-binding proteins necessary for the formation of the cell wall.

Decreased membrane permeability: The loss or modification of porins is one of the most frequent cases of antimicrobial resistance.

Enzymatic modification of antibiotics: There is a wide variety of enzymes that have the ability to modify antimicrobials, the best known are β -lactamases, resistant to beta-lactam antibiotics such as penicillins, cephalosporins, monobactams and carbapenems. Soria Segarra (2021)

In general, when talking about antimicrobial resistance, we focus on acquired resistance (point mutations in the chromosome acquired by the gastrointestinal tract) and intrinsic resistance (inherent cellular components that make bacteria resistant to certain antibiotics). Similarly, the resistome can be classified into intrinsic and mobile resistome. Intrinsic antimicrobial resistance genes as such not only confer a resistant phenotype but are also associated with bacterial physiology and metabolism. However, these genes can be captured by mobile genetic elements during the course of evolution and become mobile, therefore, mobile AMR genes can easily spread through THG. Hu Y et al (2016).

An investigation carried out by Gonzales et al (2022) on infants resulted in a high frequency of fecal commensal bacteria resistant to quinolones, ESBL, type blaCTX-M. Concluding that it reflects the extent of the dissemination of bacteria with antimicrobial resistance and its eventual role in limiting the therapeutic use of antimicrobials in this population. Which leads us to reflect on the use of antibiotics in the early stages of life, the negative influence that it has on this individual who is already sensitized, which results in his body not responding to new infections. to the treatment of choice or need higher potency antibiotics to combat them.

Another study conducted in hospitalized adult patients demonstrated that *Citrobacter koseri* is no longer predominantly a urinary pathogen but is now causing nosocomial infections. In this study *C. koseri* showed a high resistance to gentamicin, which is alarming since, Enterobacteriaceae are sensitive to aminoglycosides, besides the fact that this therapeutic option would no longer be available. Céspedes, L. D., Fonseca, Y. M. C. (2022) This is an example of how the use of antibiotics indiscriminately affects the stages of life, these patients were exposed to several changes in antimicrobial treatment which severely modified their health status and response to infections.

Conclusions

The intestinal microbiota is essential in human health; currently there is talk of achieving its balance through healthy lifestyles, mainly in a healthy diet and the use of probiotics. Obviously one of the predisposing factors that most affects its balance are antimicrobials, which in an effort to cure infections and stop the advance of bacteria contribute to the development of multi-resistance genes. One of the steps to take into account is to achieve control of bacterial infections, facilitate rapid and effective diagnosis through the clinical method, reduce hospital stay, reduce invasive procedures with new technology that shorten steps but expose the patient to nosocomial infections

and correctly use the antibiogram as a tool to establish adequate therapy starting with antibiotics that fight the infection but are correct.

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