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The Role Of Probiotics in the Symptomatic Treatment Of Covid-19

Research Article

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Abstract

The purpose of this systematic review of the literature was to analyze the possible purpose of probiotics in the treatment and prevention of Covid-19. Numerous studies have evaluated the effects of gut bacteria on the immune system, somewhat regulating the host response to lung infections. This mechanism is now well established and is called the gut-lung axis.

Keywords: Covid-19; Probiotics; Intestinal Bacteria.

Introduction

Coronavirus disease is an emerging disease that has been plaguing the planet for more than a year. It originated in Hubei province in late 2019 and has spread across the planet. This new virus belongs to the beta coronavirus family. It is now commonly known as SARS-Cov-2 (Lake, 2020). Covid-19 has a very high transmissibility rate and has a clinical manifestation with symptoms ranging from mild to severe with a typical radiological picture. This is an RNA virus and has projections on its surface that give the virus a corona-like appearance, hence the term coronavirus. Several dtudi showed an equality of genetic material (about 79%) between another virus of the Sars-Cov family that caused an epidemic in 2002-2003 [1]. SARS-Cov-2 has a similarity in the genetic material of the nucleocapsid to SARS-Cov. Middle Eastern respiratory syndrome or MERS disease was caused by another very similar type of virus called MERS-Cov. Both of these viruses use the ACE-2 receptor to enter the cell [2]. These receptors are expressed in the renal and gastrointestinal tract. In fact, there is evidence to support the ubiquitous presence of the virus, in fact it was found in the faeces and respiratory secretions of some patients even after a month from the onset of symptoms. Further clinical studies reveal the presence of Covid-19 in the feces of some affected patients. Furthermore, diarrhea is frequent in patients with Covid-19, this test shows the presence of an involvement of the intestine-lung axis. Therefore the gut microbiota could be affected [3].

The intestine is populated by bacteria, viruses, fungi, in fact there are about 1014 resident microorganisms. The main four phyla present in the intestine are Actinobacteria, Firmicutes, Proteobacteria and Bacteroidetes. The colon, on the other hand, has bacteria from the Bacteroidaceae, Prevotellaceae, Rikenellaceae, Lachnospiraceae and Ruminococcacea families. Intestinal bacteria play a key role and help the host organism thanks to its trophic and protective actions. In fact, the microbes obtain a habitat and nourishment from the intestine of the host, while the microbes help the host to regulate physiological functions and to develop a protective immunity against pathogens [4].

For this reason, alterations in the intestinal microbiota, called "dysbiosis", is one of the contributing causes of diseases such as IBD, diabetes, depression, cardiovascular diseases, etc. Similar to the intestine, microorganisms are also present in the lungs. Bacteroidetes, Firmicutes and Proteobacteria predominate in the lungs. Very interesting was the discovery that the intestinal microbiota is able to influence the health of the lungs through an exchange of mediators, all this is known as the "gut-lung axis". The influence of this axis is two-way, as intestinal toxins and metabolites can affect the lung, while pulmonary ones can affect the intestine.

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Therefore, inflammation in the lungs can affect the intestinal microbiota. Hence the idea that SARS-Cov2 could have an influence on the intestinal microbiota. Various studies have shown that some respiratory infections have an impact on the composition of the gut microbiota.

Covid-19 has several clinical manifestations from asymptomatic to more severe manifestations such as pneumonia and acute respiratory distress syndrome (ARDS). Several clinical demonstrations have shown that the gut microbiota plays a key role in the development of ARDS. The lack of different species of intestinal bacteria is associated with many diseases. In fact, elderly people lose various intestinal bacterial species and this leads to the emergence of beneficial bacteria such as Bifidobacteria. Since most of the elderly affected by Covid-19 have adverse outcomes, it has been hypothesized that the gut microbiota could influence the course and clinical manifestations of Covid-19.

The food an individual takes influences the composition of intestinal bacteria, thereby reflecting their health. In fact, several studies show how individuals who consume animal fats and proteins have a different intestinal microbiota from those who consume vegetable fats and proteins. Some external events such as inflammation and stress can produce changes in the gut microbiota, which shows how both diet and some external events can cause changes in the gut microbiota. For this reason, some foods or supplements can modify and improve the composition of the intestinal microbiota. Indeed, prebiotics can cause changes in composition and improvements in both intestinal species diversity, digestion and immunity. In humans especially in the elderly (Kleessen et al., 1997; Bouhnik et al., 2007). Prebiotics can cause immune changes by transforming. In addition to the effects on the composition of the microbiota, prebiotics also produce noticeable changes in immune and metabolic markers by decreasing pro-inflammatory cytokines. It has been observed that the consumption of whole grains decreases insulin resistance and decreases the production of IL-6. In contrast, an increase in IL-10, an anti-inflammatory cytokine, was observed following the intake of corn starch. The beneficial effects of prebiotics are expressed through the production of short-chain fatty acids and a strengthening of the lymphoid tissue associated with the gastrointestinal tract. Recent studies have shown how the intestine-lung axis is connected and influenced by diet. In fact, a diet rich in fiber certainly has an influence on the intestinal microbiota, but changes are also observed in the lung microbiota. Like prebiotics, probiotics have a similar action, obviously maintaining beneficial effects on the health of the organism.

Probiotics are species belonging to the genera Lactobacillus and Bifidobacterium and include many different strains such as L. johnsonii, L. fermentum, L. reuteri, L. paracasei, L. rhamnosus, L. acidophilus, L. plantarum, B. longum, B. short, B. bifidum and B. animalis subsp. Lactis. Some foods such as yogurt or dairy are rich in probiotics. In fact, yogurt decreases the amount of intestinal pathogenic bacteria such as E.Coli and Helicobacter. Sometimes lactobacilli and bifidobacteriaare used to treat traveler'sdiarrhea. Probiotics improve and regulate innate immunity by acting on the Tool Like Receptor and activating the respective communication pathways. Studies on animal models, on mouse Treg cells, which inhibited the allergic response, induced the allergic response after the administration of probiotics. Therefore the diet regulates the intestinal microbiota and the lung microbiota can also influence immunity. Therefore a weighted diet that can improve the gut microbiota has an ameliorative effect on patients with Covid-19. Therefore the aim of this work is to evaluate how probiotics through the lung-intestine axis can influence the symptoms of Covid-19.

Material and Methods

The study was conducted utilizing the main scientific databases (PUBMED, MEDLINE, and WEB of SCIENCE). The time window considered for the electronic search was from 1st March 2019 to 1st April 2021. The term "probiotics" was first combined with "Covid-19" .The web search was assisted using MESH (Medical Subjects Headings). The criteria for this review are described in PRISMA flow diagram. The purpose of this review is to answer to the following questions using a PICO method (P: patient problem/population; I: intervention; C: comparison; O: outcome):

Are probiotics useful in treating Covid-19 symptoms?

The following inclusion criterion were used: articles in English, human studies and clinical trials. Two independent people search with the same keywords all article and select the article founding. The risk of bias in this phase is solved by an independent author that conduct the same search. The phase of screening is carried out by the two independent research that excluded the article duplicated, review and animal study. The article found in this phase are 13. 3 articles are excluded because are duplicates and they do not respect the topic proposed in this review.The phase of eligibility is conducted by other two reviewers. These authors compare the article founding and select the article that asked the PICO. Articles which did not contain data regarding aloe vera and mouthwashes are excluded. The authors read first the abstract of all articles, excluded which did not respect the inclusion criteria, after read the complete test of the remains articles. In this phase are excluded 2 articles. In this phase the risk of bias is solved by an independent author, completely external and unknown to the authors. The number of articles remaining in this phase are 14. One article is excluded because did not. The synthesis of data is carried out by the authors. All data were extracted. The author reads first the abstract of all articles, after read the complete test of the articles. All the reviewers extract the data regarding effect of probiotics in the treatment of Covid-19. Articles which not contain the data and the previous keywords were excluded. All doubts, regarding the included articles, are solved contacting the author.

Result

Akur's study is a systematic review and examines the role of probiotics in treating Covid-19 symptoms. The study examines the effects of probiotics on in vitro, animal and human models. The analysis of the various studies has shown how possible a use of probiotics as a preventive or symptomatological measure in patients with Covid-19 [6]. The Dhar study showed how a personalized diet causes an improvement in the intestinal microbiota, all of which cause an improvement in the immune profile and could cause an improvement in the symptoms of immunocompromised and elderly patients with Covid-19 [7]. Myrtuyana's study states that several nutrients including probiotics have a proven ability to increase the ability of the immune system. Among the main

nutrients are Zn, vitamin D, vitamin C, curcumin, cinnamaldehyde, probiotics, selenium, lactoferrin, quercetin, etc. All these nutrients, taken in the right concentration, help the immune system prevent viral infections and prevent serious complications of some diseases due to a hyper-inflammatory state. For this reason it can be useful for prophylactic purposes against Covid-19 [8]. Sundaraman's study evaluates the use of some nutrients against Covid-19. In this review, the possible beneficial and therapeutic effects of Covid-19 in the prevention and management of possible complications are evaluated and studied. Furthermore, several studies taken into consideration in this review affirm the possible effect of probiotics in modulating the intestinal microbiome, thanks to the increase in the production of interferon as an antiviral agent, thus preventing Covid-19. All this happens thanks to the presence of the intestine-lung axis, a regulatory axis influenced by the intestinal microbiome [9]. The Infusino study evaluated the possible interaction between supplements, probiotics as a possible preventive aid for Covid-19 and as an aid to symptoms. These substances, if used sparingly, can have beneficial effects on the body. Studies selected by the author have also shown that some bacteria release products against respiratory viruses, triggering the immune response. For this reason it has been hypothesized that these bacteria may have a regulatory/modulatory role against endothelial damage and systemic inflammation due to Covid-19. Further studies will have to be carried out on the effectiveness of probiotics as food supplements and to be able to effectively evaluate their beneficial effect for the treatment of Covid-19 [10].Bottari's study also evaluates the possible effect of probiotics on Covid-19 infections, thanks to the fact that they have a regulatory effect on inflammatory processes and on innate and adaptive immunity. Probiotics act on intestinal cells by stimulating the secretion of IgA, the activation of phagocytosis and above all the maturation of dendridic cells. All of this could lead to the modulation of systemic inflammation. This study also talks about the intestine-lung axis and therefore the improvement of the intestinal microbiome could also lead to an improvement in inflammation and lung function. However, further studies, aimed at knowing which probiotic strain is effective at the lung level, are needed [11]. Gohil's study also suggests the ability of probiotics to act on the immune system, including in the respiratory system. Emerging studies suggest the ability of probiotics to regulate immune responses in the respiratory system. In fact, several studies have shown the effectiveness of probitics on viral infections of the respiratory tract. All the articles analyzed in this review evaluated the influence that intestinal probiotic bacteria have on lung immunity. Therefore, this study also hypothesized how the possible administration of probiotics can attenuate the symptoms of Covid-19, acting on the balance of intestinal bacteria [12]. Dhar hypothesized the possible influence of probiotics on Covid-19 disease. Since elderly patients have intestinal dysbiosis and since Covid-19 disease has been potentially fatal in this category, it has been hypothesized that the intake of probiotics may affect the progression of the virus. In fact, by acting on the diet it is possible to improve the immune profile of immunocompromised patients. In fact, a clinical study on probiotics could be created to evaluate the efficacy on the progression of symptoms [13]. The study of Angurara probiotics, too, evaluates the effects of probiotics by regulating the immune mechanism of the intestinal microbiome, which regulate and modulate the immune response in patients with Covid-19. Probiotics have numerous beneficial effects and are easy to find, which is why they can be used to treat Covid-19 [14]. The Oliamat study states that there is now several evidence to support that probiotics can act on immunity by preventing or stemming the presence of infections. In fact, this study evaluates the effectiveness of probiotics in the prevention of respiratory tract diseases. In fact, these data are very encouraging regarding the use of probiotics for the treatment of Covid-19 [15]. Conte's study estimates that consuming fiber and probiotics can help reduce inflammation and strengthen the immune system against Covid-19 [16]. Packnahad's study was very interesting as it carried out a literature review on 24 studies, classifying the effectiveness of probiotics on 3 categories and levels:shorten the period and severity of infections, the incidence and all possible complications associated with viruses.In fact, probiotics have shown beneficial effects on this category of patients [17]. Khaled's study evaluated the effectiveness of probiotics on treating Covid-19 disease. It is now established that probiotics and prebiotics have functional benefits in the treatment of some viral infections, such as seasonal flu, the purpose of this study is to evaluate the possible influence on the progression of the disease from Covid-19 [18].Sahin's study showed the possible role of the gut microbiota in treating respiratory tract infections. This study evaluates the possible effect of probiotics in the treatment of Covid-19 disease. The strengthening of the intestinal microbiota, through the intake of probiotics, leads to a strengthening of the immune defenses and therefore could attenuate the Covid-19 pathology [19]. Mahoti's study evaluated the possible effect of probiotics on the immune response and on the alleviation of symptoms of viral diseases of the upper respiratory tract. The main cause of the onset of symptoms is due to an over induction of the immune system. In this study the possible effects of taking probiotics on the modulation of the immune system and therefore on the improvement of symptoms are analyzed. In fact, the possible effects of probiotics on the immune response in pre-clinical studies have been analysed [20].

Conclusion

Probiotics have been studied in different clinical studies and are effective in improving the immune response. In fact, the improvement of the immune response causes better protection against viral infections [21]. The intake of probiotics, maintain the homeostasis of intestinal bacteria, all this causes a production of interferon and a mitigation of the immune response. All the studies analyzed, albeit pilot and non-randomized studies, showed the effectiveness of taking probiotics on improving respiratory symptoms in Covid-19 patients. In fact, the administration of lactobacilli and bifidobacteria cause an improvement in the intestinal microbiota [22]. Therefore the administration of probiotics can potentially improve the immune status of the individual. Each effect on the individual and each released cytokine are specific to the bacterial strain of probiotics. For this reason it is necessary to carry out a specific analysis in order to identify the most suitable probiotic strain for the patient's immune status [23].

In fact, specific probiotic strains must be administered in case of Covid-19. Therefore, studies will be necessary to identify the intestinal flora and to be able to identify the host response to probiotics, also based on the genetic model. Future clinical studies will serve to characterize the basic individual microflora and the individual genetic pattern, under which the individual responds to probiotics. In fact, all these studies confirm the effectiveness of probiotics in fighting viral infections, therefore its action against

Covid-19 is also conceivable. In fact, the presence of a lung-intestine axis is now established, thanks to which a scab of information occurs between the two systems [24].

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