Considering role of probiotic on respiratory disease Is Probiotic Possible to Treat COVID-19

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Considering Role of Probiotic on Respiratory Disease: Is Probiotic Possible to Treat COVID-19?

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Abstract

Background: COVID-19 is a new variant of the corona virus known as a pandemic disease. The number of cases has increased every day around the world. Unfortunately, treatment in management has not been satisfactory.

Purpose: This study aims to examine the role of probiotics in respiratory disease and the possibility of managing COVID-19 through an analysis of its function.

Method: This study is a review. Quality journals until 2020 were searched in the Pubmed database for the keywords 'respiratory' or 'asthma' or 'pneumonia' or 'lung' or 'influenza' and 'COVID-19'. Compiled data includesthe author, type of study, type of probiotic, duration of intervention, target population, results, conclusion and side effects that occurred

Results: We analyzed 9 experimental studies. Some studies related to respiratory disorders used the Lactobacillus Sp as probiotic. One research used Fructooligosacharide as additional ingredient. The research use different doses and timing of interventions 14 days - 6 months. The diseases covered in this report are asthma, pneumonia, and influenza. Probiotics can reduce symptomps, duration in hospitality risk, and quality of life.

Conclusion: The ability of probiotics in the management of respiratory diseases provides hope for the management of COVID-19, of course, it is balanced with further research that is able to analyze clear dosages, types and roles.

Keywords: *Respiratory disease, Role, Probiotic, COVID-19,*

Introduction

Covid-19 is a health problem in the world. Globally, there have been 88,383,771 confirmed cases of COVID-19, including 1,919,126 deaths, reported to WHO. There were 818,386 cases with a total of 23,947 deaths in Indonesia. The number of these cases continues to increase and changes every day[1]. Cases in East Java reached 92,613 cases [2]. Outbreaks of viruses and pathogens originating from zoonoses in the future are likely to continue[3].

Handling COVID-19 is currently at an unsatisfactory stage. There is no standard treatment for this disease and supportive treatment is the only strategy. Further, expanded clinical trials with better designs are still

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needed to evaluate the efficacy of this treatment although such treatments will be quite challenging to undertake in an epidemic era. One of the alternative treatments available is Probiotics. Probiotics are believed in previous studies to have benefits in overcoming health problems. Probiotics are live microorganisms that can be found in fermented foods and cultured milk, and are known as "health friendly bacteria," which exhibit a variety of beneficial health properties such as prevention of intestinal disease, boosting the immune system, for lactose intolerance and gut balance. microbes, exhibiting anti-hypercholesterolemic and antihypertensive effects, reducing postmenopausal disorders, and reducing diarrhea[4]This evidence appears to be adequate regarding the prevention and treatment of certain conditions while being only promising or even controversial when it comes to others. However, the development of probiotics for human consumption is still in its early stages.

Further research, in the form of controlled human studies, is needed to determine which probiotics and doses are associated with greatest efficacy and for which patients, and to demonstrate their safety and limitations [5]. The main focus of Probiotics is on three things, health improvement, infection control and disease management, through the use of various types of direct use of Probiotics or with the use of foods containing Probiotics[6].

At this time, there is not enough evidence to recommend specific anti-COVID-19 treatments. The decision to use this drug during the COVID-19 pandemic must be based on careful consideration of the potential benefits and risks for the patient. This study aims to examine the role of probiotics in respiratory diseases and the possibility of managing COVID-19 through an analysis of their functions.

Method

Participants in this study were all ages ranging from pediatric patients to adult patients. The experimental research included in this review. The data compiled are the first author, year of publication, method, types of probiotics, target population, and conclusion. A systematic search on the PubMed database, carried out for studies from the start of the database to 2020. We searched article using language in English with a searching strategy of applying 'asthma' or 'lung' or 'pulmonary' or 'pneumonia' or 'respiratory disease' or 'probiotic' and 'COVID-19'. Duplicate articles were eliminated. We screened potentially eligible trials by article titles and abstracts obtained from broad search, and then, the full text of these screened trials was assessed for eligibility according to inclusion and exclusion criteria.

Results

A study from Ahanchian et al (2016), used a randomized, double-blind, placebo-controlled, randomized clinical trial in 72 children aged 6-12 years for 60 days. The probiotics used were Lactocare ® containing ®, synbiotics containing 1 billion CFU / capsule, Lactobacillus casei, Lactobacillus rhamnosus, Streptococcus thermophilus, Bifidobacterium breve, Lactobacillus acidophilus, Bifidobacteriuminfantis, Lactobacillus bulgaricus, and Fructooligosacharide. Synbiotics (a mixture of seven strains of probiotics plus fructooligosacharide can have an effect on reducing episodes of viral infection in children with asthma. [7]

Del Giudice et al (2017) used placebo-controlled, double-blinded, and randomized for 40 children for 4 weeks using 1 sachets/day. The probiotic used were Bifidobacteria, B longum BB536, (3x109 CFU), B infantis M-63 (1x109 CFU),and B. breve M-16 V (1x109 CFU) as a powder in 3 mg sachets. Bifidobacteria mixture can be increased significantly AR symptoms and quality of life in children with pollen-induced AR and intermittent asthma.[8]

Moura et al (2019) used a pilot longitudinal experimental and nonrandomized study for 30 patients from six to 17 years at least 60 days. All patients received beclomethasone at the initial visit, and one group also received a probiotic containing Lactobacillus reuteri (n = 14). Giving probiotics as an adjunct therapy for the treatment of children and adolescents with asthma improves the patient's clinical condition.[9]

Zeng et al, 2016 [10] used open-label, randomized, controlled multicenter trial for 235 respondents critically ill adult patients expected to receive mechanical ventilation for ≥48 hours. Probiotics used contain Bacillus subtilis and Enterococcus faecalis (Medilac-S). Patients were randomized to receive a probiotic capsule of 0.5 g three times daily via a nasogastric feeding

tube plus a standard preventive strategy or a standard prevention strategy alone, for a maximum outcome of 14 days. VAP progress is evaluated daily, and throat swabs and gastric aspirates are cultured at baseline and once or twice a week there after. Therapy with the probiotic bacteria B. Subtilis and E. faecalis is an effective and safe way to prevent VAP and acquisition of PPMO colonization in the stomach.

Mahmoodpoor et al, 2019 [11] used clinical trial for 100 critically ill adult patients who underwent mechanical ventilation for> 48 hours. The patients in the probiotic group received 2 capsules probiotic preparations and the control group received placebo daily for 14 days. Probiotic used *Lactobacillus* species (*casei*, *acidophilus*, *rhamnosus*, *bulgaricus*), *Bifidobacterium*species (*breve*, *longum*), and *Streptococcus thermophilus*. Probioticsfor the prevention of VAP is inconclusive but such an approach can reduce its length ICU and inpatient hospital.

Leyer et al, 2009 [12] used double-blind, placebo-controlled study for 326 children (ages 3–5)were treated twice a day for 6 month. Probiotic used Lactobacillus acidophilus NCFM (N 110), or L acidophilus NCFM withBifidobacteriumanimalissubsplactis Bi-07Respondentswere randomly assigned a placebo(N 104), Lactobacillus acidophilus NCFM (N 110), or L acidophilus NCFM in combination with Bifidobacteriumanimalissubsplactis Bi-07(N 112). Daily dietary probioticsupplementation for 6 months is a safe and effective way to reduce fever, rhinorrhea, and coughand duration and incidence of antibiotic prescription, as wellnumber of days absent from school due to illness, for children 3up to 5 years of age.

Bianchini et al, 2020 [13] used a prospective, randomised, and single-blind study for 87 patients. Probiotic used LGG Lactobacillus rhamnosus GG (Dicoflor 60 Immuno D3, Dicofarm, Italy), containing 1 billion LGG / drop, QIV is associated with adequate immunogenicity in children and adolescents with T1D in the presence of a good safety profile. Although systematic administration of LGG does not result in improved humoral response to influenza vaccine, probiotics have important anti-inflammatory effects.

Wang et al, 2018 [14] used randomized, double-blind, placebo-controlled pilot trial for 196 nursing home residents aged 65 and older. They are randomized received probiotic studies - 2 capsules or placebo (calcium carbonate) every day for 6 months. Probiotic used Lactobacillus rhamnosus GG (estimated 10 billion colony forming units of L. rhamnosus GG per capsule). Feasibility of a trial assessing the effects of probiotics on reduce influenza and other respiratory infections in treatment houses for residents aged 65 years and over.

Discussion

Most of them use lactobacillus Sp as a probiotic in research. Previous research supports the potential of lactobacilli to regulate the immune system, increase intestinal metabolic capacity and maintain the balance of the gut microbiota. However, the species and specific characteristics of the lactobacilli strains that provide probiotic benefits are still not well understood [15]. There are recommendations about probiotics containing Lactobacillus rhamnosus GG (LGG) against acute gastroenteritis and against antibiotic-related diarrhea[16]. One research used Fructooligosacharide as additional ingredient. Fructo-oligosaccharides (FOS) are medium-chain carbohydrate compounds known as prebiotics with natural functional ingredients. Several studies have shown the functional properties of FOS, such as decreased cholesterol and blood glucose levels, decreased blood pressure, better absorption of calcium and magnesium, as well as inhibiting the production of reductase enzymes which can contribute to cancer, stimulating the growth of non-pathogenic intestinal microflora (bifidobacteria). and boosts the immune system[17].

The dosage used also varies. Various dosages for Lactobacillus sp. and other probiotics have been studied in clinical trials. In general, higher probiotic doses (ie, more than 5 billion CFU per day in children and more than 10 billion CFU per day in adults) were associated with more significant study results. There is no evidence that higher doses are unsafe; however, they may be more expensive and unnecessary. The dosage of S. boulardii in most studies has ranged between 250 mg and 500 mg per day. Probiotics are generally sold as capsules, powders, tablets, liquids, or in foods. The specific amount of CFU contained in a particular dosage or serving of food may vary between brands. Patients should be advised to read product labels carefully to make sure they are getting the

right dose [18]

Probiotics have been explored in a number of clinical trials which are increasing exponentially for their health effects. Underpowered clinical trials are another problem in the probiotic field[16]. Most research used to study children and adults with almost similar effectiveness though respiratory diseases often attack children. Infants and young children have higher resting metabolic rates and oxygen consumption per unit of body weight than adults because they have a larger surface per unit due to body weight and because they are growing rapidly [19].

Most of the studies found a reduction in symptoms, risk of hospitalization, risk of ICU and nasal symptoms including the respiratory symptoms present in Covid-19, namely fever, rhinorrhea, and cough. Probiotics exert their beneficial effects by modulating the host's immune response, maintaining gut homeostasis and producing interferon thereby suppressing viral cytokine-induced storms. In fact, immune stimulation and cytokine expression are strain specific, and can vary according to the probiotic bacterial consortium[20]. Probiotics are live microorganisms that provide health benefits when consumed in sufficient quantities, including subtle immune activity and clearing of respiratory tract infections [21]. The main points of the role of probiotics are health promotion, infection control and management. disease [6].

All studies reviewed in this article did not analyze and report side effects of probiotic administration. There are studies that report side effects of probiotics such as minor gastrointestinal symptoms, such as stomach cramps, nausea, soft stools, flatulence, and taste disturbances, which occurred in subjects receiving probiotics[22]. Most probiotics are safe. There are rare occurrences of sepsis, endocarditis, and liver abscess during Lactobacillus use; In addition, fungemia has been reported with S boulardii, especially in patients with severe comorbidities. The most common side effects of probiotics are constipation, flatulence, hiccups, nausea, infections, and rashes [23].

Most of the studies agree and support probiotics in respiratory disease in general. This shows possible applications in the management of COVID-19. Probiotic research in the form of a randomized control trial needs to be carried out in the management of COVID-19. Several systematic reviews underscore the need for studies that address the role of clear, recommended doses and the broader affordable population. Better designed randomized controlled trials with larger sample sizes need to be done to improve the quality of research[24].

Much remains to be learned about the determinants of the various immune responses induced by different strains of bacteria. Deeper knowledge of the interactions between specific probiotics and existing microbiota, along with an understanding of how the dialogue between microbes and innate management systems becomes a beneficial / protective response is needed before we can achieve clinically effective bacteria-based strategies which maintains and improves respiratory health[25]. Physiology and pathology of the respiratory tract and digestive tract are closely related. The similarity of these two organs may be the reason why dysfunction in one organ can cause disease in other organs. In this sense, probiotics can act as immunomodulatory agents and activators of the body's defense pathways suggesting that probiotics can affect the severity and incidence of disease at the location of the distal intestine. There is more evidence that probiotics given orally are able to provide an immune response in the respiratory system [26].

Conclusion

Probiotics have many great benefits related to the respiratory system. This is likely to be able to support health services during the Covid-19 period. Recommendations for further research are randomized control trials that are able to analyze the ability of probiotics, dosages and their processes in the management of respiratory diseases. This research is expected to be able to be an alternative and supportive therapy during a pandemic.

Ethical Clearance: This manuscript has passed the ethical test process in Faculty of Medicine Universitas Airlangga.

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