

THE EFFECT OF PROBIOTICS TO ENHANCE THE IMMUNITY TO COMBAT THE RESPIRATORY INFECTIONS IN THE ELDERLY WITH COMORBIDITIES.

Keerthana T ¹, S. Ray ², Ramya AKL ³

¹ SHP, Rutgers, State University, ² CAS, Rutgers State University, ³ Microbiologist

ABSTRACT

Background: The greatest challenge the mankind is facing currently is the development of the respiratory infectious disease. The risk of respiratory infections has radically increased over the years. According to the National Center for Health Statistics (2020), respiratory diseases is highest in persons aged >85 years and is 57% and 85% lower in those aged 75 to 84 years and 65 to 74 years, respectively. Respiratory-disease mortality rates across these age groups were within 15% of each other.

Objective: To identify the effect of probiotics on the immunity to combat respiratory diseases in elderly people (60yr and above) with comorbidities.

Methods: A review of relevant studies was conducted using Medline/PubMed, EMBASE, Cochrane, and Google Scholar. Finally, after advanced search using keywords such as “probiotics, immunity, respiratory diseases, viral respiratory infection, older adults,” availability and relevancy based on title and year of study a total of 10 articles were analyzed for systematic review.

Results: The results suggested the positive effect of the probiotics which is indirectly related to the enhancement of innate immunity and to combat various respiratory diseases in adults with comorbidities.

Conclusion: The adequate dose of probiotics in elderly with comorbidities and compromised gut microbiota can combat with respiratory diseases and viral infections.

INTRODUCTION

In the spread of respiratory viral infection, the vulnerable population is elderly people with comorbidities. Many of them are trying to understand the nature of the infection and practicing methods to stay away from the infection. A probiotic is one of the most essential elements that can boost up the immunity. So, from the systemic review of literature, the derivation that probiotics can improve the immunity against respiratory diseases and viral infection in elderly people with comorbidities is analyzed. Gut microbiota diversity is decreased in old age and Covid-19 has been mainly fatal in elderly patients, indicating to the role the gut microbiota may play in this disease.

According to Isolauri et al in 2001, the establishment of indigenous microflora depends upon the generation of immune physiological regulation in the gut. The potential mechanisms of probiotic therapy are promotion of a nonimmunologic gut defense barrier, this includes the stabilization of increased intestinal permeability and altered gut microecology. The findings of this study imply that certain immunomodulatory properties of probiotic bacteria must be characterized while developing clinical applications for extended target populations.

In 2010 according to the findings of Seiya et al in their studies, stated that the consumption of yogurt fermented with *Lactobacillus bulgaricus* enhanced natural killer cell mechanism and lowered the risk of infection of common cold in elderly individuals.

Monachese et al in their studies in 2010, mentioned that the greatest challenges in the developing country is the infectious diseases. This consent report summarizes the potential probiotic to help millions of people to combat the infectious diseases at affordable prices.

In 2014, Lehtoranta et al in their studies review the current knowledge on the effects of the probiotics on the respiratory virus infections and to provide possible insights on the antiviral mechanisms of the probiotics. The results from these experimental studies states that probiotics exert effects directly on the probiotic virus interaction or through stimulation

of the immune system. Due to lack of the adequate investigation the role of the probiotics on specific viruses has not been identified yet.

Frei et al in 2015, concluded that the possible benefits of the probiotics, prebiotics, or their combination exert potent effects on the immune system

Osamu et al demonstrates in their studies in 2018, that the unique mechanism by which viruses are excluded through the activation of type 1 interferon production by probiotics and Para probiotics via the activation of dendritic cells. These are expected to be among the rational adjunctive options for the treatment of various viral diseases.

In 2019, Negi et al described the interactions of the host with the microbiota are complex, numerous and bidirectional. The gut microbiota is supposed to significantly regulate the development and function of the innate and adaptive immune system. Improving the gut microbiota may be prophylactic way to minimize the impact of the disease in old and immunocompromised patients.

In 2020, Zuo et al in their studies by performing shotgun metagenomic sequence analyses of the fecal samples of 15 COVID patients found the persistent alterations on the fecal microbiome during the hospitalization when compared to controls. They are also associated with severity of the disease. Few strategies to alter the gut microbiota may reduce disease severity.

Aravind et al in 2020, in their studies on COVID 19 described the unique role of probiotics to modulate the gut microbe and establish gut homeostasis and production of interferon as an antiviral mechanism. The regulatory role of probiotics on gut-lung alliance and mucosal immune system for the potential antiviral mechanisms is reviewed.

According to Shabazi et al studies in 2020 probiotics are nowadays well recognized to emphasize immunity and neutralize inflammation by restoring symbiosis within the gut microbiota. Inflammation is a natural biological response to the activation of the immune system. This inflammation can be caused by various infectious and noninfectious agents

which may lead to cell damage and several diseases. Probiotics protect against various diseases, including respiratory infections.

The goal is to establish a robust understanding of the effect of the probiotics on the immunity to combat against the respiratory diseases and to understand the influence of probiotics on the elderly people with comorbidities, by undergoing systemic analysis of the research articles.

METHODS

A review of relevant studies was conducted to evaluate the effectiveness of prescription opioids among elderly population of age 60 years and above of United States. Articles from Medline/PubMed, Science direct, Wiley online library, PsycINFO, EMBASE, Cochrane, and Google Scholar PRISMA was used to illustrate the process of selection. The articles were searched using advanced search option with keywords such as probiotics, immunity, respiratory diseases, viral respiratory infection, older adults. This search first yielded 1186 journal articles. After carefully screening of articles depending on the title and availability of full text article, about 80 articles were analyzed. All the duplicate articles, unmet inclusion criteria, exclusions were exempted, and paid citations were only viewed for abstracts. After the exclusions, there were 31 full text articles which were reviewed and analyzed and 16 articles were finally selected for further review analysis.

Inclusion and exclusion criteria:

Out of 16 abstracts, 6 abstracts are excluded, and these are based on the

- a. The study (1) did not mention anything about immunity against infections.
- b. The study (2) used a vaccine response which is not relevant to the research topic.
- c. The study (1) mentioned no association between the probiotics and immunity against viral respiratory infections.
- d. The studies (2) based on the inclusion of young and infant population.

RESULTS

Ten articles are included in this systematic review. Six were systemic review studies, one was narrative study, two were meta-analysis and one was case control study report. Population size ranged from as low as 15 to 85 for meta-analysis and case control study, and about 11 to 15 articles were reviewed in the systematic analysis, narrative analysis and metanalysis studies included in our study.

In one of the studies the participants were categorized into two independent studies, with fifty-seven of median age 74.5 years and eighty-five healthy elderly individuals of median age 67.7 years. The case control study report included fifteen patients diagnosed with COVID 19 from Hongkong. The analyzed review articles state the importance of the probiotics for the improvement of gut microbiota which enhances the innate immunity of the elderly with comorbidities.

The ten review papers advocate the association between the intervention probiotics and the improvement of the innate immunity. The more clinical trials and adequate research would be predicted to generate more statistically significant correlation reports.

Probiotics are the live microorganisms when administered in the adequate quantities into host impart the benefits the gastrointestinal health. The intestinal microbial balance tends to develop and modulate the immune function promoting the overall health of the individual. The researchers now have the substantial evidence on probiotics promoting the immune mechanisms in the host and the importance of the human microbiota is been recognized and most of the diseases are treated alongside with probiotic treatments.

The mechanisms of the probiotic on immunity to combat the respiratory diseases however needs great amount of research and trials. The gastrointestinal tracts act as the barriers against the foreign agents causing infections from food and microbiota. The stimulation of the immunophysiologic mechanism starts with the indigenous microflora. The

probiotic effects are mediated through the immune regulation through balanced control of proinflammatory and anti-inflammatory cytokines.

SUMMARY

S. NO	AUTHOR/YEAR	METHODS	FINDINGS	COMMENTS
1.	Isolauri et al 2001	Systemic review	These results suggest that specific immunomodulatory properties of probiotic bacteria should be characterized when developing clinical applications for extended target populations.	The data shows that participants show variations in the immunomodulatory effects due to probiotic bacteria.
2.	Makino et al 2010	Meta-analysis (n=57 and n=85)	The consumption of yogurt fermented with <i>Lactobacillus bulgaricus</i> enhanced natural killer cell mechanism and lowered the risk of infection of common cold in elderly individuals.	The yogurt fermented with <i>L. bulgaricus</i> OLL1073R-1 may be a new beneficial food for the elderly

3.	Monachese et al 2010	Systemic review	The importance of the human microbiota in retaining health is now recognized, as is the concept of replenishing beneficial microbes through probiotic treatments. The study have indicated that probiotics can reduce the duration of diarrhea and improve gut barrier function.	This consent report summarizes the potential probiotic to help millions of people to combat the infectious diseases at affordable prices.
4.	Lentoranta et al 2014	Systemic review	Twenty-eight trials reported that probiotics had beneficial effects in the outcome of respiratory tract infections (RTIs) and five showed no clear benefit. Only 8 studies registered examining viral etiology from the respiratory tract infections, and one of these described a significant decrease in	The probiotics seem to be therapeutic in respiratory illnesses, the role of probiotics on specific viruses has not been investigated adequately. Due to the lack of confirmatory studies and wide-ranging data available, more randomized, double-blind, and placebo-controlled trials in different age populations investigating

			<p>viral load. Based on these studies, probiotics may exert antiviral impacts directly in probiotic-virus interaction or via stimulation of the immune system.</p>	<p>probiotic dose response, comparing probiotic strains/genera, and interpreting the antiviral effect mechanisms are obligatory.</p>
5.	Frei et al 2015	Narrative review	<p>The probiotics, prebiotics, or their combination exert potent effects on the immune system</p>	<p>The immunological mechanisms underpinning probiotics, prebiotics, and synbiotics effects continue to be better defined with novel mechanisms</p>
6.	Osamu et al 2018	Metanalysis	<p>The efficacy of probiotics and para probiotics for the prevention or treatment of infectious diseases, which have been increasing in incidence in recent years.</p>	<p>The state of knowledge regarding the immunomodulatory effects of probiotics has recently advanced and various studies have especially focused on the interactions between commensal bacteria and the mucosal immune system.</p>

7.	Negi et al 2019	Systemic review	The interactions of the host with the microbiota are complex, numerous and bidirectional. The gut microbiota is intended to considerably regulate the development and function of the innate and adaptive immune system.	It explains the association between the gut microbiome and innate memory
8.	Zuo et al 2020	Case control studies (n=15 and placebo n=15)	These bacteria are bacteremia-associated bacteria, indicating susceptibility for severe disease course due to potential secondary bacterial infection.	Few strategies to alter the gut microbiota may reduce disease severity.
9.	Sundaram et al 2020	Systemic review	The findings show probiotics and probiotic-derived factors have promise for enhancing health benefits and regulation of host homeostasis,	This study confirms that immune stimulation through probiotics potentially promote prolonged resistance to virus infections and diseases in humans.

			including immune health.	
10.	Shabazi et al 2020	Systemic review	The potential role of probiotics in the treatment of viral respiratory infections, including the COVID-19 disease, as major public health crisis in 2020, and influenza virus infection, and in therapy of neurological disorders like multiple sclerosis and other mental illnesses.	Probiotics protect against various diseases, including respiratory infections.

CONCLUSION

The intake of probiotics has shown evidence and modest effects on the viral respiratory infection. Although the mechanisms were not perspicuous, there is proof from animal models that probiotic shows positive influence on innate immunity to pathogens causing infections.

COVID-19 CLINICAL STUDY AND OUTCOME:

Covid-19 pandemic has driven the world to the verge. The sooner we understand the patterns and epidemiology of the disease the better we will be prepared the next time. It is remarkable to

know that the general imbalance of gut microbiota called “dysbiosis” is the implicated reason in such COVID-19 elderly patients with comorbidities.

Study of gut microbiota has driven our knowledge in the field of chronic and infectious diseases. Gut microbiota diversity and the existence of beneficial microorganisms in the gut may play a crucial role in regulating the path of this infectious disease. The elderly patients with compromised immunity, and with other co-morbidities like type-2 diabetes, cardiovascular disorders perform poorly in combating Covid-19.

For observing the role of probiotics on enhancing the immunity in elderly patients (60yr and above) with comorbidities, given some suggestions to those patients to take probiotics (yogurt) in their daily routine. Taking the respiratory issues on the main light in this survey, the data was collected of the patients (study group = 10 and placebo=10) with pre and post infection .Two groups of patients were selected randomly, who were on the intervention on the yogurt-based diet. Based on those observations, moderate changes in the health were observed. The overall improvement was observed on intervention group than the placebo. Diabetic patients who took probiotics got back to their stable/pre infection state, whereas those who did not still have shown some variations in their blood sugar levels after the recovery from the respiratory illness. Based on this survey on the data collected and observed from these patients, it seems that probiotics may have some impact on the improvement of respiratory health.

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