

Unlocking the Power of Probiotics: A Potential Game-Changer in Allergic Rhinitis Management

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ABSTRACT

OBJECTIVE: To study effects of probiotics on clinical symptoms of the allergic rhinitis and their remission in comparison with conventional treatment.

Study Design: Randomized Clinical Trial

Place and Duration of the study: Department of ENT & Head and Neck Surgery, PIMS hospital, Islamabad, from January 2021 to June 2021.

METHODOLOGY: After approval from ethical review board, the study was started by recruiting 102 patients. The patients randomized into the two groups: Control group (group A) and treatment group (group B). Group A in which patient was given Nasal spray, Montelukast, and Anti allergic and Group B in which oral Probiotics 4 billion colony forming units/g once daily was given along with the other medication for first four weeks and then Nasal spray, Montelukast and Probiotic given for the next four weeks followed by only Nasal spray and probiotic for the last four weeks. The study lasted 12 weeks, after treatment began. Severity of AR was assessed at each visit using the Specific Symptoms Score (SSS) and Nasal Symptom Scores (NSS).

RESULTS: We find age of patients in group A and B was as 24.25 ± 8.93 vs 25.86 ± 8.78 ($p=0.361$). In group A 47.1% were male & 52.9% were female and in group B 49.0% were male and 51.0% were female. The nasal symptom score in group A and B at baseline was as 13.84 ± 0.78 vs 14.12 ± 0.82 ($p=0.086$), at 4 weeks was as 12.76 ± 0.79 vs 11.86 ± 0.94 ($p=0.000$), at 8 weeks was 10.78 ± 0.86 vs 8.96 ± 0.82 ($p=0.000$) and at 12 weeks was 9.73 ± 0.78 vs 6.00 ± 0.80 ($p=0.000$). Similarly, the specific symptoms score in group A and B at baseline was 42.43 ± 1.75 vs 42.80 ± 1.67 ($p=0.274$), at 4 weeks was as 36.25 ± 1.73 vs 33.69 ± 1.66 ($p=0.000$), at 8 weeks was 27.31 ± 1.74 vs 21.69 ± 1.69 ($p=0.000$) and at 12 weeks was as 21.22 ± 1.89 vs 6.69 ± 1.69 ($p=0.000$).

CONCLUSION: Probiotics are beneficial in improving symptoms (nasal symptoms and specific symptoms scores) in patients with allergic rhinitis along with decreased remission of the symptoms after completion of therapy.

Key Words: Allergic rhinitis, clinical symptoms, conventional treatment, nasal symptom score, probiotics, remission, specific symptom score

INTRODUCTION: Allergic rhinitis (AR) affects 10 % to 30% of world's population. When person is exposed to allergen, IgE-mediated inflammatory responses in nasal mucosa are triggered, resulting in allergen sensitization and development of atopic reaction¹.

Allergy is deficiency in "allergen-specific T regulatory cells" that allows T helper 2 "Th2" cells to become polarized. Interleukins such as IL-13, IL-5 and IL-4 are produced by Th2 cells and are responsible for the allergic inflammation².

Because AR is complicated multifactorial illness involving both adaptive and innate immune responses,

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underlying immunological processes are not yet completely explored. AR belongs to group of the type I allergic disorders that are defined by increase in the serum immunoglobulin E "IgE" levels³.

Pruritus, sneezing, nasal congestion and rhinorrhea are symptoms of the condition. Mold spores, animals, mites and house dust are all important triggers that cause symptoms to reappear on a regular basis. Pollen exposure is the most common cause of seasonal or intermittent illness⁴.

Allergic rhinitis is often a self-limiting condition. Symptomatic alleviation often requires medical intervention. Probiotics, intranasal corticosteroids, decongestants, antihistamines and allergen avoidance are some of the current therapy options⁵.

Probiotics are live microorganisms that provide physiologic benefits after being administered to the host. Because of their broad availability, few side

effects, and inexpensive cost, probiotics might be an alternate treatment option for AR. Probiotics help to stop and cure allergic illness by altering the intestinal environment⁶.

Lactobacilli are thought to trigger Th1 cell reactivity and hence ameliorate allergy illnesses, thereby enhancing quality of life⁷.

Antihistamines are considered to be first line of therapy for AR, however they may induce drowsiness and impair cognition and the performance in youngsters. Corticosteroids are also effective for minimizing inflammation in the AR, although they may disrupt development and growth in children^{8,9}.

Although some drugs have been shown to provide symptomatic relief, total symptom resolution is not always attained. AR symptoms vary, based on seasonal variations in environment's allergic load and individual susceptibility to the environmental allergens. Probiotics have recently gained popularity as a supplemental technique for a variety of health benefits¹⁰.

Thus, this study aimed at investigating whether a probiotic mixture could be able to relieve nasal, pharyngeal, ocular and lung symptoms in patients with allergic rhinitis.

METHODOLOGY: It was a single-Centre, randomized clinical trial conducted on the Allergic Rhinitis Patients presented in the OPD of Department of ENT & Head and Neck Surgery, Pakistan Institute of Medical Sciences, Islamabad from January 2021 to June 2021. Both males and females older than 10 years and younger than 60 years with More than 02 years history of the moderate to the severe persistent AR symptoms were included. The patients who were suffering from non-allergic rhinitis, pregnant, consumed probiotics within last 12 weeks, undergone treatment with systemic corticosteroids within the last 06 months or antibiotics within last 30 days, history of recent surgery (03 months duration), use of other immune modulating or anti-inflammatory medication, existing disease of respiratory airway including nasal polyposis, asthma and COPD were excluded from the study.

An ethical approval was taken from hospital ethics committee before he starting the study. Patients were filtered from OPD of ENT Department, PIMS, Islamabad & their data was recorded on a proforma. The patients randomized into the two groups consisting of conventionally treated patients [Control group (group A)] and patients treated with probiotic [Treatment group (group B)]. Group A in which patient was given

Mometasone nasal spray 2 puffs in each nostril (200mcg) per day, tablet Cetirizine 10mg per oral at night and tablet Monteleukast 10mg once daily, for the first 4 weeks. For subsequent four weeks, Mometasone nasal spray 2 puffs in each nostril (200mcg) per day and tablet Monteleukast 10mg once daily was prescribed while in last 4 weeks of treatment only Mometasone nasal spray 2 puffs in each nostril (200mcg) per day was given. In group B same protocol was followed as in group A but also added Ecotec probiotic sachet 4billion colony forming units for whole span of treatment (12 weeks).

The study lasted 12 weeks and patients were followed on monthly basis. On initial visit, at the time of patient enrolment, "Scoring Allergic Rhinitis Index" SSS "specific symptom score" was recorded on proforma to determine degree and severity of the allergic rhinitis. Subsequently patients were followed at 4 weeks, 8 weeks and 12 weeks and "Scoring Allergic Rhinitis Index" SSS "specific symptom score" was recorded on proforma.

The data was analyzed in SPSS Version 25. Qualitative variables like gender were presented as frequency with percentage. Quantitative variables like age, NSS and SSS were presented as mean with standard deviation. Chi square test and t-test was applied to compare improvement in symptoms between both groups. The P value = 0.05 was considered significant.

RESULTS: In our study we enrolled 102 patients 51 in each group. The mean age of patients in group A was 24.25 ± 8.93 years and in group B was 25.86 ± 8.78 years with insignificant p value ($p=0.361$).

In group A 24(47.1%) were male & 27(52.9%) were female and in group B 25(49.0%) were male and 26(51.0%) were female with insignificant p value ($p = 0.843$).

At baseline the mean nasal symptom score in group A was 13.84 ± 0.78 and in group B was 14.12 ± 0.82 with insignificant p value ($p = 0.086$). At 4 weeks the mean nasal symptom score in group A was 12.76 ± 0.79 and in group B was 11.86 ± 0.94 with significant p value ($p = 0.000$).

At 8 weeks the mean nasal symptom score in group A was 10.78 ± 0.86 and in group B was 8.96 ± 0.82 with significant p value ($p = 0.000$). At 12 weeks the mean nasal symptom score in group A was 9.73 ± 0.78 and in group B was 6.00 ± 0.80 with significant p value ($p = 0.000$).

Table 1: Results of Nasal Symptom Score in Study Groups

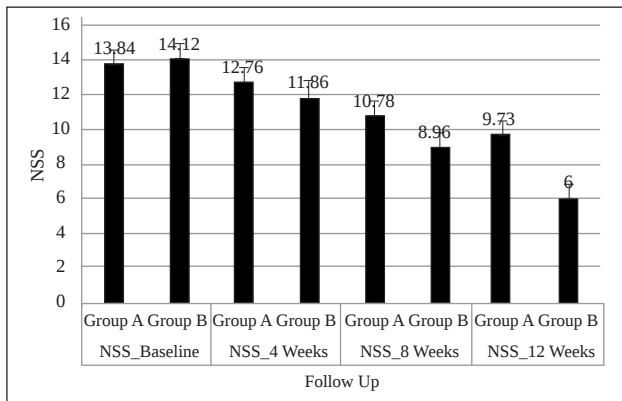
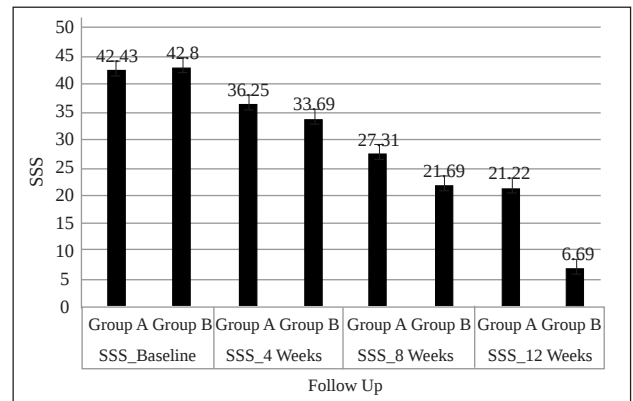
NSS	Groups	N	Mean	SD	p value
Nasal Symptom Score Baseline	Group A (Control Group)	51.00	13.84	0.78	0.086
	Group B (Treatment Group)	51.00	14.12	0.82	
Nasal Symptom Score_4 Weeks	Group A (Control Group)	51.00	12.76	0.79	0.000*
	Group B (Treatment Group)	51.00	11.86	0.94	
Nasal Symptom Score_8 Weeks	Group A (Control Group)	51.00	10.78	0.86	0.000*
	Group B (Treatment Group)	51.00	8.96	0.82	
Nasal Symptom Score_12 Weeks	Group A (Control Group)	51.00	9.73	0.78	0.000*
	Group B (Treatment Group)	51.00	6.00	0.80	

*Significant (p<0.05)

Table 2: Results of Specific Symptom Score in Study Groups

NSS	Groups	N	Mean	SD	p value
Specific Symptom Score Baseline	Group A (Control Group)	51.00	42.43	1.75	0.274
	Group B (Treatment Group)	51.00	42.80	1.67	
Specific Symptom Score_4 Weeks	Group A (Control Group)	51.00	36.25	1.73	0.000*
	Group B (Treatment Group)	51.00	33.69	1.66	
Specific Symptom Score_8 Weeks	Group A (Control Group)	51.00	27.31	1.74	0.000*
	Group B (Treatment Group)	51.00	21.69	1.69	
Specific Symptom Score_12 Weeks	Group A (Control Group)	51.00	21.22	1.89	0.000*
	Group B (Treatment Group)	51.00	6.69	1.69	

*Significant (p<0.05)

**Figure 1: Results of Nasal Symptom Score in Study Groups****Figure 2: Results of Specific Symptom Score in Study Groups**

At baseline the mean specific symptom score in group A was 42.43 ± 1.75 and in group B was 42.80 ± 1.67 with insignificant p value ($p = 0.274$). At 4 weeks the mean specific symptom score in group A was 36.25 ± 1.73 and in group B was 33.69 ± 1.66 with significant p value ($p = 0.000$).

At 8 weeks the mean specific symptom score in group A was 27.31 ± 1.74 and in group B was 21.69 ± 1.69 with significant p value ($p = 0.000$). At 12 weeks the mean specific symptom score in group A was 21.22 ± 1.89 and in group B was 6.69 ± 1.69 with significant p value ($p = 0.000$). The use of probiotic significantly improved the symptoms of allergic rhinitis.

DISCUSSION: Allergic rhinitis (AR) is most prevalent disorders in world, affecting 10% to 50% of population. According to different studies, prevalence of asthma and AR is believed to be between 20% and 30%. It has a bad impact on patient's health, as well as quality of the sleep and function of person, as well as numerous yearly expenditures for managing the illnesses that individual consumes^{11,12}.

Antihistamines are administered as first-line treatment for AR since histamine is most prevalent mediator of condition. AR has additional effects than the common illnesses like cardiovascular disease, diabetes, respiratory infections, migraine and depression because of symptoms like reduced productivity, increased drowsiness, learning difficulties, insomnia, sleep disturbances, itching and sneezing and work concentration on work and activities of school¹³.

AR is kind of type I hypersensitivity "IgE-mediated illness" that is caused by mast cell degranulation. Basophils and Mast cells' abandoned mediators are catalysts for process. The expense of controlling AR is larger than chronic and common illnesses like URTI "upper respiratory tract infection" and diabetes on annual basis¹⁴.

Probiotics are living bacteria that aid in regular functioning of colon and may boost mucosal immune system to avoid atopy symptoms and allergy⁴. Probiotics' effectiveness in contrast to traditional therapies like antihistamines, anti-leukotrienes, systemic and topical corticosteroids, and the immunotherapy is unknown.

Despite the fact that probiotics activate immune system at mucosal surface and stop the formation of atopy and inflammatory responses caused by AR illness, there is no agreement on their anti-inflammatory benefits⁴. Therefore, we conducted this study at the "Department of ENT Head and Neck Surgery, Pakistan Institute of Medical Sciences, Islamabad" to study the effects of Probiotics on the clinical symptoms of AR and their remission in comparison with the conventional treatment.

We find age of patients in group A and B was as 24.25 ± 8.93 vs 25.86 ± 8.78 , $p=0.361$. In group A 47.1% were male & 52.9% were female and in group B 49.0% were male and 51.0% were female. The nasal symptom score in group A and B at baseline was 13.84 ± 0.78 vs 14.12 ± 0.82 ($p=0.086$), at 4 weeks was 12.76 ± 0.79 vs 11.86 ± 0.94 ($p=0.000$), at 8 weeks was 10.78 ± 0.86 vs

8.96 ± 0.82 ($p=0.000$) and at 12 weeks was 9.73 ± 0.78 vs 6.00 ± 0.80 ($p=0.000$). Similarly, the specific symptoms score in group A and B at baseline was 42.43 ± 1.75 vs 42.80 ± 1.67 ($p=0.274$), at 4 weeks was 36.25 ± 1.73 vs 33.69 ± 1.66 ($p=0.000$), at 8 weeks was 27.31 ± 1.74 vs 21.69 ± 1.69 ($p=0.000$) and at 12 weeks was as (21.22 ± 1.89 vs 6.69 ± 1.69 , $p=0.000$).

According to Sadeghi-Shabestari et al, AR is most frequent disorders worldwide. Probiotics are living microorganisms that aid in the regular functioning of the gut when used as directed. Their findings showed that probiotics had no discernible therapeutic impact on AR patients after just a few weeks of medication. The efficiency of probiotics in treatment of AR patients seems to be influenced by the length of therapy and various bacteria species¹¹. These findings not matched with our study results as the duration of our study was short.

Probiotics were given as supplement with the antihistamines in individuals with the AR for 24 weeks in a research by Leu et al. Both control and experimental groups had considerably decreased symptoms after the 24 weeks, while the experiment group's change in symptoms was extra significant than control group's during first 12 weeks¹⁶.

Patients who took probiotics had a substantial reduction in nasal discharge, according to Xiao et al.¹⁷, which was comparable to our findings. In another trial, Jalali et al. found that adding probiotics to chronic AR patients' nasal corticosteroid medications enhanced their quality of life considerably¹⁸.

Kang et al separately assessed the effectiveness of NPV-1703 without the anti-AR drugs and completed both TNSS and QoL evaluations in a research. The TNSS and RCAT scores of NVP-1703 both improved significantly. NVP-1703 is first probiotic combination to be shown to be beneficial in individuals with symptomatic AR without requirement for additional treatment or rescue medicine. Their findings provide solid evidence for usefulness of probiotics in treatment of AR¹⁹.

Anania et al reported probiotics have been shown to be useful in reducing symptoms and enhancing quality of life in individuals with AR in many clinical studies. However, since most studies have revealed substantial variation in terms of strains, dose, timing, and results, the existing data does not support use of probiotics as a main preventative measure for allergic disorders²⁰.

Probiotics might be useful in treatment and prevention of AR. The therapeutic effectiveness of probiotic treatment is dependent on a variety of parameters, including the bacteria used, the mode of administration, dose, and regimen, as well as other underlying host characteristics²¹. Furthermore, the most advantageous probiotic strain must be chosen, as well as the duration of treatment, but these questions need more research to be answered. A probiotic fusion protein might be a unique way to increase the efficiency of allergic rhinitis therapy.

Additional research is needed to determine the clinical effectiveness of probiotics, the process for choosing microorganisms, the design of acceptable study populations, and the safety of employing probiotics. The mechanisms of action of the probiotics in modifying immune response must be investigated further.

CONCLUSION: Probiotics are a good therapeutic cure for allergic rhinitis; however the underlying processes need to be researched further.

We conclude that probiotics are beneficial in improving symptoms in patients with allergic rhinitis along with decreased remission of the symptoms after completion of therapy in short term follow-up.

Declaration:

Conflict of interest: Authors declare no conflict of interest.

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REFERENCES:

1. Watts AM, West NP, Smith PK, Cripps AW, Cox AJ. Probiotics and allergic rhinitis: a Simon two-stage design to determine effectiveness. *J Alternative Complementary Med.* 2016; 22(12):1007-12.
2. Miraglia Del Giudice M, Indolfi C, Capasso M, Maiello N, Decimo F, Ciprandi G. Bifidobacterium mixture (B longum BB536, B infantis M-63, B breve M-16V) treatment in children with seasonal allergic rhinitis and intermittent asthma. *Ital J Pediatr.* 2017;43(1):1-6.
3. Ren J, Zhao Y, Huang S, Lv D, Yang F, Lou L, et al. Immunomodulatory effect of Bifidobacterium breve on experimental allergic rhinitis in BALB/c mice. *Exp Ther Med.* 2018; 16(5):3996-4004.
4. Zajac AE, Adams AS, Turner JH, editors. A systematic review and meta-analysis of probiotics for the treatment of allergic rhinitis. International forum of allergy & rhinology; 2015: Wiley Online Library.
5. Yameen M, Angulo A, Bello A, Arce A, Varon DS, Varon J. Conventional and Alternative Treatment Options for Allergic Rhinitis. *Curr Respir Med Rev.* 2018;14(1):29-34.
6. Ahmed M, Billoo AG, Iqbal K. Efficacy of probiotic in perennial allergic rhinitis under five year children: A randomized controlled trial. *PaK J Med Sci.* 2019;35(6):1538.
7. Lin T-Y, Chen C-J, Chen L-K, Wen S-H, Jan R-H. Effect of probiotics on allergic rhinitis in Df, Dp or dust-sensitive children: a randomized double blind controlled trial. *Ind Pediatr.* 2013;50(2):209-13.
8. Church MK, Church DS. Pharmacology of antihistamines. *Ind J Dermatol.* 2013;58(3):219.
9. Luhulima F, Karyana I, Sumadiono S. Probiotic therapy on children with allergic rhinitis. *Paediatr Indones.* 2013;53(5):264-7.
10. Schaefer M, Enck P. Effects of a probiotic treatment (*Enterococcus faecalis*) and open-label placebo on symptoms of allergic rhinitis: study protocol for a randomised controlled trial. *BMJ open.* 2019;9(10):e031339.
11. Sadeghi-Shabestari M, Moghaddam YJ, Rezapoor H, Sohrabpour M. Effect of probiotics on allergic rhinitis: A randomized, controlled, clinical trial. *Galen Med. J.* 2020;9:e1918.
12. Mårtensson A, Abolhalaj M, Lindstedt M, Mårtensson A, Olofsson TC, Vásquez A, et al. Clinical efficacy of a topical lactic acid bacterial microbiome in chronic rhinosinusitis: a randomized controlled trial. *Laryngoscope Investigative Otolaryngol.* 2017;2(6):410-6.
13. Lin W-Y, Fu L-S, Lin H-K, Shen C-Y, Chen Y-J. Evaluation of the effect of *Lactobacillus paracasei* (HF. A00232) in children (6–13 years old) with perennial allergic rhinitis: a 12-week, double-blind, randomized, placebo-controlled study. *Pediatr Neonatol.* 2014;55(3):181-8.
14. Peng Y, Li A, Yu L, Qin G. The role of probiotics in prevention and treatment for patients with allergic rhinitis: A systematic review. *Am J Rhinology Allergy.* 2015;29(4):292-8.
15. Jan R-H, Chen C-J, Chen L-K, Wen S-H, Lin T-Y. Is the effect of probiotics on allergic rhinitis confined to *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, or dust-sensitive children? A randomized prospective double-blind controlled trial. *Tzu Chi Med J.* 2011;23(2):51-4.
16. Nishimura I, Igarashi T, Enomoto T, Dake Y, Okuno Y, Obata A. Clinical efficacy of halophilic lactic acid bacterium *Tetragenococcus halophilus* Th221 from soy sauce moromi for perennial allergic rhinitis. *Allergol Int.* 2009;58(2):179-85.
17. Xiao JZ, Kondo S, Yanagisawa N, Takahashi N, Odamaki T, Iwabuchi N, et al. Probiotics in the treatment of Japanese cedar pollinosis: a double-blind placebo-controlled trial. *Clin Exp Allergy.* 2006;36(11):1425-35.
18. Güvenç IA, Muluk NB, Mutlu FB, Epki E, Altıntoprak N, Oktamer T, et al. Do probiotics have a role in the treatment of allergic rhinitis? A comprehensive systematic review and Metaanalysis. *Am J Rhinology & Allergy.* 2016;30(5):e157-e75.
19. Kang M-G, Han S-W, Kang H-R, Hong S-J, Kim D-H, Choi J-H. Probiotic NVP-1703 alleviates allergic rhinitis by inducing IL-10 expression: a four-week clinical trial. *Nutrients.* 2020;12(5):1427.
20. Anania C, Di Marino VP, Olivero F, De Canditiis D, Brindisi G, Iannilli F, et al. Treatment with a Probiotic Mixture Containing *Bifidobacterium animalis* Subsp. *Lactis* BB12 and *Enterococcus faecium* L3 for the Prevention of Allergic Rhinitis Symptoms in Children: A Randomized Controlled Trial. *Nutrients.* 2021;13(4):1315.
21. Yang G, Liu Z-Q, Yang P-C. Treatment of allergic rhinitis with probiotics: an alternative approach. *N Am J Med Sci.* 2013;5(8):465