Volume-10 / Issue-I/June 2022/ISSN No.-2321-3450
ORIGINAL RESEARCH ARTICLE
DOI: httpp://doi.org/10.36611/upjohns/volume10/Issue1/6
Date received: 28.5.2022 / Date published: 30.6.2022

A STUDY ON THE ROLE OF PROBIOTICS IN NASAL ALLERGY

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ABSTRACT

INTRODUCTION:

One of the major components of the commensal microbial flora, which is being frequently used as probiotics in the intestinal tract of humans, is Lactobacilli. It exerts health benefits beyond inherent basic nutrition, and its role in increasing the immunomodulating capacity of the host is widely accepted. In the treatment of allergic diseases, the beneficial effect of probiotics has been demonstrated.

OBJECTIVE

This study was aimed to observe the effectiveness of probiotics in reducing the symptoms of nasal allergy.

METHODS

Total 50 patients suffering from Allergic Rhinitis (AR) were administered with probiotics for a period of six weeks post which the VAS and IgE scores of the symptoms (Rhinorrhea, Sneezing, and Nasal obstruction) were statistically analyzed. The pre and post treatment VAS and IgE scores were collected and analyzed.

RESULTS

It showed that there was a reduction in the scores after the administration of probiotics.

CONCLUSIONS

This prospective study demonstrated the presence of significant improvement in the VAS and IgE scores among the following nasal symptoms - Rhinorrhea, Sneezing, and Nasal obstruction with the administration of probiotics in the patients suffering with AR.

KEYWORDS

Allergic rhinitis, probiotics, nasal obstruction, rhinorrhea and sneezing.

INTRODUCTION

An inflammatory disorder of the nasal mucosa, Allergic Rhinitis (AR), is induced by exposure to an allergen, triggering Immunoglobulin E (IgE)-mediated inflammation. The four major symptoms - rhinorrhea, sneezing, nasal itching, and nasal congestion - characterize AR and may be associated with comorbid conditions like asthma, atopic dermatitis, and nasal polyps. While 20–30% of the Indian population suffer from AR, 15% of them develop asthma. Management of AR includes following the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines, and the treatment is a combination of allergen avoidance, pharmacotherapy, and allergen immunotherapy [1]. One of the major components of the commensal microbial flora, which is being frequently used as probiotics in the intestinal tract of humans, is Lactobacilli. It exerts health benefits beyond inherent basic nutrition, and its role in increasing the immunomodulating capacity of the host is widely accepted [2]. In the treatment of allergic diseases, the beneficial effect of probiotics has been demonstrated. The interaction between the probiotics and the immune system of the host results in modification of the natural course of allergic disease, which is why the probiotics are a profitable therapeutic treatment of AR [3].

Review Process: Double blind Peer Reviewed by Reviewer Board Members

"Hygiene hypothesis," postulates that by feeding probiotics to infants at risk for allergic diseases, atopic march could be altered. Immunomodulatory mechanisms are induced by the probiotics through the stimulation of gut-associated lymphoid tissue. Probiotics induce dendritic cell maturation for restoration of balance of Th1:Th2, through the production of Interleukin (IL) 12 and Interferon (IFN) γ, or by suppression of Th2 responses through the reduction of IL-4 and specific Immunoglobulin E (sIgE) production. A 50% decrease in the frequency of clinical eczema was reported with the supplementation of Lactobacillus rhamnosus strain GG (ATCC 53103) (LGG) [4].

It was demonstrated that stimulating the production of Immunoglobulin A (IgA) by certain strains of Lactic Acid Bacteria (LAB) also increases the number of IgA secreting cells, type I and II interferons and IL-12, and Interleukin-18 (IL-18). Interaction of gram-positive cell wall components (peptidoglycans and lipoteichoic acid) with surface receptors (CD14 and Toll-like receptor 2) of mononuclear phagocytes may inhibit T-helper subset 2 cell-skewed immune responsiveness, suppress IgE synthesis, and stabilize the mucosa barrier. LAB preparations can effectively enhance immunity and stimulation of IL-12 production in humans [5]. In this study, we aimed to study and observe the usefulness of probiotics in reducing the symptoms of nasal allergy.

METHODS

This is a prospective observational study with a duration of one-year analysis of administration of a course of probiotics to a population of adult patients (n=50) experiencing the symptoms of mild-to-moderate AR. Informed consent was obtained from the patients, who were explained about the study. Institutional Ethics Committee approval was obtained before the start of the study.

PATIENTS

The patients were prescribed with probiotics over a course of six weeks. For the sake of convenience only one brand and one concentration of probiotic was used in the study (Lactobacillus paracasei and Lactobacillus fermentum– 4 billion cells). No other antiallergy treatment were prescribed during the course of the study. Symptoms included were: nasal obstruction, rhinorrhea, and sneezing. Investigations of the patients included the subjective scoring of their symptoms pre-treatment and six weeks post treatment. It will be Visual Analog Scale (VAS) (1–10 severity scale of nasal symptoms - Rhinorrhea, Sneezing, and Nasal obstruction). Pre-treatment total IgE and post treatment total IgE values were done and compared.

INCLUSION CRITERIA

All adult patients within the age group of 18–60 years with a history of perennial AR. Only patients with history of respiratory allergy were included. No test was done to determine the allergens except serum IgE. The subjects were non-smokers and did not consume tobacco in any form. Patients who were previously using tobacco and have quit since last three months were also considered for the study. Patients who have not tried specific long-term treatment for allergic rhinitis were included. Patients who had occasional anti allergics and also who have tried prevention strategies and not found relief were also included.

EXCLUSION CRITERIA

The following subjects were excluded: Patients with allergic asthma or allergy to probiotics or any of its components or having other causes of nasal obstruction (Deviated Nasal Septum, Polyps, Mass in nasal cavity, Atrophic rhinitis, etc). Patients with severe symptoms of AR or with seasonal AR. Patients with history of food allergy and contact allergy were not included in the study. Pediatric patients were also excluded.

STATISTICAL ANALYSIS

The patients were subjected to VAS and IgE scores both pre and post treatment to analyze the extent of the antiallergic activity after the probiotic intervention. The resultant was normalized.

Normality of data assessment is necessary for the application of many statistical tests because normal data is an underlying assumption in parametric testing. Normality must be followed irrespective of the sample size for meaningful conclusions and assumptions. Once normality of a data is established, it must be analyzed to see if the mean is applicable as the representative value of the data or not. In case of the means being applicable, they are then compared with parametric test, otherwise medians are used to compare the groups using nonparametic methods [6]. Shapiro–Wilk test was utilized for finding the normality.

RESULTS

Over the course of one year, a sample size of (n=50) adult patients experiencing the symptoms of mild-to-moderate AR were enrolled, on whom VAS and IGe scores were collected. After the probiotic course of six weeks, the scores were again collected (Table 1).

1.Scores of VAS and IgE before and after intervention

Pt Sl no	Pre Rx VAS score	Pre-treatment IgE score	Post Rx VAS score	Post treatment IgE score
1.	7	453	2	247
2.	7	512	2	134
3.	8	398	3	278
4.	6	256	3	245
5.	7	314	2	213
6.	8	520	3	156
7.	6	413	3	198
8.	5	674	1	256
9.	6	703	1	319
10.	7	517	2	495
11.	8	678	4	412
12.	6	213	2	167
13.	7	367	3	112
14.	6	187	2	153
15.	6	298	1	174
16.	7	471	2	264
17.	7	342	3	375
18.	7	523	2	215
19.	8	671	3	313
20.	5	365	1	211
21.	6	732	3	345
22.	7	764	3	274
23.	6	543	2	182
24.	6	389	6	356
25.	7	498	4	183
26.	6	294	2	153
27.	6	378	3	102
28.	7	476	4	217
29.	7	523	3	265
30.	7	287	2	173
31.	6	365	2	112
32.	6	647	3	453
33.	7	369	4	168
34.	6	823	3	345
35.	6	432	2	124
36.	6	213	1	119
37.	7	476	3	184
38.	8	512	3	311
39.	6	601	2	264
40.	7	638	2	478
41.	6	128	2	113
42.	7	372	3	312
43.	7	538	1	211
44.	6	249	1	145
45.	5	535	5	351
46.	6	376	2	121
47.	6	437	2	158
48.	6	128	3	146
49.	7	218	2	175
50.	6	383	1	243

Through Shapiro–Wilk test (Table 2), it was understood that the data must be subjected to non-parametric test – the Wilcoxon Signed Rank Test (Table 3&4). It depicted a significant mean difference between IgE and VAS score with respect to pre and post treatment, thus rejecting the null hypothesis. The trial showed a significant reduction in VAS and IgE scores in the AR patients after the administration of probiotics. Even though in some patients there was no significant reduction in total IgE scores, better VAS scores were noted suggestive of symptomatic improvement.

1. Tests of Normality

Tests of Normality					
	Shapiro-Wilk				
	Statistic	df	Sig. (p-value)	Result	Tests of Normality
Pre Rx VAS score	.846	50	.000	Significant	Deviate from Normal Distribution
Post Rx VAS score	.877	50	.000	Significant	Deviate from Normal Distribution
Pre treatmentIGe score	.982	50	.648	Not Significant	Follows Normal Distribution
Post treatment IGe score	.925	50	.003	Significant	Deviate from Normal Distribution

Shapiro-wilk test was conducted to determine normality.

If sig. value (p –value) < 0.05 then the data deviate from normal distribution.
If sig. value (p –value) > 0.05 then the data follows normal distribution.

2. Wilcoxon Signed Ranks Test

Null Hypothesis (H0)

There is no significance mean difference between Rx VAS score with respect to pre and post treatment

Ranks				
		N	Mean Rank	Sum of Ranks
Post Rx VAS score - Pre Rx VAS score	Negative Ranks	48[a]	24.50	1176.00
	Positive Ranks	0[b]	.00	.00
	Ties	2[c]		
	Total	50		
a. Post Rx VAS score < Pre Rx VAS score				
b. Post Rx VAS score > Pre Rx VAS score				
c. Post Rx VAS score = Pre Rx VAS score				

Test Statistics[a]	
	Post Rx VAS score - Pre Rx VAS score
Z	-6.123[b]
Asymp. Sig. (2-tailed)	.000
a. Wilcoxon Signed Ranks Test	
b. Based on positive ranks.	

3. Wilcoxon Signed Ranks Test

Null Hypothesis (H0)

There is no significance mean difference between IGe score with respect to pre and post treatment

Ranks				
		N	Mean Rank	Sum of Ranks
Post treatment IGe score - Pre treatmentIGe score	Negative Ranks	48[a]	26.39	1266.50
	Positive Ranks	2[b]	4.25	8.50
	Ties	0[c]		
	Total	50		
a. Post treatment IGe score <Pre treatmentIGe score				
b. Post treatment IGe score >Pre treatmentIGe score				
c. Post treatment IGe score = Pre treatmentIGe score				

Test Statistics[a]	
	Post treatment IGe score - Pre treatmentIGe score
Z	-6.072[b]
Asymp. Sig. (2-tailed)	.000
a. Wilcoxon Signed Ranks Test	
b. Based on positive ranks.	

From the above table significant value (p- value) is 0.000 < 0.05, reject null hypothesis. It means that there is a significance mean difference between IGe score with respect to pre and post treatment.

Software: IBM SPSS V.20.0

DISCUSSION

The symptomatic disorder, AR, is induced after allergen exposure due to an IgE-mediated inflammation of membranes lining the nose. AR brings societal and considerable economic burdens. It is a global health problem. The incidence of AR in the western countries is 1.4–39.7%. Triggers of AR could be varied like hairs of domestic animals, dust mites, insects, pollens and moulds; occupational triggers like latex; tobacco smoke; automobile exhaust including ozone, oxides of nitrogen and sulphur dioxide; aspirin and other non-steroidal anti-inflammatory drugs. The absenteeism associated from AR results in greater economic losses than those of other common conditions such as migraine, diabetes, and asthma [1].

It was evident that many commensal microbes discarded the genes for survival in the microenvironments, while simultaneously developing genes which are beneficial for the host with no/little benefit to self, displaying the symbiotic co-evolution of the commensal microbes with the host. Allergies could be due to the alterations in microbial diversity. The Food and Agriculture Organization (FAO)/World Health Organization (WHO) defined probiotics as “live microorganisms which confer a health benefit on the host when administered in adequate amounts” [7]. In the treatment of allergic diseases, the beneficial effect of probiotics has been demonstrated. The interaction between the probiotics and the immune system of the host results in modification of the natural course of allergic disease, which is why the probiotics are a profitable therapeutic treatment of AR [3].

Yang G, et al., reviewed that although conventionally only a single probiotic strain (Lactobacillus acidophilus, L. paracasei, L. casei, L. rhamnosus, L. johnsonii,etc) could reduce AR, recent times witnessed the utilization of more than one strain of probiotics (LactobacillusGG (LGG) and L. gasseri, L. acidophilus and Bifidobacterium lactis) in AR treatment [3].

In the double-blind, randomized, placebo-controlled study by Wang IJ, et al., pediatric atopic dermatitis patients were randomized to receive L.

paracasei (LP), L. fermentum (LF), LP+LF mixture, or a placebo for 3 months. Changes in Family Dermatology Life Quality Index (FDLQI), Children's Dermatology Life Quality Index (CDLQI), and Severity Scoring Of Atopic Dermatitis (SCORAD) scores in the different groups and at different visits were evaluated along with levels of IgE, IFN-γ, IL-4, TGF-β, and TNF-α, and urine biomarkers. It was reported that children receiving LP, LF, and LP+LF mixture showed lower SCORAD scores than the placebo group ($p<0.001$), which continued to four months even after discontinuing the probiotics. IgE, TNF-α, urine eosinophilic protein X, and 8-OHdG levels decreased, whereas IFN-γ and TGF-β increased in the probiotic groups. The FDLQI and CDLQI scores were lower in the LP, LF, and LP+LF mixture group than in the placebo group ($p=0.02$ and 0.03) [8].

The heat-killed L. paracasei displayed similar effect when administered for the treatment of house dust mite induced perennial allergic rhinitis. Peng G-C, et al., randomized patients to receive live or heat-killed LP33 variant or a placebo, to a total of 90 patients with a history of AR who showed sensitization to house dust mites as evaluated by skin testing. Three arms were created in which the interventions were heat-killed LP33 variant, live variant, and the placebo. The intervention was given for 30 days, and the result concluded that the efficacy of the heat-killed LP33 was non-inferior to the live variant. Although there were no obvious side-effects reported for either of the active treatment group, it was reported the heat-killed LAB was much safer than the live LAB [5].

In our study, we found significant improvement in VAS score post administration of six weeks course of probiotics. The total IgE score also showed significant difference. In a few patients, even though there was no much difference in total IgE scores, clinical symptomatic improvement was noted. There could be some placebo effect in a few patients. This study precludes that the probiotics can be an effective add-on therapy/ supportive treatment for relieving symptoms of AR in patients, who suffer from the same. Its therapeutic value has to be proven by randomized controlled trial with larger patient subgroups. We did not separate the symptoms while observing difference in VAS score. This study forms the basis for further investigations in this field.

CONCLUSION

This prospective study demonstrated the presence of significant improvement in the VAS and IgE scores among the following nasal symptoms - Rhinorrhea, Sneezing, and Nasal obstruction with the administration of probiotics in the patients suffering with AR. Further studies with greater sample sizes are necessary to establish the extent of the use of probiotics in AR as well as in other therapeutic areas. The treatment duration with its safety and effectiveness of probiotics in relieving specific symptoms of AR has to be further investigated.

FUNDING

No funding was obtained for the conduct of the study.

CONFLICT OF INTEREST

The authors declare that there were no conflict of interest whatsoever in the conduct of this study.

INFORMED CONSENT

Written informed consent was obtained from all study participants.

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How to Cite the article
Prashanth Veerabhadraiah etal, A Study on the Role of Probiotics In Nasal Allergy, UPJOHNS June 2022; 10(1)- 35-41 DOI: httpp://doi.org/10.36611/upjohns/volume10/Issue1/6