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SYNERGISTIC EFFECT OF PROBIOTICS ON TREATMENT OF ALLERGIC RHINITIS

ENT

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ABSTRACT

Background: A variety of disorders, including allergic rhinitis (AR), are brought on by allergen exposure and an immune-mediated response. The quality of life for individuals who are on current AR medications could be impacted by unfavorable side effects. Live bacteria called probiotics have been utilized as supplemental diets to treat and prevent a variety of immunological illnesses. In addition to normal medication, our goal was to look into the synergistic experimental and immunologic things of probiotics in the prevention and handling of AR. **Materials And Methods:** The Sino-nasal Outcome Test (SNOT-22), Serum IgE (IU/ml), and Absolute Eosinophil Counts (per mm3), which patients or their parents filled out, were investigated at baseline after 1, 3, and 6 months of standard treatment for allergic rhinitis in this single-blind trial, which included 100 patients diagnosed clinically by ARIA. **Results:** We discovered a substantial improvement in subjective symptoms and a decrease in all SNOT - 22 scores after taking probiotic supplements (p-value<0.05). Blood values (TOTAL IgE and AEC) did not significantly improve, but there was a tendency for Total IgE and AEC to decline in the Probiotic supplemented group. **Conclusion:** The study demonstrated that probiotics modify the immune response of the body and improve AR patients' symptoms with quality of life. Due to study heterogeneity and inconsistent outcome measures, the data available today is still insufficient.

KEYWORDS

Probiotics, Total IgE, SNOT 22, Allergic Rhinitis, AEC (absolute eosinophil counts).

BACKGROUND

Rhinorrhoea, sneezing, nasal obstruction, and/or nasal itching lasting more than an hour on most days for two or more consecutive days are all considered to be two or more symptoms of rhinitis. Allergies account for about 50% of all occurrences of rhinitis. Inflammation is brought on by an immunological reaction mediated by gamma globulin E (Ig E) to certain allergens. The immune reaction includes the liberation of inflammatory mediators, cell activation, and recruitment to the nasal mucosa [1].

The incidence of allergic illness is a critical issue in contemporary medicine and public health [2][3]. Epidemiological studies show that over the past three decades, the prevalence of AR has progressively climbed in more advanced, "Westernized" civilizations and affects the world's population [4]. Allergic rhinitis is reported to affect (20 – 30) % of people in India [5].

The mainstays of AR treatment are allergen avoidance and medicine, such as immunotherapy and anti-inflammatory therapy, which, although offering symptomatic relief, have some undesirable side effects (dryness, sleepiness, and insomnia) that lower our quality of life. Finding alternative treatments is fascinating. Thus, probiotics may represent a cutting-edge therapy for allergic rhinitis.[6]

Probiotics are living bacteria that can be found in natural foods and which, when given to the host, have beneficial physiological effects [7]. A new study indicates that probiotics may be utilized as a preventative adjuvant for various conditions such as atopic dermatitis, infectious and antibiotic-associated diarrhea, and vaginal infections during pregnancy [8,9,10]. Probiotics are useful in treating a number of immunological and allergen-mediated disorders. Probiotics can have pro- or anti-inflammatory effects depending on whether they activate or inhibit type 1 T-helper cells. Interleukin-10 (IL-10) levels are predominantly increased by probiotics, which reduce inflammatory responses [11].

Numerous investigations into the possible usefulness of probiotics in the supervision of AR have produced contradictory findings. There is disagreement on the use of probiotics in AR as a result. Recent evaluations [12,13] suggest that probiotics may have a considerable positive impact on AR management, with the probable to enhance patient value of life and lower drug use.

AIMS & OBJECTIVES

To calculate the probiotics' additional impact on the standard treatment for allergic rhinitis (AR).

METHODS

Following approval from the Institutional Ethics Committee, this prospective randomized single-blind case-control comparative study was carried out from September 2019 to August 2020 at Tertiary Care Hospital Prayagraj, Uttar Pradesh, India. Before taking part in the trial, every patient (or their parent) had to complete an informed permission form in writing. 100 individuals (10–40 years old) with clinical signs of allergic rhinitis were enrolled in accordance with ARIA guidelines [4].

STUDY SUBJECT AND STUDY DESIGN

The Sino Nasal Outcome Test (SNOT) [14] and clinical examination were used to select patients with rhinorrhoea, sneezing, nasal blockage, and nasal itching who presented to the ENT OPD. Total IgE, Absolute Eosinophil Count, DLC, and CRP were all examined in the blood sample. Patients with chronic rhinosinusitis, nasal masses, tuberculosis, diabetes, hypertension, renal disease, and HIV patients with impaired immune systems were not included in the study.

Systemic antihistamines (levocetirizine and montelukast), local decongestants, chromones for the eyes, and inhaled corticosteroids (fluticasone propionate) in the smallest doses necessary to control the symptoms were the conventional treatments for allergic rhinitis. Patients were divided into two groups at random using a computer-based random table, group (A) and group (B) who met the inclusion criteria.

Group A- AR patients were given Cap Probiotic BD (5 billion Lactobacillus preparation) in addition to standard AR treatment (case).

Group B - patients with AR were given a placebo (control) along with

standard treatment for Allergic Rhinitis for the same period.

Follow-up

All subjects were required to bring all empty packages from the previous appointment in order to measure treatment adherence. Both patient groups underwent clinical evaluations and had their absolute eosinophil counts (per mm3) and Ig E (IU/ml) levels assessed after 1, 3, and 6 months.

Statistical Investigation

The statistical analysis was performed using SPSS for windows version 22.0 software (Mac, and Linux). The findings were present in number and percentage analyzed by frequency, percent, and Chi-square test. Chi-square test was used to find the association among variables. The critical value of P indicating the probability of significant difference was taken as <0.05 for comparison.

RESULTS

Out of 112 patients with allergic rhinitis who took part in the trial, 100 (89%) finished it. Age, weight, gender, family history, allergic symptoms, and other general characteristics did not vary between the two groups in terms of demographic factors. Patients in Groups A and B had respective mean ages of 25.5±7.17 and 26.9±8.7 years.

Table 1: Baseline Characteristics Of Patients.

Characteristics	Group A (case)	Group B (control)
Female	21	19
Male	29	31
Age (Mean ± SD)	25.5±7.17	26.9±8.7
SNOT22	46.62±11.49	45.16±12.92
TOTAL IgE	619.48±563.88 IU/ml	617.55±579.32 IU/ml
AEC (Absolute eosinophil counts)	301.48±122.68 /mm^3	289.26±115.855 /mm^3

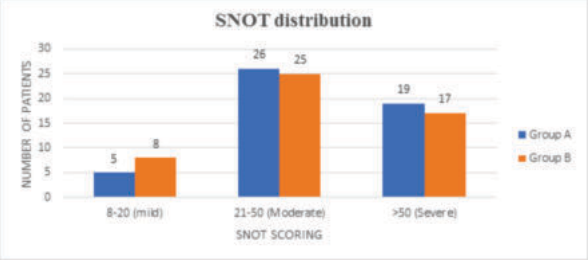

Figure 1: Baseline SNOT Distribution

Table 1 and Figure 1 show the baseline characteristics of the patients as well as the baseline SNOT distribution.

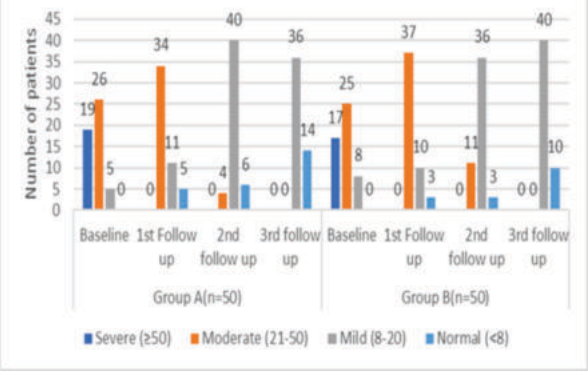

Figure 2: SNOT Distribution of patients during treatment.

Figure 2 shows that Group A improved more than Group B in terms of SNOT scoring. After the third follow-up with Probiotics, 36(72%) patients had mild SNOT scores (8-20) and 14(28%) patients had normal SNOT scores (<8) while 40(80%) patients had mild SNOT scores (8-20) and 10(20%) patients had normal SNOT scores (<8) after the third follow-up with placebo and standard AR treatment.

Table 2: Comparison Of SNOT Value Changes From Baseline (1st Day) To Different Follow-up Periods Of Study In Group A And Group B.

SNOT	Group – A				Group – B			
	Mean	SD	z-value	p-value	Mean	SD	z-value	p-value
Baseline	46.62	11.49	-	-	45.16	12.92	-	-
1st Follow-up	23.18	7.11	12.27	<0.05	24.12	6.56	10.27	<0.05
2nd Follow-up	15	4.75	17.98	<0.05	17.16	4.94	14.31	<0.05
3rd Follow-up	9.56	3.51	21.81	<0.05	11.34	3.27	17.94	<0.05

As shown in **Table 2**, the mean changes from baseline to the first, second, and third follow-ups were significant in both groups (Group A and Group B). However, group A's change was more significant than group B's change, with z-values of (|z|=17.98 vs |z|=14.31) and (|z|=21.81 vs |z|=17.94) for the second and third follow-ups, respectively.

Table 3: Comparison Of SNOT Value Changes In Mean, SD, z-value, And P-value In Both The Groups.

SNOT	Group A		Group B		z-value	p-value
	Mean	SD	Mean	SD		
Baseline	46.62	11.49	45.16	12.92	0.60	0.55
1st Follow-up	23.18	7.11	24.12	6.56	0.69	0.49
2nd Follow-up	15.00	4.75	17.16	4.94	2.23	0.026
3rd Follow-up	9.56	3.51	11.34	3.27	2.62	0.009

Table 3, When comparing groups, the mean SNOT score of Group A and B was found to be the same at baseline, but after the second (3 months) and third (6 months) follow-ups, score of Group A was less than that of Group B, and the difference was statistically significant (p-value = 0.026 & 0.009), respectively.

Table 4: Comparison Of Total IgE Changes From Baseline (1st Day) To Different Follow-up Of Study In Group AAnd Group B

Total IgE	Group – A				Group – B			
	Mean	SD	z-value	p-value	Mean	SD	z-value	p-value
Baseline	619.49	758.99	-	-	617.55	579.32	-	-
1st Follow-up	574.72	657.88	0.31	0.75	582.86	511.56	0.32	0.75
2nd Follow-up	549.19	684.28	0.49	0.63	564.29	559.65	0.47	0.64
3rd Follow-up	527.95	669.93	0.64	0.52	553.06	517.88	0.59	0.56

As shown in **Table 4**, the mean changes in Total IgE from baseline for both groups were statistically insignificant. However, with the z-value (|z|=0.64 vs. |z|=0.59), the reduction of Total IgE was greater in group A than in group B. The Total IgE values differed between the groups, with Group A having a higher baseline mean Total IgE than Group B. The difference, however, was not statistically significant (p value=0.99). Furthermore, at the first, second, and third follow-ups, Group A's mean Total IgE was decreasing faster than Group B's, and the difference was not statistically significant.

Table 5: Comparison Of AEC Changes From Baseline (1st Day) To Different Follow Up Of Study In Groups

AEC	Group – A				Group – B			
	Mean	SD	z-value	p-value	Mean	SD	z-value	p-value
Baseline	301.48	122.68	-	-	289.26	115.85	-	-
1st Follow	272.38	122.09	1.19	0.23	275.06	130.65	0.58	0.57
2nd Follow	254.62	108.39	2.02	0.04	257.00	109.32	1.43	0.15
3rd Follow	256.82	102.26	1.98	0.51	250.40	110.04	1.72	0.08

As shown in **Table 5**, the mean changes in AEC from baseline to the first and third follow-ups in Group A were not significant but statistically significant (p value=0.04) from baseline to the second follow-up. The mean changes in AEC from baseline to the first, second, and third follow-ups in Group B were statistically insignificant. However, the scale of change in group A was better than that in group B, with z-values (|z|=1.19 vs. |z|=0.58), (|z|=2.02 vs. |z|=1.43), and (|z|=1.98 vs. |z|=1.72) in the first, second, and third follow-ups, respectively. When the AEC values of the groups were compared, it was discovered that Group A had higher mean AEC values than Group B at baseline. Still, the difference was not statistically significant (p value=0.61), and at the first, second, and third follow-ups.

DISCUSSION

Intranasal corticosteroid sprays are the primary treatment for moderate-to-severe AR and are most successful at controlling AR symptoms [15]. Patient adherence to medicine is the main challenge in the management of AR. Probiotics may improve the harmony of gut microorganisms and control immunological reactions, according to research. Only five studies [17–20] that evaluated the impact of probiotics on patients with PAR were found by Guvencet al [16]. According to these researchs, probiotics may be beneficial for treating or preventing PAR in kids. The clinical effects of administering probiotics to adults were only studied in one single research [20], which looked at PAR. The efficacy of probiotics in the treatment of PAR adults has not, however, been the subject of a definitive study [21]. Patients in Group A had a mean SNOT value of 46.62±11.49, whereas those in Group B had a value of 45.16±12.92; respectively, there was no statistically significant difference between these two groups (p value=0.55). In contrast, the post-treatment mean SNOT values of Group A and B in the second follow-up were 15.00±4.75 and 17.16±4.94 (p value0.05) respectively, and 9.56±3.51 and 11.34±3.27 (p value0.05) in the third follow-up respectively, and the difference between these two groups was highly significant. In a related study, Jalali et al. [22] discovered that while the overall mean pre-treatment SNOT score in the control and placebo groups was 49.0±16.1 and 48.9±15.1, respectively, the post-treatment (after 8 weeks) means SNOT score in the control and placebo groups was 16.71±5.92 and 27.47±4.90 (p value0.01). When compared to placebo yoghurt, BB536-supplemented yoghurt considerably improved eye symptoms, according to a different study by J.Z. Xiao et al. [23] However, there were only 40 patients in this trial, and there were three follow-ups at 4, 9, and 14 weeks. Giovannini et al. [24] studied the advantages of 187 children with allergic rhinitis and/or asthma who had been consuming fermented milk containing one species of Lactobacillus for 12 months, with p values of 0.037 and 0.022, respectively. In order to alter the gut microfloral environment, Wang et al. [25] used the probiotic L. paracasei (LP-33) to conduct a randomized clinical trial. They discovered that this strain improved the quality of life for those with perennial allergic rhinitis. Similar outcomes were obtained from Rossi et al.'s clinical experiment [26] on the safety of co-treatment with probiotics and SLIT (sublingual allergen immunotherapy) and their beneficial effects on allergic symptoms. Additionally, the frequency of healthy days increased while medication ratings significantly decreased. Nineteen sufferers of allergic rhinitis took part in a single-blind, placebo-controlled experiment in a study by Moazzen et al. [27] According to the intervention, the mean SNOT scores for the interventional group were 40.66±22.57, 15.11±10.34, and 11.13±9.36, respectively, whereas for the placebo group they were 52±24.06, 18.62±11.84, and 14±18.36.

Only 7% of the 100 patients in the current study's pre-treatment state had a sum IgE level of 188 IU/ml, whereas 93% had one that was higher. Total IgE levels higher than 188 IU/ml were present in 46 (92%) patients in Group A and 47 (94%) patients in Group B. In Group A, the pre-and post-treatment Total IgE levels were 619.48 IU/ml and 481.15 IU/ml, respectively, while in Group B, they were 617.55 IU/ml and 553.06 IU/ml, respectively. This shows a reduction in Total IgE levels due to probiotic treatment, however it was statistically insignificant (p-value = 0.83). When compared to the intra-group variation, the change in Total IgE levels from baseline was statistically negligible**.** J.Z. Xiao et al. [23] examine the effect of yogurt fortified with a probiotic strain and discovered no important intra-group differences in the levels of total IgE (mean IgE in Placebo was 149.6±206.9 and 190.2±316.7 IU/ml, and interventional 90.3±60.7 and 99.0±63.1 before and after treatment, respectively), or JCP specific IgE from baseline in either group. The difference in JCP-specific IgE from baseline at week 4 between the BB536 Group (-0.78±2.07) and the placebo group (0.56±2.61), however, showed a trend toward decrease (p = 0.081). Lin et al. [28] looked into how Lactobacillus salivarius affected the use of medicine and clinical symptoms in children with allergy rhinitis (AR) who were 6 to 12 years old. There were no statistically significant differences in blood and immunologic profile (IgE) levels between the groups before and after treatment. Kang et al. [29] compared the efficacy of NVP-1703 probiotic mixture *(B. longum* IM55 and *Lactobacillus plantarum* IM76) with a placebo for 4 weeks in a study in adults with perennial AR. There was a significant improvement in TNSS and Rhinitis Control Assessment Test (RCAT) scores and the level of dust mite-specific IgE was also significantly lower in the NVP-1703 group compared with the placebo group. Giovanini et al. [24] looked at whether pre-schoolers with allergic asthma and/or rhinitis may have their health improved over time by consuming fermented milk with particular Lactobacillus cases and found no difference.

In our study, the pre-treatment mean AEC (Absolute eosinophil count) was 301.48±122.68/mm3 and 289.26±115.855/mm3, while the post-treatment mean AEC was 256.82±102.26/mm3 and 250.40±110.04/mm3 in groups A and B, respectively. The difference was found to be statistically insignificant, with p-values of 0.51 and 0.08 in the intra-group and p-value = 0.76 in the inter-group. Although the trend in different AEC evaluations was decreasing.

Lactobacillus helveticus SBT2171 (LH2171) was used in a study by Yamashita et al. [30]. In a related trial, J.Z. Xiao et al. [23] found that, although not statistically significant, the eosinophil rate was lower in the probiotic group compared to the placebo group. In a study by Lin et al. [28] examining the impact of Lactobacillus salivarius on clinical symptoms and drug use in children with allergy rhinitis (AR) aged 6 to 12 years, it was found that there was no difference in eosinophil levels between the probiotic-treated and placebo-treated groups.

The effectiveness of orally administered Lactobacillus acidophilus strain L-92 (L- 92) in perennial allergic rhinitis was investigated by Ishida et al. [31]. Bifidobacterium longum BB536 was used for 14 weeks during the research conducted by Xiao et al. [32] on the development of pollinosis in Japanese persons. Although the BB536 Group's eosinophil rate was found to be lower than the placebo Group's, the difference was not statistically significant. The results, according to Helin T et al. [33], were unfavourable. The patient's symptoms or medication use throughout the birch-pollen season or the next two months were not improved by the treatment. The symptoms brought on by the apple in the oral challenge tests were not significantly impacted by the medication. According to Aldinucci C et al [34], there was no discernible difference in the proliferation index between the three groups. The yoghurt-fed group's cultured PBMC produced more IFN gamma and less IL-4. Plasma cytokine concentrations had attained and stayed at baseline. The NPT, specific serum IgEs, and the prick test were not changed. After yoghurt eating, mucociliary transit time (MCTt) and symptom score clearly improved. **Hu et al** [35] showed that probiotics and L-glutamine can effectively regulate the level of gastrointestinal peptides in the treatment of children with AR and restore the balance of intestinal microflora along with the barrier function of the intestinal mucosa for the purpose of treatment.

Luo and colleagues' meta-analysis [36] of 28 studies on AR patients found that probiotics significantly reduced symptom severity and improved quality of life. The outcomes also demonstrated that probiotics restored a normal type 1 polarization in the T helper cell 1/T helper cell 2 ratio. However, the IgE levels that are specific to allergens were unaffected by probiotics. The researchers also deduced that probiotic supplementation decreased nasal symptoms and improved patients' quality of life based on their findings. However, the research found that a number of the results displayed significant heterogeneity.
Another meta-analysis of probiotics used in the AR treatment was carried out by Yan and colleagues [37]. Only RCTs, or randomized controlled trials, were chosen by these researchers. In total, 30 RCTs totaling 2708 patients were examined. The results revealed that both the nasal symptom severity and the nasal ratings of rhinitis quality of life significantly decreased in patients receiving probiotic treatment. However, probiotics had no impact on total and allergen-specific IgE levels, eosinophil count, or ocular symptoms.

Probiotics' impact on AR patients was the subject of a systematic study conducted by Iftikhar and colleagues [38]. Only three systematic reviews, out of the 419 articles that these researchers reviewed, qualified for the review and reported that probiotics in managing AR patients improved quality of life, total nasal symptom and ocular symptom scores, and total daily symptom scores.

CONCLUSION

According to the study, probiotics boost the body's immunological response, and we saw a more satisfying effect on allergic reaction regulation than with conventional therapy. These preliminary results from a small research population imply that probiotics plus anti-allergy therapy may enhance the effectiveness of anti-allergy therapy. To validate and further develop these findings, though, additional study is needed.

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