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ORIGINAL ARTICLE

Role of Multistrain Probiotic as Supportive Therapy in Reducing the Frequency and Severity of Respiratory Infections in Children

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ABSTRACT

Background: Respiratory tract infection is a disease that can result in high mortality and morbidity. Factors related with severe respiratory infections in children comprise the age of young children, male sex, malnutrition, incomplete vaccination status and breastfeeding only children. This analysis targets the Role of multi-strain probiotics as supportive therapy in reducing the frequency and severity of respiratory infections among children.

Place and Duration: In the Pediatric Medicine department of Abbasi Shaheed Hospital, Karachi for six months duration from January 2021 to June 2021.

Methods: This was a randomized controlled study in 74 children aged 2 months to 5 years with respiratory infections receiving standard therapy and multi strains probiotics versus standard therapy and placebo. The assessment regarding treatment was done in both groups. Results following 7 days of adjuvant treatment alienated into group I (n = 37) (standard therapy and multi strains probiotics) and II Group (n = 37) (placebo and standard therapy). The factors evaluated in this analysis included subject characteristics, duration of stay, duration of fever, dyspnea, withdrawal, C-reactive protein, rales, breast history and probiotics use. The analysis of data was accomplished using SPSS version 20.0.

Results: The males were 51.4% and females were 49.6%), breastfeeding (83.8% in Group-I vs 67.6% in Group-II), children who were not malnourished (81.1% in Group-I vs 86.5% in Group-II), and children who completed vaccination history (91.9% in Group-I versus 78.4% in Group-II). As shown in Table 1 in groups I and II, correspondingly, the mean concentration of CRP in subjects diagnosed with respiratory infections was not statistically significant in 1st group (30.10 (20.01-44.60 mg / l), relative to Group II (28.23 (19.20-46.12 mg / l), respectively (P = 0.39).Multivariate analysis with Ancova showed that probiotics can significantly decrease the time of Rale by 5.84 hours (p = 0.021, CI 95% -10.90 - (- 0.87).

Conclusions: In this study, it was found that multi strains probiotic therapy significantly reduced the duration of Rale among children with infections of the upper respiratory tract.

Keywords: Respiratory tract infections, children, multi strain probiotics, efficiency.

INTRODUCTION

Respiratory tract infections (RTIs) persist to be the chief causes of mortality and morbidity worldwide in children of all ages[1]. Many children under two years of age have more than one RTI in the 1st twelve months of life, and a quartier in developed countries suffer from prolonged or recurrent infections[2-3]. Respiratory disorders are a major cause of concern for parents in preschool and medical visits at school age, leading to comfort and hospitalization. In addition, due to the ineffectiveness of antibiotics against viruses, they result in an unnecessary antibiotics prescription in pediatric practice[4]. Improper and widespread usage of antibiotics can result in the advancement of resistance to bacterial and alter the standard equilibrium of the human microflora, facilitate the pathogens colonization and reduce the accessibility of vaccines against viruses. The RTI economic impact is also weighty in countries. This is why RTI in children remains a major public health problem worldwide. The WHO states probiotics as living microorganisms that, when directed in appropriate quantities, benefit the health of the host. The furthermost communal cast-off probiotics are Bifidobacterium and Lactobacillus species, followed by Enterococcus, Streptococcus, Bacillus, Escherichia coli and Propionibacterium. Some yeast strains are also castoff as probiotics, for example Saccharomyces cerevisiae and Saccharomyces boulardii are often used to manage gastrointestinal disorders[5-6]. A well-characterized probiotic should be clearly definite along with the species, type and description of the strain, and specify the microbial culture conditions. Probiotic products can be framed as tablets, capsules, powders (regulated as dietary supplements) and as food ingredients (e.g., yoghurt, kefir, medicines). Probiotics are definite as live microorganisms that are directed in adequate amount which can offer the better health benefits. Probiotics such as Lactobacillus or Bifidobacterium species known to have health properties and non-pathogenic Escherichia coli have been widely developed[7-8]. L. rhamnosus GG and Lactobacillus reuteri have a mechanism that modulates the allergic immune system in the respiratory tract and prevents infectious diseases[9]. Bayer Mulsid TB et al. probiotics contain Streptococcus, Bifidobacterium and Lactobacillus administer to patients with severe respiratory tract infection for 6 to 24 months, patients receiving probiotics had a significantly shorter duration of hospital stay (P <0.007) compared with the group of control, less duration of dyspnea (less than 0.001 P-value), chest wall retraction disappeared faster (less than 0.001 P-value), and the rales duration was more rapidly in the group of probiotics than in the control group (P <0.001). Esposito S done the same study which examined the part of various probiotics such as Streptococcus thermophilus, Bifidobacteriumlongum and Lactobacillus acidophilusb in subjects with upper respiratory tract infections in children of 2 months to 5 years, led to improved rhonchi and subcostal retractions proved to be statistically significant for probiotics compared to placebo. Becina PGA presented several results in 2016 with the probiotics L. rhamnosus, Lactobacillus casei, L. bulgaricus, L. acidophilus, Bifidobacteriumbreve, Streptococcus thermophilus, Fructooligosaccharide (FOS) and B. infantis in patients with moderate respiratory tract infection for 2 months to 4 months[10]. There was no statistically substantial variance in length of hospital stay, improvement in dyspnea, fever, and withdrawal in the probiotic group for 1 year compared with placebo.

Unfortunately, these studies did not mention the response of inflammation subsequent to the multi strain probiotics administration, which were evaluated as markers of infection on the basis of improvement in C-reactive protein (CRP) and blood count (CBC). The level of CRP was used as a determinant of the severity of respiratory infections with a 97.6% sensitivity, 33.9% specificity, a PPV of 10.5% and a negative predictive value of 99.4% in Chalmers JD et al study[11].

Relying on the gicen data, this analysis was done to establish the role of multi strain probiotic as supportive therapy in reducing the severity and frequency of respiratory infections in children.

MATERIAL AND METHODS

In this study, an experimental, randomized clinical trial (RCT) was conducted in the Pediatric Medicine department of Abbasi Shaheed Hospital, Karachi for six months duration from January 2021 to June 2021. Childhood age 2 months to5 years diagnosed with respiratory infections according to revised WHO criteria were included. For selection of patients; We use consecutive sampling was used. The criteria of inclusion was as follows: children aged two months to five years and parents were ready to contribute in this analysis and have signed informed consent. The criteria of elimination were patients using immunosuppressants, immunodeficiency states, respiratory infections with comorbidities, and patients receiving a probiotic minimum two weeks prior to treatment. A total of 206 patients were selected with severe respiratory infections and only 74 patients were selected in the study. The excluded patients were HIV patients, patients with congenital heart disease, respiratory distress suffered patients and cerebral palsy. 74 patients were chosen and were then randomized to two groups of 37 patients who all received additional probiotic or placebo therapy in addition to the standard antibiotic therapy. Estimates of the size of the respondents, a = 0.05 of significance level; the preferred 95% of confidence interval (CI) and 80% of power resulted in a 37 patients as the sample size in each group. The selected patients are randomly assigned to a placebo or intervention group. The standard treatment for respiratory infections was I.V administration of ampicillin 50 mg / kg body weight / times every 6 hourly and 7.5 mg / kg body weight gentamicin /every 24 hourly. Group I, the intervention group includes people receiving multi strain probiotics (B. longum, L. acidophilus, Streptococcus thermophilus every 1x107 cfu / gr) in the granules form in a package, 2 times daily for five days at three hours intervals after normal administration of antibiotics. Group II received a combination of placebo and standard therapy that looked like a probiotic. Rendering to the growth curve by WHO in 2006 grounded on Waterlow, the nutritional status is classified as malnutrition <90% and malnutrition> 90%. The patient's clinical outcomes were assessed every 12 hours, including duration of stay, fever time, dyspnea, rales duration and subcostal retraction. The SPSS 20.0 software was applied for analysis of data. One-dimensional analysis was applied to identify key patient characteristics counting minimum-maximum, rate distribution and median. The Shapiro-Wilk test was applied for the normality test, and Levene test for the similarity of variance test. The Bivariate analysis was performed by means of Mann-Whitney test and the multivariate analysis by the Ancova analysis. The level of significance is assessed by P <0.05.

RESULTS

Sex, Age, nutritional status, breastfeeding and vaccine status were achieved uniformly in both groups. The males were 51.4% and females were 49.6%), breastfeeding children (83.8% in Group-I vs 67.6% in Group-II), children who were not malnourished (81.1% in Group-I vs 86.5% in Group-II), and children who completed vaccination history (91.9% in Group-I vs 78.4% in Group-II). As shown in Table 1 in groups I and II, correspondingly, the mean concentration of CRP in subjects diagnosed with respiratory infections was not significant statistically in group I (30.10 (20.01-44.60 mg / l), relative to Group II (28.23 (19.20-46.12 mg / l), respectively (P = 0.39).

Table 1: Baseline features of the patients shown in Table-I

Characteristics	Group I (N = 37)	Group II (N = 37)
median (min-max), month and Age	17 (7-48)	19 (5-46)
Sex, n(% Male	20 (54.1)	18 (48.6)
Female	17 (45.9)	19 (51.4)
Breastfeeding, n (%) Yes	31 (83.8)	25 (67.6)
No	6 (16.2)	12 (32.4)
Malnutrition, n (%) Yes	7 (18.9)	5 (13.5)
No	30 (81.1)	32 (86.5)
Complete immunization, n (%) Yes	34 (91.9)	29 (78.4)
No	3 (8.1)	8 (21.6)

However, following administration of the probiotic therapy on 3rd day, the median CRP was 2.82 mg / L (1.21-4.31) compared with 3.75 mg / L (2.74-5.09) in the group of placebo. The reduction in concentration of CRP was also not significant statistically among group I 26.85 (18.06-44.89 mg / L)) and group II 24.46 (17.24-41.20 mg / L) (p = 0.14) (Table 2). Though, in the Bivariate analysis, we institute that the duration of the rales was statistically significantly different among the two groups (p = 0.034)

(Table 2). A multivariate analysis (Ancova) was performed to get the variables that influence the rales duration.

Table 2: Bivariate analysis of various variables into the Group I correlated with Group II shown in Table-II

Variables	Group I (N=37)	Group II (N=37)	p
Duration of stay (hour), median (min-max)	129 (126-141)	134 (134-148)	0.54
Duration (hour), median (Min-max) Fever	37 (25-62)	47 (23-65)	0.23
Shortness of breath	86 (74-98)	82 (73-109)	0.06
Retraction	81 (70-111)	93 (81-109)	0.068
Rales	74 (61-94)	80 (74-110)	0.034
C-Reactive Protein (CRP) (mg/L), median (min-max) After Diagnosis	30.10 (20.01-44.60)	28.23 (19.20-46.12)	0.39
Third Day	2.82 (1.21-4.31)	3.75 (2.74-5.09)	
Decline of CRP (mg/L), median (min-max)	26.85 (18.06-44.89)	24.46 (17.24-41.20)	0.14

Table 3 shows Multivariate analysis with Ancova that probiotics can significantly decrease the period of Rale by 5.84 hours (p = 0.021, CI95% -10.90 - (- 0.87).

Table 3: The multivariate analysis by Ancova between variables that predictable to effect the rales duration shown in Table-III

Variables	B	CI 95%	P-value
Probiotic	-5.84	10.90 - (- 0.87)	0.021
Breastfeeding	-0.89	-7.59 – 5.76	0.760

DISCUSSION

Respiratory tract infections occur mainly in children under 5 years of age, malnourished men and incomplete vaccinated children. The utilization of broad-spectrum antibiotics can alter the commensal microflora balance in the gastrointestinal tract[11-12]. In a previous study, administration of probiotics was not recommended after three hours of antibiotics. In our research, probiotics were administered three hours after IV administration of antibiotics to evade the effect of antibiotics on probiotics. Araujo GV et al. Regarding the probiotics use versus placebo in children with RTIs, there were 3 significant RCTs that reduced disease symptoms (p <0.05). Leier GJ et al. Users of probiotics were alienated into 2 groups as single (L. acidophilus) and combined (B. animalis and L. acidophilus) and compared in terms of fever 53.0% and 72.7%, 41.4% vs 62.1% with cough and 28.2% with rhinorrhea in placebo group, respectively. Skovbjerg S et al. the use of a probiotic (S. sanguinis, L. rhamnosus) in children with respiratory infections[13-14]. They improved in 36.6% of subjects compare with only 5.8% in the group of placebo. Kumpu M et al. showed that the duration of the disease was significantly lower in the group using probiotics (L. rhamnosus GG) than in the group of placebo (P <0.001). Skovbjerg S et al and Leier GJ et al have shown a statistically significant reduction in symptoms, these analysis have a broad range of confidence. Both used a dissimilar respiratory infection definition in their studies[15-16]. In this analysis, there was no statistically significant difference in duration of hospital stay, duration of dyspnea and fever, withdrawal time, and CRP outcomes. Conversely, there was a statistically significant differentiation in the rales duration between the intervention group (group I) and the placebo group (group II). The clinical difference between 12 hours (0.5 days) and 24 hours (1 day) can benefit patient comfort, hospital costs and hospital services especially for patients having no health insurance[17-18]. Becin's PGA study had similar results to our study, and her RCT showed that probiotics (L. rhamnosus, L. casei, , B. breve, Streptococcus thermophilus, B. infantis, L. acidophilus, L. bulgaricus all with 109 cfu / gr, FOS)) as an additional therapy for respiratory infections to improve results. According to Bayer-Muslid TB and Gathcheco FN, children aged 6 to 24 months receiving standard therapy and Ohhira® OMX probiotics had statistically significantly shorter duration of stay (P <0.007), duration of dyspnea (P) in severe respiratory infections compared with controls in the intervention group. <0.001), and the subcostal retraction disappears faster (P <0.001). The release of pro-inflammatory cytokines such as TNF-α, IL-6 and IL-1 was consistent with damage to the lung parenchyma and will therefore be correlated with the severity of respiratory tract infection[17-18]. The C-reactive protein (CRP) is synthesized by the liver in retort to tissue damage. It is a protein that reacts faster, is sensitive, easy to measure, has a short half-life, fast reaction time, and its catabolism is not affected by the inflammation type. In this study, no adverse effects were observed when taking probiotics or placebo[19-20]. Wang Y et al, Araujo GV et al concluded that the probiotics had a safety profile as most RCTs had no adverse effects. Mild side effects such as regurgitation, decreased appetite, mild abdominal pain, dry skin, nausea, diarrhea, rash and constipation[21-22].

This analysis has some limitations because fecal cultures were not tested before and after probiotic administration to detect an increase or decrease in probiotic colony numbers. In our analysis, fever measurements were made on entrance in the hospital; No previous antibiotics given history has been made. Given these restrictions, additional studies should provide larger sample sizes and complete data to evaluate the efficacy of probiotics as an additional therapy for respiratory infections.

CONCLUSION

Children 2 months to 5 years of age with severe respiratory infections who received standard therapy and multi strain probiotics had a shorter duration of treatment than those who were given placebo and standard therapy.

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