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Original Research Article

STUDY ON ROLE OF PROBIOTICS IN RECURRENT RESPIRATORY INFECTIONS

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Abstract

Background: Respiratory tract infections (RTIs) represent one of the main health problems in children. Probiotics are viable bacteria that colonize the intestine and affect the host intestinal microbial balance. Accumulating evidence suggests that probiotic consumption may decrease the incidence of or modify RTIs. Aims: The aim of this on health effects of probiotics in patients with RTI, with a focus on viral respiratory infections. **Materials and Methods:** A double-blinded, randomised, placebo-controlled study was conducted. During the 6-month intervention study period 400 children of age 3-6 years were recruited into the study who received daily Probiotics containing lactobacillus acidophilus and Bifidobacterium lactis. **Results:** There was a significant reduction in the duration of total RTI symptoms (days) in the active group compared with the placebo. The incidence rate of RTI symptoms is significant without using probiotics. **Conclusion:** Supplementation with a probiotic provide a strategy to reduce the incidence of RTIs in 3–6-year-old children attending preschool facilities.

INTRODUCTION

Respiratory tract infection (RTI) is one of the most common infectious diseases of viral or bacterial origin. The disease is divided into upper respiratory tract infections (URTI) (affecting sinuses, nose, and throat causing sinusitis, pharyngitis, tonsillitis) and lower respiratory tract infections (LRTI) (affecting windpipe and lungs causing Pneumonia). It represents a global health challenge.

Probiotics have shown a positive response in clinical treatment for several diseases. Inhibition of coronavirus, rotavirus, hemagglutinin type 1 and neuraminidase type 1 (H1N1) influenza virus, and HIV in vitro and reduction of viral load in vivo, using Lactobacillus has been well established. Probiotics are defined as live microorganisms that confer health benefits for the host and contain immunostimulatory substances such as lipoteichoic acid, peptidoglycan and nucleic acid, which are Toll-like receptor (TLR) ligands, and muramyl dipeptide, which is a Nod-like receptor ligand.

Considering the beneficial effects of probiotics in virus infections, specific probiotics have been suggested to be effective in alleviating the duration and severity of acute rotavirus gastroenteritis.[1] In addition, increasing evidence shows that probiotics are beneficial in RTIs.[2], which, in most cases, are of viral origin. However, the mechanisms behind these effects are largely unknown. The aim is to present health effects of probiotics in patients with RTI, with a focus on viral respiratory infections.

MATERIALS AND METHODS

A double-blinded, randomised, placebo-controlled study was conducted. During the 6-month intervention study period 400 children of age 3-6 years were recruited into the study who received daily Probiotics containing lactobacillus acidophilus NCFM and Bifidobacterium Bi07. Written informed consent was obtained from parents prior to participation in the study. Children were excluded if they were taking medication or immunostimulatory products or any form of probiotic prior. None of the children received the flu vaccine during the study period.

We collected background information on the family, their environment, the child's nutrition habits, and illnesses. During the study parents recorded any respiratory symptoms (fever, runny nose, sore throat, cough, chest wheezes, earache) daily in a symptom diary. They also reported absences from the day care centre, doctor's diagnosis, and prescriptions of antibiotics.

URTI symptoms included sneezing, sore throat, cough, runny and blocked nose. Each distinct episode was the time period (in days) covering the continuous display of symptoms, separated from another episode by a minimum of 24 h. LRTI was confirmed by a

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paediatric physician, and LRTI duration was the number of days between the physician confirmed onset and absence of symptoms. Secondary end points were changes in plasma cytokines, salivary IgA and urine metabolites. Parent-reported symptoms included diarrhoea (⩾3 loose stools in a 24-h period), vomiting and stomach aches.

As a pilot study there was no a formal sample size calculation. For the primary end point analysis, incidence rate ratio (number of episodes divided by the number of days in the study) and mean difference in the duration of URTIs and LRTIs, absence from preschool and number of visits to paediatric centre for RTIs during the intervention period with 95% confidence intervals (CIs) were calculated using a generalised linear model (GLM) that included treatment as a single predictor.

RESULTS

400 children were enrolled. Three children did not provide any records and withdrew from the study. Nine children were excluded from the PP analysis; six due to non-authorised treatment usage and three due to non-completion of the follow-up period.

Table 1: Baseline demographics

Gender	**Without probiotics**	**With probiotics**
Girls	100	100
Boys	100	100
Age (years) [a]		
Girls	4.8 ±0.4	4.8 ±0.7
Boys	5.0 ±0.4	5.1 ±0.6
BMI (kg/m^2)[a]		
Girls	15.8 ±0.3	15.5 ±0.9
Boys	15.2 ± 0.6	15.5 ± 0.8
Eczema	2 ± 0.1	7 ±0.9
Atopic disease	2 ± 0.1	6 ± 0.2
Food allergy	0	3 ± 0.3

Baseline data for both groups appears comparable.

Table 2: Duration of URTI symptoms, absence and paediatric physician visits

	Without probiotics	**With probiotics**
URTI symptoms		
Mean (s.d.), days	43± 3	22±4
P-value	0.006	
Individual URTI symptoms		
Sneezing		
Mean (s.d.), days	10 ± 3	2 ± 1
P-value	0.010	
Cough		
Mean (s.d.), days	23.5 ±5	11.9 ± 3
P-value	0.006	
Runny nose		
Mean (s.d.), days	21.4 ± 6	11.5 ± 5
P-value	0.072	
Blocked nose		
Mean (s.d.), days	9.8 ± 5	4.9 ± 4
P-value	0.285	
Sore throat		
Mean (s.d.), days	2.8 ± 3	1.9 ±1
P-value	0.332	
Absence, physician visits		
Absence from preschool due to URTI		
Mean (s.d.), days	14.2 ± 4	7.5 ±4
P-value	0.070	
Number of physician visit due to URTI		
Mean (s.d.)	2.9 ± 3	1.6 ± 2
P-value	0.082	

Abbreviations: CI, confidence interval; ITT, intention to treat; URTI, upper respiratory tract infection.

There was a significant reduction in the duration of total URTI symptoms (days) in the active group compared with the placebo.

Table 3: Incidence rate of URTI symptoms and absence

	P-value
URTI symptoms	0.002
Individual URTI symptoms	
Sneezing	<0.001

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Cough	<0.001
Runny nose	0.005
Blocked nose	0.600
Sore throat	0.235
Absence	
Absence from preschool	0.007

The incidence rate of URTI symptoms is significant without using probiotics.

DISCUSSION

Children supplemented with a combination of the Lab4 probiotic consortium and vitamin C for 6 months attending preschool facilities showed a reduced incidence and duration of URTI symptoms. Studies with probiotics alone have shown variable results for URTIs, with some reporting significant reductions in incidence and duration while others observed little or no effect.[4,5,6] Positive effects on URTI have been reported in response to Lactobacillus casei DN-114 001, Lactobacillus rhamnosus GG and for Lactobacillus acidophilus NCFM alone or in combination with Bifidobacterium animalis sp lactis Bi-07 at doses ranging from 109 to 1010 colony-forming units per day while limited evidence exists suggesting that supplementation with low dose vitamin C (<0.2 g per day) may reduce common cold duration as discussed by Hemila et al.[7] A probiotic consortium combined with multi-vitamins and minerals in adults showed a 13.6% reduction in the incidence of combined URTI and LRTI symptoms.[8] There was no impact on LRTI or gastrointestinal symptoms in this study although benefits have been reported elsewhere.[9,10]

Children receiving the Lab4/vitamin C combination had fewer days of absence from preschool and unscheduled visits to the paediatric physician, suggesting that combined supplementation may reduce the severity of infections. Reductions in preschool absence have been reported with probiotics and with a vitamin C (150 mg per day), echinacea and propolis combination.[10] Fewer children receiving the supplement were treated with oral antibiotics similar to that seen in other probiotic studies, and there was a significant reduction in the number of days that cough medicine was used which highlights the potential socio-economic benefits associated with the combination supplement.[3]

Metabonomics is a new approach providing a systematic analysis of the chemical products or metabolites in biological samples, such as urine, blood and faeces, and is considered as a very sensitive measure of an organism's phenotype. In this study, no changes in the urinary metabolite profiles of healthy preschool children were observed between the placebo and active groups. The major metabolites identified in 1H NMR spectral data agreed with those observed in healthy children.[11]

Both probiotics is known to modulate the immune system, and the combination probably mediates a response through immune-modulation although the absence of any significant changes in cytokines levels between the active and placebo groups in our study may suggest the existence of an alternate mechanism. Although there were no significant differences in salivary IgA levels between the active group and placebo, Cáceres et al.[6] observed increased faecal IgA levels in Lactobacillus rhamnosus HN001-supplemented children but was unable to associate this with any improvements in URTI symptoms. The trend towards a reduction in IL-2/IL-5 and IFN-γ levels may suggest a shift towards an anti-inflammatory state in the supplemented group, and this is consistent with the abilities of both the Lab4 consortium and vitamin C to induce an anti-inflammatory response in immune cells extracted from the blood of healthy subjects.[12]

Subgroup analysis of our population on the basis of gender revealed reduced URTI symptoms in boys that corresponded with reduced plasma levels of IL-12p70, IL-12p70/IL-10, IL-2/IL-10 and IL-12/IL-5, indicating a more anti-inflammatory basal immune status. Positive effects of both probiotics and vitamin C on RTIs have been seen in adolescent and adult male subjects, and it is known that X-chromosome-specific immune-modulatory genes mediate male-specific immunological responses during prepubescence.[13,14]

As this was a pilot study with a small number of participants, it was not powered to detect all statistically significant differences, and an unwillingness to provide blood or saliva reduced the samples size for the secondary end point analysis. Also, the impact of the intervention at the time of an infection was not evaluated in this study.

CONCLUSION

Supplementation with a probiotic provide a strategy to reduce the incidence of URTIs in 3–6-year-old children attending preschool facilities. These results are encouraging and need to be confirmed in a larger study population. Taken together, the present study suggested that probiotic consumption may decrease the incidence and illness duration of RTI episode. The optimal probiotic strains, dosing, administration form, time of intervention, and long-time follow-up should be considered in future clinical trials. And studies are needed to explore the mechanisms of such action of probiotics on RTI in children.

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