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EFFICACY OF PROBIOTICS IN REDUCING ANTIBIOTIC-ASSOCIATED DIARRHEA IN CHILDREN

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Abstract

Objectives: The objective is to identify the optimal probiotic strains and dosage schedules and to comprehensively evaluate the impact of probiotics in reducing the frequency, severity, and duration of antibiotic-associated diarrhea (AAD) in children.

Materials and Methods: At a tertiary care hospital in Islamabad, Pakistan, 200 children between the ages of 1 and 12 who had taken antibiotics participated in the current study, which was a randomized placebo-controlled trial. Two groups of participants were created, one for the probiotic and one for the placebo. While the placebo group received the placebo in the form of empty sachets, the probiotic group received the multispecies probiotics as a supplement. After gathering data on AAD incidence, prevalence, and severity, statistical analysis was performed.

Results: The children in the placebo group had a high risk of AAD (35%, $p<0.01$), while the children in the probiotic group had a reduced rate of 15%. Additionally, there was a substantial decrease in the overall duration of AAD from 4.8 days in the placebo group to 2.5 days in the probiotic group ($p<0.05$). Additionally, probiotic supplementation decreased the severity of diarrhea and demonstrated an excellent safety profile.

Conclusion: Because probiotics have fewer adverse effects, the study demonstrated that they are useful in both preventing and treating AAD in children.

Keywords: Probiotics, antibiotic-associated diarrhea, children, prevention, gut health.

INTRODUCTION

Antibiotic-associated diarrhea (AAD)is a common disorder affecting the population, especially the youths and the other sensitive groups whose gut flora is comparatively underdeveloped. Since antibiotics are essential in the management of infection, they interfere with the normal gut flora, thus causing side effects like diarrhea. As for AAD, frequency varies between 5 to 30% based on age, type of antibiotics, and the overall conditions of the patient (1). According to recent research, probiotics which are defined as live bacteria that, when consumed in sufficient amounts, help the consumer's health may be used to treat and manage this illness. Other researchers have demonstrated that diet

changes can be utilized and are beneficial in treating and preventing new occurrences and reducing the rising tendency and severity of AAD in children (2, 3).

There are several ways by which probiotics can provide protection. Probiotics promote and establish the friendly bacteria inside the stomach and intestines, suppress the growth of deleterious bacteria, and enhance the elaboration of short-chain fatty acids that help strengthen the stomach and intestinal lining (4). This is especially important for kids since the composition of microorganisms in the gut has yet to develop fully and can be easily disrupted. Łukasik et al. (2022) emphasized the importance of multispecies containing probiotics strains to decrease the incidence of AAD, reporting lower clinical scores in children (1). Furthermore, Maity and Gupta (2021) signaled that other randomized controlled trials also proved the effectiveness of Alkalihalobacillus clausii in the maintenance of gut health, noting that species selectivity and specific focus on children's probiotic needs might be beneficial (2).

However, clinical applications of probiotics in the clinical setting are not without some challenges. More study is required to identify consistency because variances have been caused by different types of studies, probiotic strains, and quantities. Meta-analysis directed by Liao et al. (2021) identified and analyzed data from the randomized placebo-controlled trials and suggested that probiotics have a prophylactic effect and can decrease AAD in children and adults (3). However, the study pointed out that the impact of a particular probiotic may vary depending on the strain of the probiotic. Goodman et al. (2021) corroborated these observations by explaining that strain selection should be stringent to produce the best therapeutic results (4).

Probiotics, especially in pediatrics, have been noted to alleviate diarrheal incidences, and they have also been noted to minimize the duration and severity of diarrhea. Parmar (2024) observed that children who took probiotics had fewer complications and less hospitalization than the placebo group, reducing healthcare expenditure (5). Similarly, Shyoran et al. (2024) stated the positive impact of probiotic yogurt in pediatric patients and successful modification in gut microbiota, which ensured the potential of probiotics in the usual clinical care setting (6).

Because of the inadequate treatment of AAD, probiotic use is on the rise worldwide. In a multicenter, randomized controlled trial, Konowal et al. (2020) emphasized the preventative role of probiotics, specifically referring to the prevention of Clostridium difficile-associated diarrhea, where the main outcome was a severe form of AAD (7). This correlates with De Castro et al. (2020), who recommended Bacillus clausii for antibiotic-induced diarrheal conditions in children of Asian origin (8). These findings further support the application of probiotics in different areas of health care close to clients, particularly in areas with limited technological advancement in developing medical products such as technologies and equipment.

However, it's highlighted that the dosage, time, and duration of the probiotics have a direct impact on the efficacy. Zhang et al. (2022) also stated that early intervention with probiotics was even more effective in preventing AAD than late interventions focusing on older people and children (9). In order to determine the best probiotics for preventing diarrhea linked to Clostridium difficile, Ma et al. (2020) conducted another network meta-analysis of the literature. The authors emphasized that in order to improve the results, the research should concentrate on the specific strain (10).

The probable safety profile of the probiotics further adds to its advantage as an adjuvant therapy. The systematic review and meta-analysis by Fadin et al. (2023) revealed that most children tolerate probiotic interventions well with few side effects (11). This places probiotics in a better position than pharmacological treatments, which are more associated with side effects. Łukasik et al. (2020) built on this, suggesting that probiotics should be incorporated into the pediatric care clinical practice guidelines to counteract antibiotics' negative effects on a child's well-being (12).

However, extensive research is still needed to fill all existing gaps in the knowledge. Ferguson and Taylor (2022) have stressed the need to identify the proper dose, frequency, and probiotic strains to provide the highest therapeutic effect (13). Doar and Samuthiram (2023) echoed these groups' sentiments and urged them to determine the most effective strain and formulation for such people (14). Schnadower et al. (2021) also noted that other studies demonstrated that probiotics help to

decrease the duration and severity of diarrhea and recommended additional large-scale clinical trials to confirm such findings more effectively (15).
Finally, the use of probiotics in the treatment of children is an area of great potential in managing AAD, a major side effect of antibiotic administration. Although there is pre-existing proof of their effectiveness, the necessity for future research cannot be overemphasized in a bid to mainstream their use through standard protocols. Overcoming these challenges, probiotics could be established as the key element of AAD treatment and a safe, efficient, and affordable option for children globally.

Objective: To assess how well probiotics work to lower the frequency, severity, and length of antibiotic-associated diarrhea (AAD) in kids. The objectives of this study are to determine the specific probiotic strains and their dosages before advising the dosing and mode of administration of the resulting probiotics as a scientific therapeutic tool for pediatric care to enhance healthier gastrointestinal outcomes.

MATERIALS AND METHODS

Study Design: The effectiveness of probiotics in reducing antibiotic-related diarrhea in children was evaluated using a randomized placebo-controlled experiment. The respondents were split between the group that was given the probiotic supplement and the control group or the placebo group.
Study setting: This study was conducted at multiple centers including Rahber Medical and Dental College Lahore, Pakistan and Indus Hospital, Karachi, Pakistan.
Duration of the study: The study was conducted for six months in the middle of the year, from January, 2024 to June, 2024.

Inclusion Criteria

Participants included only children aged between 1 and 12 years who had been treated with antibiotics for any bacterial infections. The participants were chosen based on inclusion criteria such as they had to have no chronic gastrointestinal disease, and in the case of children, the guardian had to consent to participate in the study.

Exclusion Criteria

Exclusion criteria were coexisting diarrhea, immunocompromised status, and concomitant use of probiotics in children. Furthermore, patients with severe malnutrition or those requiring critical care were excluded from the study.

Methods

Patients who were willing and able to participate in the study after providing signed written consent through their guardians were recruited and assigned randomly to the two groups using a computer-generated allocation sequence. The intervention group was given a microbiota composed of Lactobacillus rhamnosus and Bifidobacterium breve in sachet form, which was taken orally twice daily, together with antibiotics. The control group was given a sachet that looked almost similar to the aforesaid sachet but comprised of placebo substances. The two groups were observed throughout the antibiotic course and for one week after the treatment. Parents or legal guardians documented any diarrhea by using a specific diary on the incidence, regularity, and length of the event. Details of compliance to probiotic or placebo administration were also noted.
Data were self-administered by trained healthcare professionals through weekly follow-ups and phone consultations. In cases with persistent diarrhea, stool samples were taken in order to exclude other reasons. Assessment was done based on the occurrence, duration and extent of diarrhea. With a significance threshold of 0.05, the data were statistically examined using the Statistical Package for Social Sciences (SPSS version 25). Ethical approval was sought and received from the institutional review board.

RESULTS

The study involved 200 children, 100 of whom were given probiotics and 100 of whom were given a placebo. The participants' characteristics at baseline remained similar in terms of age, gender, and the type of antibiotic, reinforcing the validity of the comparison. Supplementation with probiotics was associated with a significantly lower incidence, duration, and severity of AAD than placebo.

Incidence of Diarrhea

Out of 100, only 15% of children in the probiotic group were affected by AAD, as opposed to 35 children in the placebo group. This absolute difference shows that probiotics have a statistically significant protective role in the development of AAD ($p<0.01$). It demonstrated that children who take probiotics in addition to antibiotics are far less likely to get diarrhea. Probiotics help reduce the risk of AAD by more than half, as indicated by the computed 57% relative risk reduction. These results corroborate the future of probiotics as an effective complementary intervention to promote pediatric antibiotic treatment outcomes.

Group	Total Participants	Children with AAD	Percentage (%)
Probiotic Group	100	15	15%
Placebo Group	100	35	35%

Duration of Diarrhea

Children in the probiotic group developing AAD had milder symptoms with a duration of 2.5 days as opposed to the placebo group having a duration of 4.8 days. This difference was statistically significant at $p < 0.05$, indicating that probiotics have a dual role in AAD management. Besides, it is also shown that probiotics not only prevent the occurrence of diarrhea in individuals but also help them recover quickly if they have contracted the disease. Based on the above research, probiotics are beneficial to patients because they help reduce the amount of time taken by the body to regain normal flora after antibiotic use, hence improving patient outcomes during treatment.

Group	Children with AAD	Mean Duration of Diarrhea (days)	Standard Deviation
Probiotic Group	15	2.5	0.8
Placebo Group	35	4.8	1.2

Severity of Diarrhea

The severity of the condition was measured on the basis of the Bristol Stool Chart, with lower values presenting lesser severity. The difference between the probiotic and placebo groups was statistically significant at $p<0.05$, with the probiotic group averaging 3.2 and the placebo group 5.1. This shows that by taking the probiotics, symptoms of diarrhea are less severe when they are encountered.

Group	Mean Bristol Stool Score	Standard Deviation
Probiotic Group	3.2	0.6
Placebo Group	5.1	1.1

No adverse effects were recorded in relation to probiotic use during the study. In the present study, minor gastrointestinal side effects were reported in only 5% of the patients receiving probiotics and 7% of the placebo group, with no statistical significance. Probiotics are obviously useful in preventing and managing AAD in children, according to the evidence from randomized controlled trials. The data imply that using probiotics with antibiotics as an additional treatment option can enhance pediatric health and, at the same time, have a safety profile.

Discussion:

Probiotic use also helps prevent and reduce the frequency, duration, and severity of antibiotic-associated diarrhea (AAD) in children, according to the study's findings. These results are in line with previous research showing that the use of antibiotics may be counteracted by probiotics and thus maintain the composition and the functionality of the gut microbiota. This discussion shall outline the implications of these findings, compare them with other studies, and finally discuss the limitations and potential usage in a clinical setting.

Antibiotics used in the treatment of bacterial infections have been cited for causing imbalances in gut microflora by decreasing the richness and density of good bacteria. This imbalance predisposes the patients to diseases, including AAD. The significantly lower number of children in the probiotic group developing AAD as compared to children in the placebo group (15% and 35%, respectively) provides concrete evidence in favor of the stated hypothesis that the intake of probiotics has a positive impact in replacing the missing healthy bacteria during antibiotic therapy. Łukasik et al. (2022) showed similar data providing evidence that the use of multispecies probiotics helps to decrease the incidence of AAD in pediatrics (1). This further supports the opinion that probiotics may be useful as an additional agent during antibiotic therapy.

The reduction of diarrhea duration in the probiotic group (mean of 2.5 days) than that of the placebo group (mean of 4.8 days) shows the efficacy of the probiotics. The source of this particular benefit can probably be attributed to several factors. Probiotics can modulate the gut barrier function, they also can suppress pathogenic bacteria through competitive antagonism and manufacture beneficial substances, including short-chain fatty acids. Such mechanisms have been described by authors such as Maity and Gupta (2021), who found improved resolution of diarrheal symptoms in children who received Alkalihalobacillus clausii (2). The observed decrease in the severity of diarrhea, which was judged by decreasing the Bristol Stool Chart score in the probiotic group, also supports the idea of the protective effect of probiotics on gut function.

Another important discussion point is that the effectiveness of probiotics is limited to certain strains. In this study, a multispecies preparation of Lactobacillus rhamnosus and Bifidobacterium breve was used, but other strains have also been shown to be effective in prior studies. For example, Parmar (2024) described the positive effects of certain Bifidobacterium strains when applied to the prevention of AAD (5). The fact that different probiotic formulations provide similar outcomes confirms that the concept of restoring the microbiome is more valuable than focusing on specific strains. However, further strain-specific research is required to tailor formulations for various patient groups and clinical contexts.

The security profile of probiotics is another relevant factor of concern. In this study, the probiotics were shown to be safe, and no severe side effects were recorded. The minor side effects like bloating, as reported during this study, were only reported in a few instances in both the probiotic and placebo groups and this is in agreement with Fadin et al. (2023), who sought to clarify the safety of those probiotics in children (11). Such a favorable safety profile makes probiotics accessible for large-scale use, especially in sensitive groups, including children.

Nevertheless, some limitations of this study can be highlighted as follows despite its positive implications and findings. The research was carried out at a single hospital in Pakistan, which might have restricted the validity of the results in other hospitals. The diversity of gut microbial and dietary patterns across different geographic areas affects the effectiveness of probiotics, as mentioned by De Castro et al. (2020), who highlighted the need for region-specific research (8). Furthermore, the study aspects were restricted to six months, and no long-term impacts of the use of probiotics can be accurately observed.

Another limitation is the use of data collected from the diaries completed by the guardians. However, despite attempts to conduct follow-ups to enhance the precision of the study, results that are based on self-reports are always inclined towards some bias. Some possible directions for future investigations are utilizing more objective molecular data like microbiota characterization to support and generalize these results. In addition, no attempts were made to assess the effectiveness of any specific strategy to prevent Clostridium difficile-associated diarrhea, a severe form of AAD. Rajkumar et al. (2020)

and Ma et al. (2020) studied that some specific probiotics are good for this illness, which can be an avenue for research expansion (7, 10).

The time and length of use of probiotics have been found to be important factors in the effectiveness of the product. In this study, the probiotics were given at the same time as the antibiotics and for 7 days after the completion of the antibiotics. According to Zhang et al. (2022), the benefits of probiotics can improve with the early use of the product, especially in sensitive groups of the population, including children and adults of a certain age (9). This implies early and continued probiotic utilization in clinical practice. However, the recommended period of the probiotic intervention is still regarded as the object of further research.

These findings have important clinical implications. Introducing probiotics into the management of patients who have to take antibiotics could effectively decrease the incidence of AAD amongst children, hence enhancing the quality of the lives of such kids as well as cost savings. Moreover, the effectiveness of probiotics complements the trends in modern medicine aimed at the development of personalized medicine, as probiotic preparations can be developed for a specific patient based on age, health, and antibiotic treatment. Ferguson and Taylor (2022) hence underlined the need to establish constant individual probiotic therapy and the creation of formulations to enhance efficacy (13).

Finally, this study has demonstrated that probiotics are effective in decreasing the incidence, duration, and severity of AAD in children. The results support evidence from prior research and demonstrate that probiotics may be useful in enhancing the management of bacterial infections under antibiotic therapy. However, some limitations have remained unfilled, and consequently, more research is required, including regional differentiation, long-term results, and proper strain selection. In filling these gaps, probiotics could be used at every pediatric practice as an effective measure for dealing with one of the leading problems associated with antibiotic therapy.

CONCLUSION

Using randomized controlled trials that demonstrate a decrease in the frequency, duration, and severity of antibiotic-associated diarrhea (AAD), this research examines the potential utility of probiotics in the treatment of AAD in children. Multispecies probiotics should be considered as a safe and efficient additional supplement to antibiotic therapy, helping to restore the balance of the bacterial microflora in the gastrointestinal tract. The safety profile and the clinical effects observed make these therapeutic strategies applicable to the wide spectrum of the Pediatric population. The results of the study are consistent with the study conducted earlier, but the current study underlines the necessity to carry out further studies about the nature of the strains, dosage, and duration of the administration of marijuana to secure the most benefits. More research should also be done to take into account regional differences, such as diet and microbiota. Incorporation of probiotics into the basic form of pediatric care will help to reduce the burden of AAD heading to healthcare institutions, enhance patients' quality of life, and have a positive impact on the health systems. These findings provide the basis for developing effective guidelines to improve the use of antibiotic therapy in children.

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