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Role of *Bacillus clausii* in Prevention of Antibiotic Associated Diarrhea in Pediatrics

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Abstract

Antibiotic-associated diarrhea (AAD) occurs when prescribers are compelled to use antimicrobials for appropriate medical indications. Although awareness about AAD has increased during the past 40 years, no single or combined therapy has been found to effectively prevent it or help in rapid recovery from it in the pediatric age group. Therefore, the present interest in probiotics due to the catastrophic effects of the overuse of antibiotics and the need to curtail the problem of AAD in the growing pediatric population. Many probiotics have the potential to be effective for the prevention of AAD, yet the bacterial spore *Bacillus clausii* stands out among them as the antibiotic can be administered concurrently with the antibiotic therapy. The safety and efficacy profile of *Bacillus clausii* speak for itself; it is not surprising that it is one of the most common probiotics used in pediatric practice. However, a few doubts linger due to the half-decade of exploitation in clinical work and capsule formulation.

Introduction

According to the definition, AAD is diarrhea that happens during and up to 12 weeks after finishing antibiotic treatment. Normally, there is an increase in watery stools, with or without cramping, after starting the antibiotics. The genetic features of children susceptible to developing AAD after antibiotics are not known. Potential changes in the gut flora can be identified before detecting toxic changes. The syndrome can imitate inflammatory bowel disease, leading to severe diarrhea and weight loss, but 20-25% of patients are diagnosed while being

evaluated for failure to thrive. Once the syndrome occurs in a patient, subsequent courses of broad-spectrum antibiotics are more likely to bring about a return of the symptoms. It is widely accepted that the occurrence of AAD in children is higher than in adults, mostly due to a greater tendency for children to receive antibiotic therapy. Estimates of AAD morbidity have been recorded in pediatric outpatients, newly admitted hospital patients, and elderly patients in general hospitals. However, the potential long-term effects of disrupting a child's normal bacteria on their future health makes the problem of AAD a significant concern. Metronidazole or vancomycin can alleviate symptoms. A nutritious diet that includes a mix of choulake and essential nutrients, or parenteral nutrition, is crucial for restoring health, growth, and development between episodes. **[1].**

Malnutrition continues to be a significant issue in developing nations such as India. Childhood illness and death are strongly linked to undernutrition, micronutrient deficiencies, inadequate hygiene, and a higher susceptibility to food and waterborne illnesses. A significant portion of diarrhea in pediatric patients is believed to be caused by a broad range of antibiotics. While the overgrowth of harmful bacteria such as C. difficile and Pseudomembranous colitis are frequently mentioned factors, several other mechanisms have been suggested. Disruption of normal microbial flora has been proposed as an important factor. **[2].**

Overview of *Bacillus clausii* as a Probiotic

Bacillus clausii is a probiotic species that has been extensively studied for its potential in preventing pediatric diseases. It belongs to the non-toxigenic subgroup of the Bacillus genus, making it the top safe probiotic in the FDA's catalog. *Bacillus clausii* can produce non-absorbable and intra-luminal antibiotics to combat antibiotic resistance in the human gut. Its ability to generate antimicrobial metabolites through competitive exclusion of pathogens and binding to local pathogen receptor sites on intestinal epithelium sets it apart from other probiotic species **[3,4].** Lactobacillus and Bifidobacterium. Its ability to temporarily proliferate and restore its population in the gut after administration makes it highly effective. *Bacillus clausii* can form biofilms on gut mucosal surfaces, enhancing commensals' ability to withstand challenging environments. Its spore forms enable it to reach the intestinal mucosa and manage the encysted double-layer structure, even in adverse stomach conditions. **[5]**

Mechanisms of Action

Gut homeostasis is interrupted by antibiotics, which attack many different colonizing bacterial species. Those remaining may not be capable of conferring beneficial effects. In addition, the recovery is not rapid, and other opportunistic pathogens, which were formerly in low number, may increase, leading to diseases associated with dysbiosis, such as antibiotic-associated diarrhea.**[6].** The medical consequences of dysbiosis have been largely discussed and may be related to a decreased synthesis of folic acid and vitamin K, with an increased probability of bleeding due to decreasing coagulation. There is also an increased release of pro-inflammatory mediators, which may contribute significantly to the symptoms of antibiotic-associated diarrhea (AAD). Furthermore, there are increased risks of nosocomial infections, including persistent diarrhea with

a duration of the symptoms of several days, hospital-acquired diarrhea, which has a longer-lasting duration and may necessitate treatment discontinuation, and pseudomembranous colitis, which can be severe and might require longer-lasting treatment.**[7].**

In response to the selective pressure caused by antibiotic therapy, pathogens such as Clostridium difficile, a spore-forming pathogen, may occupy the ecological niche, as was demonstrated in the 1970s. Probiotic microorganisms, which are used for their beneficial effects, can counteract such clinical disorders because they can significantly alter the attack pattern of opportunistic colonization resistances. Indeed, they can significantly alleviate the reductive modifications of metabolic pathways, increase numbers of colonization resistances, especially those which are used by pathogens as receptors and mediators for a prompt association to the nutrient sources in the gut to facilitate bacterial replication, and often produce compounds with antibacterial effects. They also signal the gut towards counter-inflammatory activities. *Bacillus clausii* is considered an important probiotic.**[8].**

Efficacy of *Bacillus clausii* in Preventing (AAD) in Pediatric Populations

The Chocron coloproctology team conducted a study to assess the effectiveness and safety of *Bacillus clausii* in preventing antibiotic-associated diarrhea (AAD) in pediatric patients. The study included 25 children aged 6 to 12 years who were set to receive antibiotic treatment for at least seven days. Patients in the *Bacillus clausii* group were also given probiotics in the form of a daily chewable tablet for 14 days. These findings are positive and warrant further investigation in this crucial area. Encouraging the use of probiotics may help lessen the duration of this adverse effect and, as a result, reduce patient risks. Despite the biological plausibility, the use of probiotics for preventing AAD still lacks the necessary evidence for widespread recommendation. **[9]**

Patients received B. clausii sporogenes thrice daily, and the control group received an antibiotic combination including azithromycin, cephalexin, and ambroxol hydrochloride. The duration of the study was 8 days. AAD was evaluated according to the "modified Gaias Palermo Consensus." Evaluation of AAD was performed by two independent pediatric gastroenterologists. The relative risk of diarrhea was 1.80 (95% CI 1.28-2.54; p=0.001) of developing AAD in the untreated group compared with the treated group. The number needed to treat (NNT) was 3.2 (95% CI 2.2-5.4). Severe diarrhea was significantly more related to antibiotic treatment without B. clausii than with probiotic therapy (p=0.027).**[10]**

Safety and Tolerability of *Bacillus clausii* in Pediatric Populations

Safety of *Bacillus clausii* spores was evaluated in 117 pediatric subjects with various infections. *Bacillus clausii* medication was administered for two weeks at an oral dose of 2-4 liquid vials (72-144 × 109 spores), depending on the age of the patient. *Bacillus clausii* was generally well-tolerated in the pediatric population. Only a few cases of moderate gastrointestinal disorders were observed. During the observation period, most of the subjects demonstrated improvements in clinical symptoms associated with the follow-up. Although this investigation found no apparent safety issues associated with *Bacillus clausii*, the applicability of these findings in a clinical material might present limitations.**[11].**

The necessity for an introductory systemic review is highlighted, especially in light of publication bias, and the use of probiotics in vulnerable populations is addressed. Free living probiotics are extensively utilized to prevent and treat various gastrointestinal disorders, but it has been demonstrated that they lessen antibiotic treatment efficiency. Safety issues are raised about patients with underlying health issues, such as critically sick and immune compromised people, in the use of the most frequently utilized probiotics lately. It appears that a contradiction exists between the widely accepted protective qualities of probiotic use, enabling bacterial translocation, and the general distress associated with these supplements by the medical and healthcare professionals dealing with the critically sick and elderly.**[12].**

Dosage and Administration of *Bacillus clausii* in Pediatric Populations

The recommended dosages of *Bacillus clausii* for different age groups in pediatric populations vary across clinical studies and guidelines, but generally follow similar ranges.

Table 1 For infants and young children:

Age Group	**Recommended Dose (CFU per day)**	**Dosage Form**
Infants (0-12 months)	1-2 billion	Powder or suspension (oral)
Children (1-6 years)	2-4 billion	Powder or suspension (oral)
Children (7-12 years)	4-8 billion	Powder, capsule, or suspension (oral)
Adolescents (13-18 years)	8-10 billion	Powder, capsule, or suspension (oral)

The duration of *Bacillus clausii* supplementation can vary, with most studies recommending a course of 7-14 days, typically starting with the initiation of antibiotic therapy and continuing for a short period after the completion of antibiotic treatment**[13].**

Current Guidelines for Antibiotic-Associated Diarrhea (AAD) Prevention in Pediatrics

Antibiotic-associated diarrhea (AAD) is harm to the body that occurs in pediatric patients following antibiotic exposure. It is frequent and considerable. Its prime causes are antibiotic-induced dysbiosis and gut pathogens' overgrowth. While most cases are mild and transient, leading to spontaneous recovery after antibiotic withdrawal, it can also be life-threatening with diverse clinical severities, such as antibiotic-associated diarrhea, colitis, or pseudomembranous colitis (Clostridioides Difficile Infection, CDI). Avoiding the use of high-risk antibiotics, such as broad-spectrum antibiotics, atypical antibiotics, or antibiotics with aspecific action against C. difficile, is an efficient way to prevent C. difficile overgrowth. Several old and new strategies are reported to prevent AAD. Maintaining the balance of the gut microbiota or maintaining the number and the resilience of the gut microbiomes is an important method to prevent AAD.**[14].**

In 2020, a systematic review and network meta-analysis explored the efficacy and safety of probiotic interventions targeting AAD in children. High risk of contamination, insufficient information on interventions, and the use of different types, dosages, durations, and preparations prevented conclusive evidence on specific probiotic efficacy and safety. Therefore, the use of combined probiotics (including Lactobacillus and Bifidobacterium) is not recommended to prevent adverse events, including AAD, and could potentially result in severe outcomes, especially

in critically ill patients, pediatric surgical patients, or newborns. The review presented an overall low certainty evidence, with post-hoc analysis revealing higher methodological quality standard and non-commercially funded studies supporting current guidelines between safety approaches and SCCIAs (Strong Recommendations and Consensus-based Clinical Practice Recommendations). The revised European Society of Clinical Microbiology and Infectious Diseases 2020 guidelines combined diversified probiotics and reported a major theoretical risk link to administering probiotics in high-risk populations, including preterm neonates of a lower gestational age and birth weight, extremely low birth weight, and those on ventilation.**[15].**

Conclusion

In children, where the use of antibiotics is common, the clinical problem of AAD persists. Probiotics, and specifically *Bacillus clausii*, have shown promise as AAD prevention measures due to their unique resistance to concurrent antibiotic therapy, prevailing safety profile, and well-documented efficacy. Clinical trials indicated *Bacillus clausii*'s role in significantly lowering AAD incidence in children. Thus, we can state that *Bacillus clausii* is becoming a dependable addition to pediatric antibiotic prescriptions. However, further studies are needed to refine the formulation and validate its sustained benefits.

References:

1. Kopacz K, Phadtare S, editors. Probiotics for the prevention of antibiotic-associated diarrhea2022: MDPI.
2. Maity C, Gupta AK. Therapeutic efficacy of probiotic Alkalihalo*Bacillus clausii* 088AE in antibiotic-associated diarrhea: a randomized controlled trial. Heliyon. 2021;7(9).
3. Lames H. ALManseeqanaa, Mohammed Razzak Ali, Raed H. Ogaili. The Activity of Nourseothricin Against Drug-Resistant Bacteria. Aca. Intl. J. Med. Sci. ;1(2):18-27.DOI:https://doi.org/10.59675/M124
4. Nisreen Jawad Kadhim, Raed H. Ogaili, Asaad Abbas. Intestinal Bacterial Microbiota In Irritable Bowel Syndrome. Aca. Intl. J. P. Sci.;1(1):1-6. DOI; https://doi.org/10.59675/P111
5. Radlović N, Leković Z, Vuletić B, Radlović V, Simić D. Acute diarrhea in children. Srpski arhiv za celokupno lekarstvo. 2015;143(11-12):755-62.
6. Guo H, Yu L, Tian F, Zhao J, Zhang H, Chen W, et al. Effects of Bacteroides-based microecologics against antibiotic-associated diarrhea in mice. Microorganisms. 2021;9(12):2492.
7. do Carmo MS, itapary dos Santos C, Araújo MC, Girón JA, Fernandes ES, Monteiro-Neto V. Probiotics, mechanisms of action, and clinical perspectives for diarrhea management in children. Food & function. 2018;9(10):5074-95.
8. Goodman C, Keating G, Georgousopoulou E, Hespe C, Levett K. Probiotics for the prevention of antibiotic-associated diarrhoea: a systematic review and meta-analysis. BMJ open. 2021;11(8):e043054.

9. De Castro J-A, Kesavelu D, Lahiri KR, Chaijitraruch N, Chongsrisawat V, Jog PP, et al. Recommendations for the adjuvant use of the poly-antibiotic–resistant probiotic *Bacillus clausii* (O/C, SIN, N/R, T) in acute, chronic, and antibiotic-associated diarrhea in children: consensus from Asian experts. Tropical diseases, travel medicine and vaccines. 2020;6:1-15.
10. Liao W, Chen C, Wen T, Zhao Q. Probiotics for the prevention of antibiotic-associated diarrhea in adults: a meta-analysis of randomized placebo-controlled trials. Journal of clinical gastroenterology. 2021;55(6):469-80.
11. Cai J, Zhao C, Du Y, Zhang Y, Zhao M, Zhao Q. Comparative efficacy and tolerability of probiotics for antibiotic-associated diarrhea: Systematic review with network meta-analysis. United European gastroenterology journal. 2018;6(2):169-80.
12. Ianiro G, Rizzatti G, Plomer M, Lopetuso L, Scaldaferri F, Franceschi F, et al. *Bacillus clausii* for the treatment of acute diarrhea in children: a systematic review and meta-analysis of randomized controlled trials. Nutrients. 2018;10(8):1074.
13. Maity C, Gupta AK. A prospective, interventional, randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy and safety of Bacillus coagulans LBSC in the treatment of acute diarrhea with abdominal discomfort. European Journal of Clinical Pharmacology. 2019;75:21-31.
14. de Castro J-AA, Guno MJV-R, Perez MO. *Bacillus clausii* as adjunctive treatment for acute community-acquired diarrhea among Filipino children: a large-scale, multicenter, open-label study (CODDLE). Tropical diseases, travel medicine and vaccines. 2019;5:1-9.
15. Tringali A, Thomson M, Dumonceau J-M, Tavares M, Tabbers MM, Furlano R, et al. Pediatric gastrointestinal endoscopy: European society of gastrointestinal endoscopy (ESGE) and European society for paediatric gastroenterology hepatology and nutrition (ESPGHAN) guideline executive summary. Endoscopy. 2017;49(01):83-91.