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Probiotics and Functional Constipation in Children

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ABSTRACT

Functional constipation (FC) definition as by the "Rome IV" diagnostic criteria as persistently difficult, infrequent, or seemingly incomplete defecation without evidence of a primary anatomic or biochemical cause This definition required at least two of six symptoms describing stool frequency, hardness, and size; faecal incontinence; or volitional stool retention, with the stipulation that organic causes of constipation are excluded by a thorough evaluation.

Children visiting outpatients clinic with defecation-related complaint account for 3% and 25% of pediatric gastroenterology consultations.

Functional constipation aetiology is still unclear. So is typically classified into normal transit constipation (NTC), slow transit constipation (STC), and defecatory or rectal evacuation disorders. The World Health Organization defines probiotics as "live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host".

Keywords
Functional, Constipation, Probiotics, Children.

Introduction

Functional constipation

Definition

Functional constipation (FC) definition as by the "Rome IV" diagnostic criteria as persistently difficult, infrequent, or seemingly incomplete defecation without evidence of a primary anatomic or biochemical cause [1]. This definition required at least two of six symptoms describing stool frequency, hardness, and size; faecal incontinence; or volitional stool retention, with the stipulation that organic causes of constipation are excluded by a thorough evaluation [2,3].

Rome IV Criteria for the Diagnosis of Functional Constipation in Children

1. Infant and toddlers up to 4 years old:

A- At least 2 of the following present for at least one month:
- 2 or fewer defecations per week
- History of excessive stool retention
- History of painful or hard bowel movements
- History of large-diameter stools
- Presence of a large faecal mass in the rectum

B- In toilet-trained children, the following additional criteria may be used:
- At least 1 episode/week of incontinence after the acquisition of toileting skills
- History of large-diameter stools that obstruct the toilet

2. Children and adolescents (developmental age ≥4 years old)

a- At least 2 of the following present at least once per week for at least one month:*
• 2 or fewer defecations in the toilet per week
• At least 1 episode of faecal incontinence per week
• History of retentive posturing or excessive volitional stool retention
• History of painful or hard bowel movements
• Presence of a large faecal mass in the rectum
• History of large-diameter stools that may obstruct the toilet

b- The symptoms cannot be fully explained by another medical condition

* Also, the symptoms are insufficient to fulfil the irritable bowel syndrome diagnostic criteria.

Epidemiology

Children visiting outpatient's clinic with defecation-related complaint account for 3% and 25% of pediatric gastroenterology consultations [4-6]. Functional constipation (FC) is the most common defecation disorder and accounts for about 10% of children worldwide [7].

In the Western World, chronic constipation is found in 10-25% of children who visit pediatric gastroenterology clinics [8-10], 8 % in Sri Lanka and increased those who are underweight for their age. FC in children had no gender variety [7,11,12].

Physiology of Defecation and Constipation

The defecation is achieved by colonic motor patterns, which can move colonic contents in both ante grade and retrograde directions [13,14]. Defecation has four phases [15]. Phase one process, known as the recto sigmoid brake, is the basal phase and is usually characterized by an empty rectum, partly due to retrograde motor patterns. In phase two, the pre-expulsive phase, colonic contents are moved into the rectum, filling the rectum, activating the recto-anal inhibitory reflex and resulting in an urge to defecate. Phase three is the expulsive phase, the expulsion of faces by voluntary relaxation of the external anal sphincter and pelvic floor. In phase four, the anal canal pressure increases until it again exceeds the rectal pressure.

FC result from the painful passage of hard stools, which leads the child to enter a vicious cycle of withholding stools, and stool becomes more hard and hard after the reabsorption of the fluid, thus worsening constipation [16]. Disturbance in the gut microbiome is also associated with several diseases in children [17], like functional gastrointestinal disorders such as irritable bowel syndrome [18-20], and constipation [21-23].

Etiology

Functional constipation aetiology is still unclear [24]. So is typically classified into normal transit constipation (NTC), slow transit constipation (STC), and defecatory or rectal evacuation disorders. Defecatory or rectal evacuation disorders are due to pelvic floor dyssynergia (PFD), a reduction in intra-abdominal pressure, rectal sensory perception and rectal contraction [24] children with gastrointestinal motility disorders were found to display normal or slow bowel motor function [24].

Constipation also be found to be caused by low fibre intake [25], lack of physical activity obesity [26], poor socioeconomic conditions, low maternal education [27], and Stress & sleep disturbance [28] through direct and indirect effects on gastrointestinal motility, visceral sensitivity and hypothalamic–pituitary–adrenal dysfunction [29-31]. Other causes of functional constipation include the early introduction of solids or cow's Milk, illness, and change in daily food intake [32].

Treatment

Treatment of functional constipation is either non-pharmacological or pharmacological.

Non-pharmacological treatment

- The first step is family education, which includes an explanation of the physiology of defecation dynamics based on the child's developmental age.
- The second step is the toilet training program with scheduled toilet sit moments lasting 5 minutes throughout the day [33].
- Third step is behavioral therapy by reducing the phobic reactions related to defecation and painful defecation [34].
- The fourth step is pelvic muscle exercises training [35,36].

Pharmacological Treatment

Pharmacological treatment needs to relieve acute painful constipation and to prevent future constipation.

First line: PEG, with or without electrolytes, at a starting dose of 0.4 g/kg/day and adjusted to achieve the desired effect. If PEG is not available, lactulose 1-2 g/kg, once or twice a day, or 1.5-3 ml/kg/day.

Second-line treatment: [32,36]

i. Milk of magnesia 2-5 years: 0.4-1.2 once or divided

6-11 years: 1.2-2.4 g/day, once or divided

12-18 years: 2.4-4.8 g/day, once or divided

ii. Mineral oil 1-18 years: 1-3 ml/kg/day, once or divided, maximum 90 ml/day

iii. Bisacodyl 3-10 years: 5 mg/day, > 10 years: 5-10 mg/day

iv. Senna 2-6 years: 4.4-6.6 mg at bedtime, maximum dose 6.6 mg twice a day

6-12 years: 8.8-13.2 mg at bedtime, maximum dose 13.2 mg twice a day

>12 years: 17.6-26.4 mg at bedtime, maximum dose 26.4 mg twice a day

Note. PEG, polyethylene glycol.

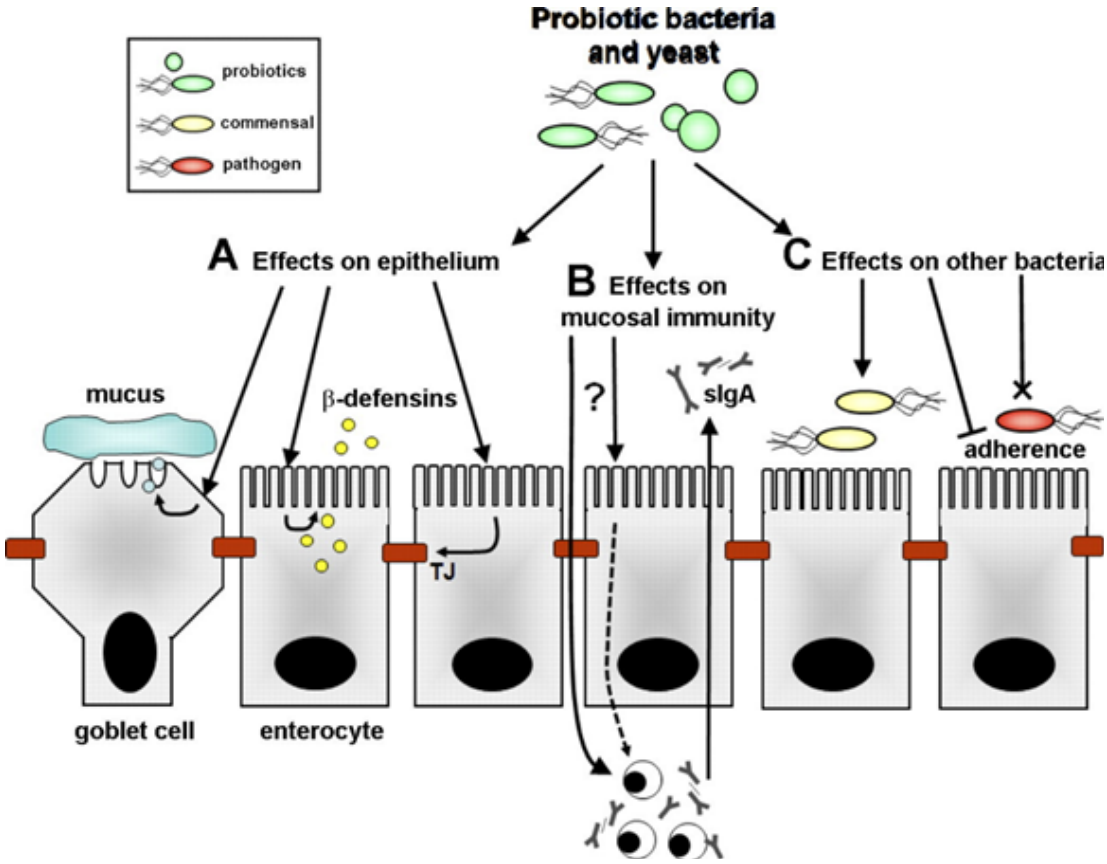
Probiotics

Definition

The World Health Organization defines probiotics as "live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host" [38].

Probiotics Development in Humans

The gut microbiome starts at birth and is affected by various factors. Mode of delivery affected gut microbiome. Microbiome development in the gut is also affected by the method of feeding, which is either breastfeeding or formula feeding; it affects the variety of foods introduced during weaning, and antibiotics or probiotics have direct and indirect effects [39]. The gut microbiome changes with age; a gradual change occurs in the first years of life and then becomes stable around three years. Some diseases like gastroenteritis and antibiotics use also directly affect the variety of gut microbiomes [40,41].



The effects of probiotic bacteria, and yeast on intestinal epithelial barrier function.

Pathophysiology

The most used natural Probiotics are *Lactobacillus* (L.), *Bacillus* (B.), and *Bifidobacterium* (BB.), while *Saccharomyces* (S.) is the most common commercial product used [42]. The main probiotics mechanism of action is controlling intestinal inflammation and inflammatory process [43,44] through immune modulations from the bacteria via releasing cytokines in the gut [45] Probiotics are reported to mediate gut motility, gastric emptying time and visceral pain via a direct effect on gut sensation and motility mechanism through calcium-dependent potassium ion channels system [46,47].

Depending on the strain of bacteria or yeast and the model used, probiotics target the epithelial barrier in the following three areas.
A: *Direct effects on the epithelium. Probiotics can increase mucin expression and secretion by goblet cells, thereby limiting bacterial movement across the mucous layer. Augmentation of β-defensin expression and secretion into the mucus by epithelial cells can prevent the proliferation of commensals and pathogens, thus contributing to barrier integrity. Finally, probiotics can enhance tight junction stability, which decreases epithelial permeability to pathogens and their products.*
B: *Effects on mucosal immunity. Probiotics can increase levels of IgA-producing cells in the lamina propria and promote secretory IgA (sIgA) secretion into the luminal mucous layer. These antibodies limit epithelial colonization by binding bacteria and their antigens, thus contributing to gut homeostasis.*
C: *Effects on other surrounding or infecting bacteria. Probiotics can alter the microbiota composition and/or gene expression, indirectly enhancing the barrier through the commensal bacteria. Furthermore, some probiotics can directly kill or inhibit the growth of pathogenic bacteria via the presentation of antimicrobial factors such as bacteriocins [48].*

Types of Probiotics

For a microorganism (i.e. bacteria or yeast) to be defined as probiotic, it should fulfil the following criteria:
i) it should have a direct beneficial effect on the host, ii) it should be non-pathogenic, iii) it should be able to survive while passing through the GIT and iv) a large number of viable organisms must be able to survive prolonged periods during storage [49].

Function of Probiotics

The main functions of probiotics are:

1. Prevention of diarrhoea like traveller diarrhoea [50], and antibiotics-associated diarrhoea.
2. Preventing pouchitis after restorative ileal pouch-anal anastomosis [51].
3. Prevention of necrotizing enterocolitis in preterm infants [52].
4. Prevention of irritable bowel syndrome symptoms and abdominal pain [53].

Discussion

In adults, some lactic acid bacteria are effective in treating chronic constipation [54,55], but the effect of it on children is unclear. In two studies in Japan, the daily consumption of LGG-fermented milk significantly increased defecation frequency, increased faecal moisture, decreased pH and ammonia content, and relieved post-Bowel motion (BM) discomfort [56,57]. The results of L. Deng et al. study showed that probiotic supplementation lowers the frequency of glycerin enema use and abdominal pain, so they recommended physicians could use probiotics in functional constipation treatment strategies [58].

In a study by Saneian H et al. and Bekkali et al., there was a significant improvement in symptoms of constipation following the lactobacillus administration. Two other studies reported faecal incontinence decreased, and no important side effect was observed with probiotics [59]. Cochrane's extensive review provides no evidence that fibre supplements, lactose-free diets, or Lactobacillus supplementation effectively manage children with recurrent abdominal pain due to chronic constipation [60].

Zoppi et al. did a culture-based study that showed that lactobacilli were significantly decreased in the faecal samples of children with constipation compared to normal children [61] , In another study, Moraes et al. and Nabi Jomehzadeh did a real-time quantitative PCR to detect lactobacilli, and they demonstrated that constipated patients had a significantly lower level of lactobacilli in their stool [62,63].

A study of Vietnamese children using fermented milk showed a significant reduction in the incidence of constipation [64]. A survey by Jadrešin O and colleagues found no benefit in adding L. reuteri DSM 17983 at a dose of 108 CFU to lactulose treatment for constipation in children [65]. Literature data show that not all types of probiotics are equal in the management of gastrointestinal disorders [66,67], not all types of probiotics products have been validated [68]. Therevbin probiotics formulation in pharmacies [69].

Conclusion

Most studies showed significant improvement in chronic constipation following probiotic use in children, but still more literature review is needed.

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