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Nonpharmacologic Treatments for Childhood Constipation: Systematic Review

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KEY WORDS

childhood constipation, systematic review, nonpharmacologic treatments, complementary treatment, alternative treatment

ABBREVIATION

RCT—randomized controlled trial

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abstract

FREE

OBJECTIVE: To summarize the evidence and assess the reported quality of studies concerning nonpharmacologic treatments for childhood constipation, including fiber, fluid, physical movement, prebiotics, probiotics, behavioral therapy, multidisciplinary treatment, and forms of alternative medicine.

METHODS: We systematically searched 3 major electronic databases and reference lists of existing reviews. We included systematic reviews and randomized controlled trials (RCTs) that reported on nonpharmacologic treatments. Two reviewers rated the methodologic quality independently.

RESULTS: We included 9 studies with 640 children. Considerable heterogeneity across studies precluded meta-analysis. We found no RCTs for physical movement, multidisciplinary treatment, or alternative medicine. Some evidence shows that fiber may be more effective than placebo in improving both the frequency and consistency of stools and in reducing abdominal pain. Compared with normal fluid intake, we found no evidence that water intake increases or that hyperosmolar fluid treatment is more effective in increasing stool frequency or decreasing difficulty in passing stools. We found no evidence to recommend the use of prebiotics or probiotics. Behavioral therapy with laxatives is not more effective than laxatives alone.

CONCLUSIONS: There is some evidence that fiber supplements are more effective than placebo. No evidence for any effect was found for fluid supplements, prebiotics, probiotics, or behavioral intervention. There is a lack of well-designed RCTs of high quality concerning nonpharmacologic treatments for children with functional constipation. *Pediatrics* 2011;128:753–761

Chronic constipation is a common problem in childhood; the estimated prevalence is 3% in the Western world.[1] It is a debilitating condition characterized by infrequent painful defecation, fecal incontinence, and abdominal pain. It causes distress to the child and family and can result in severe emotional disturbances and family discord.

The cause of constipation is multifactorial and is not well understood. Criteria for a definition of functional constipation vary widely and are based mostly on a variety of symptoms, including decreased frequency of bowel movements, fecal incontinence, and a change in stool consistency.[2]

Constipation is difficult to treat for the majority of patients and indeed is a long-lasting problem. Approximately 50% of all children who were monitored for 6 to 12 months were found to recover and successfully discontinued laxative therapy.[3] A study in a tertiary hospital showed that, despite intensive medical and behavioral therapy, 30% of patients who developed constipation before the age of 5 years continued to have severe complaints of constipation, infrequent painful defecation, and fecal incontinence beyond puberty.[4]

The first step in treatment consists of education, dietary advice, and behavioral modifications.[2] If these are not effective, then laxatives are prescribed. Although there is a lack of placebo-controlled trials showing the effectiveness of laxatives, their use in clinical practice is widely accepted.[5] The chronic nature of the disease, in combination with a lack of clear effects of laxatives and parents' general fear of adverse effects with daily medication use, is probably why 36.4% of children with functional constipation use some form of alternative treatment (eg, acupuncture, homeopathy, mind-body therapy, musculoskeletal manipulations such as osteopathic and chiropractic manipulations, and spiritual therapies such as yoga).[6]

To date, no systematic reviews of the effectiveness of nonpharmacologic treatments (fiber, fluid, physical movement, prebiotics and probiotics, behavioral therapy, multidisciplinary treatment, and forms of alternative medicine) for childhood constipation have been published. Furthermore, the published guidelines for the treatment of functional constipation are based on reviews of the literature that did not apply a systematic literature search, did not incorporate quality assessment of studies, or used a language restriction.[5,7–9] Therefore, it was our aim to investigate systematically and to summarize the quantity and quality of all current evidence on the effects of fiber, fluid, physical movement, prebiotics, probiotics, behavioral therapy, multidisciplinary treatment, and alternative medicine (including acupuncture, homeopathy, mind-body therapy, musculoskeletal manipulations such as osteopathic and chiropractic manipulations, and spiritual therapies such as yoga) in the treatment of childhood constipation.

METHODS

Data Sources

The Embase, Medline, and PsycINFO databases were searched by a clinical librarian from inception to January 2010. The key words used to describe the study population were "constipation," "obstipation," "fecal incontinence," "coprostasis," "encopresis," and "soiling." These words were combined with key words referring to the different types of interventions that were investigated in the present review. Additional strategies for identifying studies included searching the reference lists of review articles and included studies. No language restriction was applied. The full search strategy is available from the authors.

Study Selection, Data Extraction, and Methodologic Quality

Two reviewers (Drs Tabbers and Boluyt) independently screened the abstracts of all identified published articles for eligibility. Inclusion criteria were as follows. (1) The study was a systematic review or randomized controlled trial (RCT) and contained ≥10 subjects per arm. (2) The study population consisted of children 0 to 18 years of age with functional constipation. (3) A definition of constipation was provided. (4) The study evaluated the effect of a nonpharmacologic treatment, compared with placebo, no treatment, another alternative treatment, or medication, for constipation. (5) Nonpharmacologic treatments included fiber, fluid, physical movement, prebiotics, probiotics, behavioral therapy, multidisciplinary treatment, and alternative medicine. (6) Outcome measures were either establishment of normal bowel habits (increase in defecation frequency and/or decrease in fecal incontinence frequency) or treatment success as defined by the authors of the study, adverse effects, and costs. All potentially relevant studies were retrieved as full articles. Articles concerning children with organic causes of constipation and children with exclusively functional, nonretentive, fecal incontinence were excluded. Data were extracted by 2 reviewers (Drs Tabbers and Boluyt), who used structured data extraction forms. Two reviewers independently rated the methodologic quality of the included studies by using a standardized list developed for RCTs, that is, the Delphi list (Table 1). Disagreements in any of the aforementioned steps were resolved through consensus, when possible, or a third person (Prof Dr Benninga) made the final decision.

TABLE 1 Delphi List

Item No.	Question
Study population	
D1	Was a method of randomization performed?
D2	Was the allocation of treatment concealed?
D3	Were the groups similar at baseline regarding the most important prognostic indicators (age, gender, disease duration, and disease severity)?
D4	Were both inclusion and exclusion criteria specified?
Blinding	
D5	Was the outcome assessor blinded?
D6	Was the care provider blinded?
D7	Was the patient blinded?
Analysis	
D8	Were point estimates and measures of variability presented for the primary outcome measures?
D9	Did the analysis include an intention-to-treat analysis?
D10	Is the withdrawal/drop-out rate <20% and equally distributed?

Data Analyses

Methodologic quality scores were calculated as a percentage of the maximal quality score on the Delphi list. High quality was defined as a score of ≥60% (ie, ≥6 points) and low quality as a score of <60%.[10] Table 1 presents the Delphi list.

RESULTS

Study Selection and Methodologic Quality Assessment

We included 9 studies with survey data (collected in 1986–2008) for 640 children. The sample sizes of the studies ranged from 31[11] to 134.[12] Table 2 presents the characteristics of the studies included. No RCTs on the effects of physical movement, multidisciplinary treatment, or alternative medicine (acupuncture, homeopathy, mind-body therapy, musculoskeletal manipulations such as osteopathic and chiropractic manipulations, or spiritual therapies such as yoga) for children with constipation were found. All studies were hospital-based; 3 were conducted in a general pediatric department[14,18,19] and 6 were conducted in a pediatric gastroenterology department.[11–13,15–17] The studies were highly diverse with regard to the participants, interventions, and outcome measures; therefore, a meta-analysis of all included studies could not be performed. Consequently, we discuss all studies separately, including their most important methodologic shortcomings. Only 5 studies (56%) had scores of ≥6 points, which indicated good methodologic quality.

Fiber

Studies Included

One systematic review was found in which fiber was one of the options evaluated.[5] The authors included 2 RCTs comparing the effects of fiber versus placebo.[11,13] An additional search yielded 1 relevant RCT comparing fiber versus lactulose.[14] All 3 RCTs are discussed briefly.

Fiber Versus Placebo

A small crossover RCT of low quality compared fiber (glucomannan) versus placebo among children with functional constipation.[11] The study used an adequate randomization procedure, but no information on blinding of the outcome assessor was provided and an intention-to-treat analysis was not performed. Other major shortcomings that might have caused bias were the unclear definition of constipation and the unexplained high rate of loss to follow-up monitoring of 32%. Constipation was defined as a delay or difficulty in defecation for >2 weeks. If laxative therapy was instituted, then all children continued to receive the same amount of laxatives during the study. Patients filled out a daily bowel diary. Physician-rated treatment success was defined as >3 bowel movements per week and ≤1 episode of encopresis every 3 weeks, with no abdominal pain. Remarkably, the initial daily fiber intake was low for 71% of all children. Before crossover, the RCT found that the proportion of children with <3 bowel movements per week and abdominal pain was significantly smaller in the fiber group, compared with the placebo group. The proportion of children who were rated by their physicians as being treated successfully and by their parents as experiencing improvement was significantly larger after treatment with fiber, compared with placebo.

The second RCT, of high quality, compared fiber (a cocoa husk supplement) and placebo among otherwise-healthy children.[13] The study fulfilled most of the criteria for validity, such as adequate randomization and blinding and a low dropout rate (<20%) distributed equally over the 2 groups. Children filled out a daily diary. The difference in mean basal dietary fiber intake was not statistically significant. Moreover, the mean basal dietary fiber intake was close to the value recommended for children (age plus 5 g) in both groups (12.3 g/day with fiber and 13.4 g/day with placebo; *P* not reported).[13] No significant difference between the groups in the change in total colon transit time or in the mean defecation frequency per week was found. Significantly more children (or parents) reported a subjective improvement in stool consistency but not a subjective improvement in pain during defecation with fiber, compared with placebo. A subanalysis of data for 12 children with a total basal intestinal transit time of >50th percentile

TABLE 2 Study Characteristics of Included Pediatric Studies on Constipation

Study	Participants	Intervention vs Control	Study Duration	Outcome Measure	Results	Loss to Follow-up Monitoring, *n*/*N* (%)
Fiber						
Loening-Baucke et al[11] (LQ)	31 children, 4.5–11.7 y of age, with constipation for ≥6 mo, recruited from tertiary pediatric gastroenterology clinic in United States	Glucomannan (fiber), 100 mg/kg per d up to 5 g/d, vs placebo (maltodextrins)	4 wk	Defecation frequency of <3 times per wk Abdominal pain "Improved" (physician rating) "Improved" (parent rating)	Intervention: 19%; control: 52% ($P <$ .05) Intervention: 10%; control: 42% ($P <$ .05) Intervention: 45%; control: 13% ($P <$ .05) Intervention: 68%; control: 13% ($P <$ .05)	15/46 (32)
Castillejo et al[13] (HQ)	56 children, 3–10 y of age, with chronic idiopathic constipation according to Rome II criteria, recruited from tertiary pediatric gastroenterology clinic in Spain	Cocoa husk supplement (fiber), 10.4 g/d (3–6 y) or 20.8 g/d (7–10 y), vs placebo	4 wk	Change in colonic transit time Mean defecation frequency No. of patients with subjective improvement in stool consistency No. of patients with subjective improvement in pain	Intervention: 61.4 h to 43.6 h; control: 71.5 h to 61.5 h (no significance) Intervention: 6.2 times per wk; control: 5.1 times per wk ($P = .78$) Intervention: 14; control: 6 ($P < .039$) Intervention: 16; control: 11 ($P = .109$)	Intervention: 4/28 (14); control: 4/28 (14)
Kokke et al[14] (LQ)	97 children, 1–13 y of age, with ≥2 of 4 criteria for constipation (<3 bowel movements per wk, ≥2 fecal incontinence episodes per wk, periodic passage of stool at least once every 7–30 d, or palpable abdominal or rectal mass), recruited from general pediatric practice clinic in Netherlands	Fiber (10 g in 125-mL yogurt drink) vs lactulose (10 g in 125-mL yogurt drink)	8 wk	≥1 fecal incontinence episode per wk Mean abdominal pain scores Mean flatulence scores Necessity of step-up medication Taste scores	Intervention: 4%; control: 3% ($P = .084$) Week 3: intervention: 1.58; control: 1.43 ($P = .33$); week 8: intervention: 1.49; control: 1.39 ($P = .50$) Week 3: intervention: 1.9; control: 2.0 ($P = .70$); week 8: intervention: 2.0; control: 1.9 ($P = .94$) $P = .99$; absolute numbers not reported $P = .657$; absolute numbers not reported	Intervention: 1/65 (1.5), 22/65 (33.8) stopped; control: 2/70 (2.9), 11/7 (15.7) stopped
Fluid						
Young et al[15] (LQ)	108 children, 2–12 y of age, with scores of ≥8 on constipation assessment scale, recruited from pediatric gastroenterology department in United States	50% water intake increase, hyperosmolar (>600 mOsm/L) supplemental fluid treatment, or normal fluid intake	3 wk	Stool frequency Difficulty in passing stools (0 = no problem, 1 = some problem, 2 = severe problem) Stool consistency score	50% water intake increase: 3.70 times per wk; hyperosmolar fluid: 3.44 times per wk; normal fluid intake: 3.40 times per wk (significance not assessed) 50% water intake increase: 0.87; hyperosmolar fluid: 0.62; normal fluid intake: 1.06 (significance not assessed) 50% water intake increase: 6.30; hyperosmolar fluid: 5.79; normal fluid intake: not reported (significance not assessed)	?

TABLE 2 Continued

Study	Participants	Intervention vs Control	Study Duration	Outcome Measure	Results	Loss to Follow-up Monitoring, *n*/*N* (%)
Prebiotics and probiotics						
Bongers et al[16] (HQ)	38 children, 3–20 wk of age, receiving ≥2 bottles of milk-based formula per d with ≥1 of following symptoms: 3 bowel movements per wk, painful defecation (crying), or abdominal or rectal palpable mass, recruited from tertiary pediatric gastroenterology department in Netherlands	New formula with high concentration of *sn*-2 palmitic acid, mixture of prebiotic oligosaccharides, and partially hydrolyzed whey protein (Nutrilon Omneo) vs standard formula (Nutrilon 1)	3 wk Improvement of hard stools to soft stools	Mean defecation frequency Intervention: 90%; control: 50% ($P = .14$)	Intervention: 5.6 times per wk; control: 4.9 times per wk ($P = .36$)	3 wk: 3/38 (7.9); 6 wk: 14/38 (37)
Banaszkiewicz et al[17] (HQ)	84 children, 2–16 y of age. with <3 bowel movements per wk for ≥12 wk, recruited from pediatric gastroenterology department in Poland	*Lactobacillus* GG, 10^9 colony-forming units twice per d, + 70% lactulose, 1 mL/kg per d, vs placebo + 70% lactulose, 1 mL/kg per d	12 wk Mean defecation frequency at 12 wk Mean frequency of fecal soiling at 12 wk Mean frequency of straining at 12 wk	Treatment success (>3 bowel movements per wk without fecal soiling) Intervention: 6.1 times per wk; control: 6.8 times per wk ($P = .5$) Intervention: 0.8 episodes per wk; control: 0.3 episodes per wk ($P = .9$) Intervention: 1.3 times per wk; control: 1.6 times per wk ($P = .6$)	12 wk: intervention: 72%; control: 68% ($P = .9$); 24 wk: intervention: 64%; control: 65% ($P = 1.0$)	Intervention: 5/43 (11.6); control: 3/41 (7.3)
Bu et al[18] (HQ)	45 children, 0–10 y of age, with <3 bowel movements per wk for >2 mo and 1 of the following: anal fissures with bleeding, fecal soiling, or passage of large hard stools, recruited from general pediatric practice in Taiwan	*Lactobacillus casei rhamnosus* ($N = 18$), 8×10^8 colony-forming units per d; magnesium oxide (control 1), 50 mg/kg per d ($N = 18$); or placebo (control 2) ($N = 9$)	4 wk Mean frequency of abdominal pain Treatment success (defined as ≥3 bowel movements per wk without fecal soiling by fourth wk) Mean frequency of fecal soiling Proportion of hard stools Frequency of use of lactulose	Mean defecation frequency Intervention: 1.9 times per d; control 1: 4.8 times per d ($P = .04$) Intervention: 78%; control 1: 72% ($P = .71$) Intervention: 2.1 episodes per wk; control 1: 2.7 episodes per wk (significance not assessed) Intervention: 22.4%; control 1: 23.5% ($P = .89$) Intervention: 4.4 times per wk; control 1: 5.0 times per wk (significance not assessed)	Intervention: 0.6 times per d; control 1: 0.5 times per d ($P = .77$)	4/45 (8.8)

TABLE 2 Continued

Study	Participants	Intervention vs Control	Study Duration	Outcome Measure	Results	Loss to Follow-up Monitoring, *n*/*N* (%)
Behavioral therapy						
Taitz et al[19] (LQ)	47 children with fecal incontinence, with or without constipation, recruited from general pediatric department in United Kingdom	Psychotherapy vs behavior modification techniques	12 mo	Cure, improvement, or no response (see text)	Cure: $n = 22$; improvement: $n = 8$; no response: $n = 16$	17/47 (36)
van Dijk et al[12] (HQ)	134 children with functional constipation (≥2 of 4 criteria: defecation frequency of <3 times per wk, fecal incontinence ≥2 times per wk, passage of large amounts of stool at least once every 7–30 d, or palpable abdominal or rectal fecal mass) recruited from tertiary pediatric gastroenterology department in Netherlands	Behavioral therapy vs conventional treatment	6 mo Mean fecal incontinence frequency Success rate (≥3 bowel movements per wk and fecal incontinence frequency of ≤1 time per 2 wk, irrespective of laxative use)	Mean defecation frequency 22 wk: 5 vs 2.1 episodes per wk; 6 mo: 8.6 vs 6.4 episodes per wk ($P = .135$) 22 wk: 51.5% vs 62.3% ($P = .249$); 6 mo: 42.3% vs 57.3% ($P = .095$)	22 wk: 5.4 vs 7.2 times per wk; 6 mo: 5.3 vs 6.6 times per wk ($P = .021$)	20/134 (14.9)

HQ indicates high quality; LQ, low quality.

showed that the change in total intestinal transit time was significantly greater with fiber, compared with placebo (−38.1 hours [95% confidence interval: −67.9 to −8.4 hours]; $P < .015$).

Fiber Versus Lactulose

A low-quality RCT compared fiber with lactulose for 8 weeks, followed by 4 weeks of weaning, among otherwise-healthy children with constipation.[14] The study used an adequate randomization procedure, but no information on blinding of the outcome assessor was provided, no intention-to-treat analysis was performed, and the dropout rate was high and not equally distributed. Polyethylene glycol (macrogol 3350) was added if no clinical improvement was observed after 3 weeks. The RCT found no significant difference between the groups in the numbers of children with ≥1 fecal incontinence episode per week or in the mean scores (scale: 0 = not at all, 1 = sometimes, 2 = often, 3 = continuous) for people with abdominal pain or flatulence at weeks 3 and 8 of follow-up monitoring. The RCT also found no significant difference between the groups in the necessity for step-up medication or in taste scores, but absolute numbers were not reported. All included RCTs reported no adverse effects of fiber.

Fluid

One low-quality RCT that compared 3 groups, that is, 50% water intake increase, hyperosmolar (>600 mOsm/L) supplemental fluid treatment, and normal fluid intake, met our inclusion criteria.[15] No information was provided about randomization, blinding, or the rate of loss to follow-up monitoring. Furthermore, no statistical assessment was conducted, and data were reported incompletely. Similar stool frequencies were found at 3 weeks for the 3 groups, and no differences with

respect to difficulty in passing stools were found (significance not assessed). Stool consistencies were reported only for the water increase group and the hyperosmolar fluid group and were similar at 3 weeks (significance was not assessed).

Prebiotics

One systematic review was found that included 1 small, high-quality RCT comparing a standard formula (Nutrilon 1 [Nutricia Nederland BV, Zoetermeer, Netherlands]) with a formula with a high concentration of *sn*-2 palmitic acid, a mixture of prebiotic oligosaccharides, and partially hydrolyzed whey protein (Nutrilon Omneo [Nutricia Nederland BV]).[5,16] That study fulfilled most of the criteria for validity, such as adequate randomization and blinding, and inclusion and exclusion criteria were both clearly specified; however, the study was designed originally as a crossover trial but, because of the high rate of loss to follow-up monitoring (37% after 6 weeks), the results of the first treatment period only were analyzed. No significant difference between the 2 groups in the mean defecation frequency per week after 3 weeks was found. A difference in improvement of hard stools to soft stools in favor of the prebiotic group was found; however, this difference was not statistically significant.

Probiotics

One systematic review was found that included 2 RCTs evaluating the effects of probiotics.[5,17,18] The first high-quality trial was conducted to determine whether *Lactobacillus rhamnosus* GG was an effective adjunct to lactulose for treating constipation in children. The study fulfilled all criteria for validity. Children with constipation received 1 mL/kg per day of 70% lactulose plus 10^9 colony-forming units of *L rhamnosus* GG or 1 mL/kg per day of 70% lactulose plus placebo twice daily for 12 weeks.[17] There were no significant differences in rates of treatment success (defined as ≥3 bowel movements per week with no episodes of fecal incontinence) at 12 and 24 weeks between the *L rhamnosus* GG group and the placebo group. No significant differences between the probiotic group and the placebo group with respect to the numbers of episodes of fecal soiling per week at 12 weeks, frequencies of straining at 12 weeks, and proportions of children using laxatives at 24 weeks were found.

The second high-quality RCT compared magnesium oxide with the probiotic *Lactobacillus casei rhamnosus* or placebo.[18] The placebo group included only 9 patients and therefore is not discussed. The study fulfilled almost all important criteria for validity. Similar differences in defecation frequencies were found for the probiotic group and the magnesium oxide group. The clinical relevance of these differences in defecation frequencies is unclear. The RCT also found that probiotics significantly reduced abdominal pain, compared with osmotic laxatives. It found no significant difference in rates of treatment success (defined as ≥3 spontaneous defecations per week with no episodes of fecal incontinence by the fourth week) between probiotics and osmotic laxatives, compared with placebo. The RCT also found similar rates of fecal incontinence (statistical significance between groups was not assessed). It found no significant difference in the proportions of hard stools between probiotics and osmotic laxatives. Both trials did not report any adverse events for the groups receiving probiotics.

Behavioral Therapy

We found 1 systematic review (search date from inception to 2006, including 18 RCTs and 1186 children; 17 of the 18 RCTs investigated children with functional fecal incontinence and therefore are not discussed) that compared behavioral and/or cognitive interventions, with or without other treatments, for the management of fecal incontinence attributable to organic or functional constipation in children.[20] An additional search found 42 studies, of which 1 RCT met our inclusion criteria.[12]

The systematic review included 1 low-quality RCT that compared behavioral interventions (education) and a system of rewards from a pediatrician with monthly psychotherapy with a child psychiatrist.[19] The method of randomization was not stated clearly. Blinding in this case was not possible for the care provider or the patient. However, no information on whether the outcome assessor was blinded was provided. The analysis did not include an intention-to-treat analysis, and the dropout rate was >20%. All children were seen every 6 weeks for periods from 3 months to 1 year. At every visit with the child psychiatrist, the mother and the child were seen separately for 15 to 30 minutes. The authors did not provide any clear details about this psychotherapy. A total of 22 children experienced cures (≥5 bowel movements per week with no episodes of fecal incontinence per week and no use of laxatives), 8 children experienced improvement (≥3 bowel movements per week with ≤1 episode of fecal incontinence per week), and 16 did not experience improvement (<3 bowel movements per week or >1 episode of fecal incontinence per week). However, it was not clear from the study how many children in each group experienced cures, improvement, or no improvement.

One subsequent high-quality RCT compared behavioral therapy by a child psychologist (learning process to reduce phobic reactions related to defecation, which consisted of 5 sequential

steps, ie, know, dare, can, will, and do) and conventional treatment by a pediatric gastroenterologist (education, diary, and toilet training with a reward system) over 22 weeks (12 visits).[12] The study fulfilled all important criteria for validity. Both groups used similar laxative therapy. Although statistically significant increases in defecation frequency and statistically significant reductions in fecal incontinence episodes were found in both groups, no significant differences between the groups in defecation frequencies at 22 weeks and 6 months or in episodes of fecal incontinence were seen. Furthermore, no significant differences between the groups with respect to success rates were found. After 6 months, the proportion of children with behavioral problems was significant smaller in the behavioral therapy group, compared with the conventional treatment group (11.7% vs 29.2%; $P = .039$).

DISCUSSION

This systematic review clearly shows a lack of adequately powered, high-quality studies evaluating the therapeutic role of nonpharmacologic treatments. Although the first step of treatment consists of dietary advice (adequate fiber and fluid intake) and behavioral interventions, no evidence from trials suggesting any effect for fluid supplements or behavioral therapy was found. Only marginal evidence showing that fiber supplements are more effective than placebo in the care of children with constipation exists. Also, no evidence was found for prebiotics or probiotics. Moreover, no RCTs involving physical movement, multidisciplinary treatment, or alternative medicine (including acupuncture, homeopathy, mind-body therapy, musculoskeletal manipulations such as osteopathic and chiropractic manipulations, and spiritual therapies such as yoga) were found.

The results of the few, mainly underpowered, studies included in this review should be interpreted cautiously, given the lack of uniform definitions used for constipation and the methodologic limitations of the published studies. Each included trial used a different study design with respect to the duration of the study, the number of visits, the method of blinding, the outcome measures, and follow-up monitoring. Future studies with children with constipation should be conducted not only in tertiary care settings but also in primary and secondary care settings, with standardized protocols as suggested by experts in both adult and pediatric functional gastrointestinal disease. With improvements in the quality of research methods, the quality of care should improve through earlier and better recognition of constipation and improved diagnostic and therapeutic strategies. Therefore, involved researchers should use homogeneous patient populations and outcome measures, including standard definitions as described in the Rome III criteria.[21,22] Because functional constipation is a long-lasting problem in many cases, long-term follow-up monitoring is necessary for better understanding of the clinical course of the disease.[4] Growing up with a chronic disorder may impede the child's development and may affect psychological and psychosocial functioning. Therefore, quality-of-life assessments, using baseline generic and before/after disease-specific quality-of-life instruments, are important secondary outcome measures.[20]

High success rates for placebo (60%) often are reported for pediatric and adult patients with functional gastrointestinal disorders.[23,24] Despite the high response rates for placebo, there is a paucity of placebo-controlled studies with large patient samples for pediatric patients with constipation. It is well known that patients given placebo have expectations of future responses, which influences outcomes. In fact, the reported responses to placebo in RCTs might point toward the natural course of disease, fluctuations in symptoms, regression to the mean, or effects of other simultaneous treatments. Therefore, studies with such children that include groups that receive no treatment, to control for natural history and regression to the mean and to make the studies more likely to determine a real placebo effect, are necessary.

Despite the high levels of use of nonpharmacologic treatments, we did not find any comparative trial evaluating their efficacy in childhood constipation.[6] Widespread use of therapies such as homeopathy, massage therapy, and acupuncture with no evidence of efficacy emphasizes the vulnerable disposition of patients, who at times seek out such treatments because of inadequate effects achieved with conventional treatments and the misconception that complementary medicine (forms of alternative medicine) lacks adverse effects and may not interfere with prescribed medications.[6] In addition, use of these interventions is costly. A study involving adults with functional gastrointestinal diseases in the United States showed that one-third of the patients used some complementary or alternative medicine (most used were ginger, massage therapy, and yoga); the median yearly cost was $200.[25]

The main unanswered question is why well-designed trials concerning frequently used complementary treatments are lacking for one of the most prevalent, frustrating, long-lasting, pediatric gastrointestinal disorders.[1,4,6] There are some explanations. Lack of funding may play an important role. Although governments and private foundations are increasingly investigating

nonpharmacologic treatments, the available budgets are still very small, in comparison with the budgets for conventional treatment research.[6] Furthermore, blinding patients to their treatment arm could be difficult in some nonpharmacologic studies, such as studies assessing the efficacy of massage-based therapies. As in every systematic review, there is a risk that not all relevant studies were included. To minimize this risk, we performed a sensitive literature search without language restrictions.

CONCLUSIONS

We found only some evidence that fiber supplements were more effective than placebo in the care of children with constipation. This study clearly shows that there is a lack of well-designed RCTs of high quality concerning nonpharmacologic treatments for children with functional constipation. Therefore, we recommend additional, well-designed RCTs of high quality to investigate the efficacy, safety, and cost-effectiveness of the different treatment forms investigated in this review, using homogeneous patient populations and outcome measures, including standard definitions as described in the Rome III criteria.

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